ZAPORIZHYA STATE MEDICAL UNIVERSITY

DEPARTMENT OF HOSPITAL PEDIATRICS

NEONATOLOGY

(educational and methodical manual for the 5 year English speaking students of medical faculty)

ZAPORIZHYA – 2015

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Zaporizhya State Medical University

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The methodical manual is ratified on the meeting of Central methodical Council of Zaporozhia State Medical University.

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CONTENTS

EXPLANATORY MESSAGE

1. PURPOSE AND THE TASK OF SUBJECT

THE AIM OF THE COURSE:

A doctor preparation by the profession of "General Medicine" from the section of child's diseases in accordance to professional requirements to the graduating students of medical faculty in the higher medical educational establishments of Ukraine.

THE TASK OF SUBJECT:

During the hospital pediatrics course for students who studying on "General Medicine" specialty there are 10 lectures will delivered (20 educational hours), and 15 four sentinel practical classes (60 educational hours) will be conducted, 40 educational hours will be selected for independent outclass students work.

During the study there are 2 final intermediate class and the case history passing is conducted that is the students have to write by the diseases of new-born children. In completion of studying course the students pass 2 module tests from the subject of "hospital pediatrics".

In 9-10 semesters the students of " General Medicine" specialty study the diseases of new-born children, of endocrine and blood systems

Teaching of treatment questions is conducted differently for outpatient and hospital stages, for the stages of rehabilitation and clinical supervision.

The important section for the 5 year students education is the mastering of practical skills on neonatology, chidren hematology, children endocrinology which are will necessary for solving of problems in diagnostics, differential diagnostics, treatment and prophylaxis of above mentioned pathology in children.

The student mastering these skills during the all types of studying in hospital pediatrics course.

The student ought to see any diagnostic or treatment method in action, to know the ptrinciples of it, ought to complete it in certain clinical situation, to clarify the obtained results of diagnostic tests or the treatment.

In studying of hospital pediatrics course students must know:

- etiology and pathogenesis of the most widespread diseases of newborn period, haematological and endocrine diseases of child's age, methods of it diagnostics, differential diagnostics, treatment and prophylaxis.
- Features of clinical course in the most widespread diseases of newborn period, haematological and endocrine diseases of child's age, methods of it diagnostics, differential diagnostics, treatment and prophylaxis.

By finishing hospital paediatrics course students must be able:

- to estimate the state of newborn child;
- to care after a newborn child;
- to prescribe nursing regimen for the premature and injured newborns;
- to prescribe the feed fore mature and premature newborns;
- to apply the modern methods of diagnostics, treatment, rehabilitation of children in diseases of newborn period , endocrine and hemopoetic systems;
- be able to render the first aid in critical conditions which appear in newborn children in diseases of blood and endocrine system in children.

During a course considerable attention spared to basics of first aid in children's critical conditions.

TABLE OF CONTENTS OF THE PROGRAM

2.1. TEMATIC PLAN OF LECTURES ON MODULE 2

№	Topic	Amount od hours
1	The especialities of premature newborns adaptation and the feeding of prematures newborns.	2
2	Asphyxia of newborns. Birth trauma of newborns.	2
3	RDS in newborns.	2
4	Hemolytic disease in newborns	2
5	Bacterial infections in newborns.	2
	In total	10

2.2. THE PLAN OF PRACTICAL CLASSES(SEMINARS) FOR STUDENTS STUDYING ON PROFESSION "GENERAL MEDICINE"

Module #2. Neonatology.

№	Topic	Amount of hours
1	The especialities of adaptation in premature newborns. Organization of nursing and feeding in the premature children.	4
2	Asphyxia in neonates.	4
3	Birth trauma of newborns.	4
4	Respiratory system diseases in newborns	4
э	. Hemolytic and hemorrhagic diseases in newborns.	4
6	Intrauterine infections of newborns, (TORCH - infections)	4
7	Bacterial in fections in newborns	4
8	Final module control	4

2.3. PLAN OF OUTCLASS WORK IN HOSPITAL PEDATRICS FOR THE STUDENTS STUDYING BY PROFESSION OF "GENERAL MEDICINE"

#	Topic	Amount of hours
1	Adaptational reaction in newborns	1
2.	Seizures in newbornds. Causes. Urgent aid. Treatment.	2
3.	The anomalies of respiratory system development in newborns.	1
4	Replace blood transfusion operation. Indications. Methodics of conducting. Complications.	1
5.	Congenital syphilis.	1
6.	The features of antibacterial therapy in newborns.	1
7	Patients management and case history writing from the neonatology.	5
8	Preparing to the final module control in neonatology.	5
	In total	20

THE STRUCTURE OF TEST CREDIT TO THE MODULE #2.. Neonatology

Topic	Hours of lectures	Hours of classes.	Out-class Prepa-ration	Individual work
Semantic module 7. Premature newborns				
1. The especialities of adaptation in premature newborns. Organization of nursing and feeding in the premature children.	2	4	1	Examination of sick child, Writing and the defending of the educational case report.
Semantic module 8 The most wide-spreaeded non-infectious diseases of newborns.				
2. Asphyxia in neonates.	1	4	1	
3. Birth trauma of newborns.	1	4	1	
4. Respiratory system diseases in newborns.	2	4	1	
5. Hemolytic and hemorrhagic diseases in newborns.	2	4	1	
Semantic module 9. Perinatal infections.				
6. TORCH-infections in children.		4	2	
7. Bacterial infections in newborns..	2	4	1	
Patients management and the case report writing.			5	
Final module control		4	5	
In total: ECTS credits - 2,0; hours - 60; 10 of them are the lectures. :	10	32	18	

POINTS DISTRIBUTION FOR THE ASSESMENT OF STUDENTS PERFORMANCE. MODULE # 2. Neonatology.

Module # 2 (maintenence for the estimated activity)	Maximal points are possible
Semantic module 7	
Topic 1. The especialities of adaptation in premature newborns. Organization of nursing and feeding in the premature children.	12

Semantic module 8	
Topic 2. Asphyxia in neonates.	12
Topic 3. Birth trauma of newborns.	12
Topic 4. Respiratory system diseases in newborns	12
Topic 5. . Hemolytic and hemorrhagic diseases in newborns.	12
Semantic module 9	
Topic 6. Intrauterine infections of newborns, (TORCH - infections)	12
Topic 7. Bacterial in fections in newborns	12
Individual independent preparation - patients management and writing of case report.	36
Current performance in total:	120
Final module control	80
POINTS IN TOTAL FOR THE MODULE	200

Note: In mastering the topic after the traditional system the points has given to the student as follows: «5» - 20 points, «4» - 16 points, «3» - 12 points, «2» - 0 points.. Maximal amount of points for current educational performance of student are 120. A student allowed to pass the final module control in terms of performance exhibition according to the requirements of tutorial and in case of obtaining no less than 72 points for current performance during the practical classes. (12 x 6). Final module control is setting off to the student in gettting not less than 50 of 80 points.

Theme THE ESPECIALITIES OF ADAPTATION IN PREMATURE NEWBORNS. ORGANIZATION OF NURSING AND FEEDING IN THE PREMATURE CHILDREN.

Premature infants. Etiological factors of prematurety. Physiological features. Mofmorphologic and functional criteria of maturity in premature newborn children. The features of adaptational period in premature newborn children. Differential diagnosis of hyperbilirubinemias. Intrauterine growth retardation : causes, diagnostics, treatment, prophylaxis. Stages of nursing for newborn children, principles of feeding.

Emergency in urgent state: hypoglycemia, respiratory failure, enteroparesis, hyperbilirubinemia.

I**. Actuality of the theme.**

The period of gestation is one of the most important predictors of an infant's subsequent health and survival. In 2004, more than 500,000 infants, or 12.5 percent of all infants, were born preterm, which is considered birth at less than 37 completed weeks of gestation (CDC, 2005a). On the basis of new estimates provided in this report, the annual societal economic burden associated with preterm birth in the United States was in excess of $26.2 billion in 2005 (this estimate represents a lower boundary).The percentage of preterm deliveries has risen steadily over the last 2 decades. Most of this increase has been among children born at 32 to 36 weeks gestation. In the past, low birth weight has been used as an indicator for preterm birth; however, the present Institute of Medicine (IOM) committee considers low birth weight to be a poor surrogate and has specifically focused its analysis on preterm birth.Compared with infants born at term (37 to 41 weeks of gestation), preterm infants have a much greater risk of death and disability. Approximately 75 percent of perinatal deaths occur among preterm infants (Slattery and Morrison, 2002). Almost one-fifth of all infants born at less than 32 weeks gestation do not survive the first year of life, whereas about 1 percent of infants born at between 32 and 36 weeks of gestation and 0.3 percent of infants born at 37 to 41 weeks of gestation do not survive the first year of life. The infant mortality rate (IMR) per 1,000 live births for infants born at less than 32 weeks of gestation was 180.9, nearly 70 times the rate for infants born at between 37 and 41 weeks of gestation (Mathews et al., 2002). Advances in medical technologies and therapeutic perinatal and neo including those born when they are as young as a gestational age of 23 weeks. However, surviving infants have a higher risk of morbidity. Neuro-developmental disabilities can range from major disabilities such as cerebral palsy, mental retardation, and sensory impairments to more subtle disorders, including language and learning problems, attention deficit hyperactivity disorder, and behavioral and social-emotional difficulties. Preterm

infants are also at increased risk for growth and health problems, such as asthma or reactive airway disease.

Although significant improvements in treating preterm infants and improving survival have been made, little success in understanding and preventing preterm birth has been attained. The complexity of factors that are involved in preterm birth will require a multidisciplinary approach to research directed at understanding its etiologies, pathophysiology, diagnosis, and treatments. However, there are barriers to the recruitment and participation of scientists in these investigations. A critical barrier to research is the demand on clinical researchers in academic centers to provide clinical income and other duties that take them away from research. This necessitates the development of new ways to provide support to allow the time to conduct this important research.The challenge for researchers and clinicians remains to identify interventions that prevent preterm birth; reduce the morbidity and mortality of the mother or the infant, or both, once preterm birth occurs; and reduce the incidence of long-term disability in children in the most comprehensive and cost-effective manner possible.

II. Classes (pointing of planned mastering level)

1. A student must know (to familiarize): α1

- About the place of prematurity, small-for-gestational age infants in the structure of intrauterine and perinatal life;
- About statistical information in relation to morbidity, frequencies of complications, lethality, nearest and remote prognosis;
- About history of scientific study and payment of domestic scientists;

2. A student must know (master): α2

- the etiology of intrauterine growth retardation and preterm birth;
- the anatomic and physiologic features of premature children ;
- the features of adaptational period in premature newborn children;
- the mofmorphological and functional criteria of maturity in premature newborn children;
- key links of intrauterine growth retardation ;
- clinical classification of intrauterine growth retardation and preterm birth ;
- the classic clinical manifestation of intrauterine growth retardation ;
- laboratory and instrumental diagnosis of intrauterine growth retardation;
- the features of bilirubin metabolism;
- the stages of nursing for newborn children;
- the treatment principles of intrauterine growth retardation;
- the principles of feeding;
- the prophylaxis of intrauterine growth retardation and preterm birth ;

- the emergency in urgent state: hypoglycemia, respiratory failure, enteroparesis, hyperbilirubinemia.

3. A student must seize the skills: α3

- collection of complaints and anamnesis of disease;
- examination of premature newborn children and children with intrauterine growth retardation;
- formulating and substantiating the preloiminary diagnosis;
- determining a laboratory and instrumental examination plan of patient's investigation (to obedience of diagnostics standards);

By the abilities:

- interpreting the result of laboratory and instrumental investigations.
- conducting differential diagnosis among the main syndrome in premature newborn children;
- conducting differential diagnosis among intrauterine growth retardation and intrauterine (fetal) hypotrophy .
- giving recommendations in relation to the patient regimen and diet to the premature newborn children and children with intrauterine growth retardation, taking into account the stage of disease, severity of the state and concomitant pathology;
- completing the treatment plan to premature newborn children and children with intrauterine growth retardation according to the standards taking into account the stage of disease, complications and concomitant pathology.
- rendering first aid in extreme situations and exigent states.

III. Aims of personality development (educative aims):

- A student must learn to adhere to the rules of behaviour and principles of medical etiquette and deontology near a bed patient with premature newborn children and children with intrauterine growth retardation;
- to try to use hands on ability to set a psychological contact with a family of a newborn children;
- to master a sense of professional responsibility for a timely and adequate of skilled medicare.

IV. Interdisciplinary integartion:

Subject	To know	To be able
1. Previous (providing)		
Anatomy	Structure of respiratory system, central nervous system , cardiovascular system.	
Histology	Structure of pleura, lungs, alveole, brain, vascular system.	

Physiology	Normal physiology of organs and systems of newborn children, normative indices of laboratory and instrumentalinvestigational methods and their assesment.	To asses laboratory data and instrumental investigation methods .
Pathologic physiology	Key links of the pathogenesis of intrauterine growth retarda-tion and hyperbilirubinemia	To estimate the function of thyroidgland and other organsof the endocrine system
Pathologic anatomy	Morphological features of the intrauterine growth retardation development depending of stage of prematurety .	To analyze and interpret the information of a clinical examination and about additional methods of investigation
Pharmacology	Pharmacokinetics and pharmacodynamics, the side effects of preparations which use for nursing of premature newborn children and with intrauterine growth retardation, hypotrophy, respiratory failure.	To prescribe treatment depending on stage of prematurity, functional maturity, period of disea-se, to establish the indivi-dual regimen of prepara-tions taking and dosage. To precribe recipes.
Propedeutical pediatrics.	The basic stages and methods of patient clinical examination	To collect complaints, anamnesis vitae et mor-bid, to find out the basic risk factors of preterm births, coduct a patient examination to reveal the clinical signs of preterm birth,and to be able to interpret the data for additional methods of investigation.
Radiology	Normal parameters of X-ray photography of chest	To interpret data of X-ray photography
2. Followings(provided)		
Hospital pediatrics.	Clinical signs of dysadaptation, cardiovascular system, complications of hyperbilirubinemia, treatment tactics.	To reveal the clinical signs of dysadaptation of cardiovascular system, and complications of hy-perbilirubinemia and be able to prescribe treatment.

3. Interdiscipline integration		
Bronchopulmonary Dysplasia	Clinical manifestation of bronchopulmonary dysplasia.	To identify specific clinical signs of bronchopulmonary dysplasia, congenital disease of lung and conduct a differential diagnosis.
Cerebral hemorrhage	The clinical manifestation of cerebral hemorrhage	To identify specific clinical signs of cerebral hemorrhage and to conduct a differential diagnosis.
Cerebral palsy	The clinical manifestation of cerebral palsy	To identify specific clinical signs of cerebral palsy and to conduct differential a diagnosis.
Biliary atresia	The clinical manifestation of biliary atresia	To identify specific clinical signs of biliary atresia and to conduct differential diagnosis for hepatitis.

V. Contents of the theme

Fetal development is characterized by sequential patterns of tissue and organ growth, differentiation, and maturation that are influenced by the maternal environment, uteroplacental function, and the inherent genetic growth potential of the fetus. When circumstances are optimal, none of these factors has a rate-limiting effect on fetal growth and development. Thus, the healthy fetus should achieve complete functional maturity and genetically determined somatic growth, and an uncomplicated intrapartum course and a smooth neonatal cardiopulmonary and metabolic adaptation to extrauterine life can be anticipated.However, fetal growth and development do not always occur under optimal intrauterine conditions. Those neonates subjected to aberrant maternal, placental, or fetal circumstances that restrain intrauterine growth are a high-risk group and are traditionally categorized as having intrauterine growth restriction (IUGR). The cumulative effects of adverse environmental conditions and aberrant fetal growth threaten continued intrauterine survival; labor, delivery, and neonatal adaptation become increasingly hazardous. Similarly, postneonatal growth and development may be impaired as a result of IUGR and the subsequent problems encountered during the neonatal period. Neonates who have IUGR are a heterogenous group. Many with IUGR may in fact have poor intrauterine growth as

an adaptation to a suboptimal uterine environment.The terms IUGR and small for gestational age (SGA), although related, are not synonymous.IUGR is a deviation from, or a reduction in, an expected fetal growth pattern and is caused by innate reduced growth potential or by multiple adverse effects on the fetus. IUGR is the result of any process that inhibits the normal growth potential of the fetus. Fetal growth at term may be predicted by anthropometric analysis of fetal dimensions with second-trimester ultrasonography. Deviations from the predicted weight at term may result in an infant with IUGR but may not result in an infant who is SGA. The term SGA describes an infant whose weight is lower than population norms or lower than a predetermined cutoff weight (e.g., –2 SD, 5%, 10%); the cause may be pathologic, as in an infant with IUGR, or nonpathologic, as in an infant who is small but healthy. Not all infants who are IUGR are SGA: for example, in comparison with siblings, ethnically derived fetal growth curves, or their own growth potential, infants' birthweight may be less than expected despite their weight being above an arbitrary normative population growth percentile standard. A customized birthweight would take into consideration important epidemiologic variables such as parity, maternal anthropometrics, and ethnicity. (See growth curves in Appendix B.)Low birthweight as a classification includes premature infants (younger than 37 weeks), preterm infants who are SGA (younger than 37 weeks), and term (37 weeks or older) infants who are SGA. Many preterm infants are also IUGR when growth is based on fetal growth standards. These IUGR preterm infants are at increased risk for perinatal demise and neonatal complications.

FETAL GROWTH AND BODY COMPOSITION

Through anthropomorphic measurements that include fetal weight, length (crown to heel), abdominal circumference, and head circumference as well as three-dimensional fetal ultrasonography, fetal growth standards have been determined for various reference populations from various locations.Although the range of birthweight at each gestational age in these populations may vary , the overall pattern of fetal growth is representative of these and subsequent groups. Both early and late fetal growth patterns appear to be linear, beginning at approximately 20 weeks' gestation and lasting until 38 weeks; thereafter, the rate of weight gain begins to decline. Fetal growth curves based on prematurely born infants may result in inaccurate assessment of fetal growth. Premature infants often have IUGR and thus skew the fetal growth curve to standards lower than those that would have been obtained if the fetus had not been born early. The cause of the preterm labor may also cause IUGR, or alternatively the IUGR may produce fetal distress resulting in spontaneous or elective delivery.

Table Birth Weights from Six Sources

NEAREST WEEK OF GE STATION	Mean Birthweight (g ± 1 SD)					
	Denver	Baltimore	Montreal	Portland	Chapel Hill	12 U.S. Cities (Cluster Method)
28	1150 ± 259	1050 ± 310	1113 ± 150	1172 ± 344	1150 ± 272	1165 ± 109
29	1270 ± 294	1200 ± 350	1228 ± 165	1322 ± 339	1310 ± 299	1295 ± 94
30	1395 ± 341	1380 ± 370	1373 ± 175	1529 ± 474	1460 ± 340	1440 ± 115
31	1540 ± 375	1560 ± 400	1540 ± 200	1757 ± 495	1630 ± 340	1601 ± 117
32	1715 ± 416	1750 ± 410	1727 ± 225	1881 ± 437	1810 ± 381	1760 ± 128
33	1920 ± 505	1950 ± 420	1900 ± 250	2158 ± 511	2010 ± 367	1955 ± 138
34	2200 ± 539	2170 ± 430	2113 ± 280	2340 ± 552	2220 ± 395	2160 ± 202
35	2485 ± 526	2390 ± 440	2347 ± 315	2518 ± 468	2430 ± 408	2387 ± 208
36	2710 ± 519	2610 ± 440	2589 ± 350	2749 ± 490	2650 ± 408	2621 ± 274
37	2900 ± 451	2830 ± 440	2868 ± 385	2989 ± 466	2870 ± 395	2878 ± 288
38	3030 ± 451	3050 ± 450	3133 ± 400	3185 ± 450	3030 ± 395	3119 ± 302
39	3140 ± 403	3210 ± 450	3360 ± 430	3333 ± 444	3170 ± 408	3210 ± 434
40	3230 ± 396	3280 ± 450	3480 ± 460	3462 ± 456	3280 ± 422	3351 ± 448
41	3290 ± 396	3350 ± 450	3567 ± 475	3569 ± 468	3360 ± 435	3444 ± 456
42	3300 ± 423	3400 ± 460	3513 ± 480	3637 ± 482	3410 ± 449	3486 ± 463
43		3410 ± 490	3416 ± 465	3660 ± 502	3420 ± 463	3473 ± 502

From Naeye RL, Dixon JB: Distortions in fetal growth standards. Pediatr Res 12:987, 1978.

Although weight gain per day is maximal before term, when growth is expressed as percent increment per day, it is greatest during embryonic and early fetal development . In the last half of pregnancy, the fetus gains 85% of its birthweight. However, the nature of fetal growth differs between early and later fetal life. During the embryonic and early fetal growth period, tissues and organs increase in cell number rather than cell size (the hyperplastic phase of cell growth, when total DNA content increases in new tissues). Later phases of growth include a period when cell size also increases (protein and RNA content), along with continued enhancement of cell number (mixed hyperplastic and hypertrophic phase). In muscle and brain (especially the cerebellum), this phase of growth may continue through adolescence and the second year of life, respectively. The final stage of growth is a purely hypertrophic phase, when only cell size increases.

The contribution of each tissue to body weight changes during fetal and postnatal development is depicted in . Muscle represents only 25% of fetal and neonatal body weight; once full adult maturity has been achieved, it accounts for 40%

of the body's mass.] Fetal muscle growth, as well as all protein synthesis in the fetus, depends on active transport of essential amino acids across the placenta. Once provided with these precursors, fetal protein synthesis is autonomous and results in the net synthesis of proteins that have amino acid patterns determined by the fetal genome. Although the building blocks may be the same, developmentally the fetal muscle has a lower fibrillar protein content, whereas the sarcoplasmic protein concentration remains unchanged as maturation proceeds. Besides those immunoglobulins (IgG), that cross the placenta, all protein present in the fetus has been synthesized de novo by fetal tissue.

Paralleling the patterns of fetal growth, the macromolecular composition of the body also undergoes sequential patterns of change. One general trend includes a decrease of total body and extracellular water content as the fetus and infant mature . Simultaneously, there is an increment of body protein and fat content . Whereas the increase of tissue protein is gradual during development, the increment of fetal body fat is delayed until the third trimester. Once initiated, the deposition of subcutaneous and deep body adipose tissue accelerates more rapidly than the rate of protein accumulation. Infants with IUGR have a smaller percent body fat (17% versus 23%), which is mainly a reduction of subcutaneous adipose tissue rather than intra-abdominal adipose tissue.

Table Body Composition of the Reference Fetus

GESTATIONAL AGE (WK)	BODY WEIGHT (g)	Per 100 g Body Weight				Per 100 g Fat-Free Weight							
		Water (g)	Protein (g)	Lipid (g)	Other (g)	Water (g)	Protein (g)	Ca (mg)	P (mg)	Mg (mg)	Na (mEq)	K (mEq)	Cl (mEq)
24	690	88.6	8.8	0.1	2.5	88.6	8.8	621	387	17.8	9.9	4.0	7.0
25	770	87.8	9.0	0.7	2.5	88.4	9.1	615	385	17.6	9.8	4.0	7.0
26	880	86.8	9.2	1.5	2.5	88.1	9.4	611	384	17.5	9.7	4.1	7.0
27	1010	85.7	9.4	2.4	2.5	87.8	9.7	609	383	17.4	9.5	4.1	6.9
28	1160	84.6	9.6	3.3	2.4	87.5	10.0	610	385	17.4	9.4	4.2	6.9
29	1318	83.6	9.9	4.1	2.4	87.2	10.3	613	387	17.4	9.3	4.2	6.8
30	1480	82.6	10.1	4.9	2.4	86.8	10.6	619	392	17.4	9.2	4.3	6.8
31	1650	81.7	10.3	5.6	2.4	86.5	10.9	628	398	17.6	9.1	4.3	6.7
32	1830	80.7	10.6	6.3	2.4	86.1	11.3	640	406	17.8	9.1	4.3	6.6
33	2020	79.8	10.8	6.9	2.5	85.8	11.6	656	416	18.0	9.0	4.4	6.5
34	2230	79.0	11.0	7.5	2.5	85.4	11.9	675	428	18.3	8.9	4.4	6.4
35	2450	78.1	11.2	8.1	2.6	85.0	12.2	699	443	18.6	8.9	4.5	6.3
36	2690	77.3	11.4	8.7	2.6	84.6	12.5	726	460	19.0	8.8	4.5	6.1

GESTATIONAL AGE (WK)	BODY WEIGHT (g)	Per 100 g Body Weight				Per 100 g Fat-Free Weight							
		Water (g)	Protein (g)	Lipid (g)	Other (g)	Water (g)	Protein (g)	Ca (mg)	P (mg)	Mg (mg)	Na (mEq)	K (mEq)	Cl (mEq)
37	2940	76.4	11.6	9.3	2.7	84.3	12.8	758	479	19.5	8.8	4.5	6.0
38	3160	75.6	11.8	9.9	2.7	83.9	13.1	795	501	20.0	8.8	4.5	5.9
39	3330	74.8	11.9	10.5	2.8	83.6	13.3	836	525	20.5	8.7	4.6	5.8
40	3450	74.0	12.0	11.2	2.8	83.3	13.5	882	551	21.1	8.7	4.6	5.7

From Ziegler E et al: Body composition of the reference fetus. Growth 40:329, 1976.

Coinciding with the changes in the extracellular fluid space, the sodium and chloride concentrations in the fetus decline, whereas the expansion of the intracellular fluid space results in an increase in potassium concentration . The decline in total body sodium is less than that for chloride, because sodium is also a component of fetal bone. Calcium, phosphorus, and magnesium are nevertheless the major minerals in bone. By term, the total body calcium-to-phosphorus ratio is 1.7:1.8, with 98% of calcium, 80% of phosphorus, and 60% of magnesium deposited within the bone.

FETAL METABOLISM

Maternal and thus fetal nutritional deprivations can adversely affect fetal growth. The fetus depends on maternal nutrient intake as well as on maternal endogenous substrate stores as precursors for fetal tissue synthesis and as fuel for fetal oxidative metabolism. The oxygen consumed by the fetus in turn provides energy to support essential fetal work, such as maintenance of transmembrane potentials and replacement of tissue components that are continuously being renewed. In addition, fetal oxygen consumption is required for net synthesis of complex macromolecules such as DNA, RNA, protein, and lipid. Each gram of protein synthesized requires the expenditure of 7.5 cal, whereas a gram of triglycerides requires 11.6 cal. Because 4.85 cal use 1 L of oxygen, net tissue synthesis represents a substantial proportion of fetal oxygen consumption, which is approximately 4 to 6 mL/kg per minute. The energy cost of neonatal growth as measured in premature infants constitutes the energy stored in tissue plus that expended for the synthesis of that tissue. Total energy cost per gram of new tissue is approximately 5.7 cal, whereas that remaining in structural or depot macromolecules represents 4.0 cal. Therefore, 1.7 cal is expended to produce 1 g of new tissue. A similar relationship should occur in the third-trimester fetus, because energy requirements for growth should not change after birth.

Maternal metabolic adjustments during pregnancy are characterized by fuel and hormonal alterations that attempt to secure a continuous provision of substrates for use by the fetus. During normal periods of alimentation, sufficient substrates are presented to the uteroplacental circulation while maternal fuel stores are simultaneously enriched. During the third trimester, maternal insulin resistance and

decreased insulin production may partition ingested fuels toward the fetus.[When fasting occurs during pregnancy, fuel mobilization is accelerated, as is evident by the rapid rise of maternal free fatty acids and ketone bodies. This accelerated mobilization of maternal adipose tissue stores is facilitated by a rapid decline of maternal insulin levels and an enhanced secretion of human placental somatomammotropin. This latter placental hormone has lipolytic activity and may also directly diminish maternal glucose oxidation. In addition, maternal glucose use is attenuated, because free fatty acids and ketones replace glucose as a fuel in maternal tissues, whereas hypoinsulinemia reduces glucose uptake in the insulin-dependent tissues of the mother. Thus, fetal glucose provision may be continued. In addition, alternate substrates mobilized during maternal fasting, such as ketones, cross the placenta and may maintain fetal oxidative metabolism. Ketones may be oxidized or serve as precursors for fetal lipid or protein synthesis. This accelerated mobilization of maternal fuels can ensure fetal growth during short periods of maternal fasting; however, prolonged periods of starvation adversely affect fetal outcome.

The substrates used to maintain fetal oxygen consumption have been most accurately determined in the ovine fetus . Glucose accounts for approximately 50% of fetal energy production in sheep when the mother is maintained in a high nutritional plane. Amino acids, in addition to functioning as precursors for fetal protein synthesis, serve as an oxidizable fuel; they may contribute to 25% of ovine fetal oxygen uptake. Taken together, lactate and acetate may supply an additional 25%. Data from human pregnancies suggest that glucose oxidation may contribute a greater proportion of fetal energy production than in the ovine fetus.

Similarly, the fetal respiratory quotient has been estimated to be close to 1.0 in other mammalian species, which suggests that carbohydrate oxidation is the predominant source for fetal oxidative metabolism. Fasting during human pregnancy may result in an alteration of substrates presented to the fetus when maternal and subsequently fetal ketone bodies increase. Although free fatty acids, especially the essential fatty acids, must cross the placenta, their role in fetal energy production and adipose tissue growth is limited, because the essential fatty acids are probably deposited in structural tissues .

In addition to the provision of substrates for fetal oxygen consumption and growth, tissue growth also depends on an appropriate fetal endocrine milieu. Among the hormones, insulin and insulin-like growth factors have been implicated as “growth hormones” of the fetus. Because insulin does not usually cross the placenta, this growth-enhancing hormone must be of fetal origin. Insulin promotes fetal deposition of adipose and glycogen stores while potentially stimulating amino acid uptake and protein synthesis in muscle. In the absence of fetal insulin production, as in conditions such as pancreatic aplasia, transient neonatal diabetes mellitus, or

congenital absence of the islets of Langerhans, fetal growth is severely impaired. Moreover, when the peripheral action of insulin is attenuated by diminished receptor or postreceptor events, as in leprechaunism and the Rabson-Mendenhall syndrome, fetal growth may be impaired. Insulin resistance due to insulin receptor gene mutations without the phenotype of leprechaunism, and potentially due to mutations in the postreceptor phosphorylation products such as insulin receptor substrate-1 of the insulin receptor signal transduction pathway, may produce IUGR and postnatal growth retardation. As adults, these patients may manifest diabetes mellitus and other complications of hyperglycemia or hyperinsulinemia.

Fetal monogenic disorders that effect fetal insulin secretion or action may produce IUGR. Alterations of the fetal glucokinase gene, which facilitates insulin release after it senses elevated ambient glucose concentrations in the pancreas, result in IUGR when the mutation produces reduced enzyme function. Fetal weight reduction due to a loss of function mutation may be as great as 500 g. As an adult, the affected patient will manifest diabetes mellitus. If the mother also has this mutation, she probably has maturity-onset diabetes of youth and will be hyperglycemic, which may attenuate the fetal growth retardation in an affected fetus. In contrast, gain of function mutations of this pancreatic glucose-sensing enzyme enhances fetal insulin secretion and may increase fetal weight. Another genetic cause of fetal hyperinsulinism is the mutation of the sulfonylurea receptor of the potassium inward rectifier channel. Persistent activation of this channel causes fetal hyperinsulinism and enhanced fetal weight.

Pancreatic agenesis (homozygous mutation of insulin promoter factor-1) and transient neonatal diabetes (paternal isodisomy or duplication of chromosome 6q22-q33) are also associated with IUGR. The leprechaun syndrome (homozygous or compound heterozygous insulin receptor mutation) produces IUGR due to insulin resistance.

On the other hand, those neonates having prolonged periods of hyperinsulinism in utero, such as infants of diabetic mothers or infants with Beckwith-Wiedemann syndrome or persistent hyperinsulinemic hypoglycemia (nesidioblastosis), demonstrate enhanced adipose and muscle tissue mass, resulting in excessive birthweight. Amniotic fluid levels of C-peptide, a cleavage protein of proinsulin, vary directly with fetal growth status: C-peptide is reduced with IUGR and increased with fetal macrosomia.

Fetal growth hormone probably does not influence fetal growth, because there are few growth hormone receptors on fetal liver. The birthweight of a panhypopituitary fetus is not very different from that of a normal fetus. Nonetheless, fetal length may be reduced in the presence of growth hormone insensitivity as a result of a growth hormone receptor deficiency.Maternal levels of placenta-derived

growth hormone are low in cases of IUGR. Placental growth hormone increases maternal nutrient provision to the fetus and is thought to enhance mobilization of maternal substrates for fetal growth.

The final common pathway of growth hormone action is mediated by the generation of insulin-like growth factors. Insulin-like growth factor (IGF) type 1 is a single polypeptide encoded on chromosome 12. IGF1 messenger RNA (mRNA) and its receptor are present in many fetal cells and are not regulated by growth hormone. IGF2 is also a single polypeptide and is encoded on chromosome 11. Its mRNA is much (200-fold to 600-fold) more abundant in most fetal tissues than that for IGF1. IGF1 and IGF2 are 60% homologous to each other and 40% homologous to insulin. IGF1 may be regulated by substrate availability. Its level declines in fetal models of IUGR but increases in infants who are large for gestational age. Fetal levels of IGF1 correlate best with fetal weight. IGF1 and IGF2 receptor binding initiates transmembrane signaling, which activates cell metabolism and DNA synthesis.

IGF1 and IGF2 are present in fetal plasma as early as 15 weeks of gestation. Nonetheless, plasma levels may not reflect tissue-specific action, because these proteins act as competence factors for the cell division cycle in a paracrine or an autocrine, rather than an endocrine, manner. Knockout gene models deleting the IGF1 gene or the paternal IGF2 gene or both demonstrate an additive reduction of fetal growth with both gene deletions. Deletion of the paternal IGF2 gene with genomic imprinting also produces IUGR.

Partial deletion of the IGF1 gene produces severe prenatal and postnatal growth retardation as well as sensorineural deafness and mental retardation. The IUGR is symmetric. In addition, genetic variations (polymorphisms) of the IGF1 gene are also associated with symmetric IUGR. These children also have low circulating IGF1 levels. In adult life, low IGF1 levels are associated with diabetes mellitus and may explain in part the fetal-origins-of-adult-disease hypothesis.

IGFs are modulated by six IGF-binding proteins (IGFBPs), which usually attenuate or occasionally enhance IGF bioavailability and are subject to regulatory signals similar to those that regulate IGF protein synthesis.Fetal IGFBP-1 serum levels are inversely related to birthweight and may restrict the availability of IGF1 to fetal tissues. In animals, overexpression of IGFBP-1 produces IUGR. Acute fetal hypoxia and possibly fetal catecholamine release reduce IGF1 levels but increase IGFBP-1 levels in the ovine fetus.Reduced nutrient availability and lower insulin levels associated with some models of IUGR reduce fetal IGF1 levels, whereas they increase IGFBP-1 levels. Fetal IGFBP-3 serum levels usually parallel those of IGF1 and are thus increased in fetuses who are large for gestational age but reduced in fetuses with IUGR.

Maternal nutrient availability is also regulated by IGF1. IUGR is associated with reduced maternal IGF1 levels or when IGFBP-1 is increased. In mice, increasing maternal IGF1 levels results in heavier fetal weight; in sheep, maternal IGF1 infusions result in increased fetal glucose levels and enhanced placental amino acid uptake.

Reduced function or production of the IGF1 receptor (IGF1R) is associated with IUGR. This transmembrane heterotetramer is encoded at band 15q26 and is structurally similar to the insulin receptor. Hemizygosity of the IGF1R is associated with IUGR in the ring chromosome 15 syndrome.

More complex epigenetic mechanisms such as imprinting may regulate fetal growth. Abnormal expression of a normally inactive gene (loss of imprinting) is seen in Silver-Russell syndrome and transient neonatal diabetes mellitus. Silver-Russell syndrome is characterized by prenatal and postnatal growth restriction; 10% of patients have uniparental disomy of chromosome 7 (maternal). Transient neonatal diabetes manifests with IUGR and may result from overexpression of imprinted paternally expressed gene or genes at 6q24, due to paternal uniparental isodisomy of chromosome 6, paternally inherited duplication of 6q24, or a methylation (imprinting) defect.

Epidermal growth factor (EGF) in the neonate mediates mitosis and development of ectodermal and mesodermal structures; in rodents, EGF mediates eye opening and tooth eruption. EGF is a single 53-amino-acid polypeptide chain derived from the prepro-EGF peptide and may play a minor role in fetal growth and development; there is no fetal EGF RNA expression. Nonetheless, EGF receptors are abundant in the fetus, autophosphorylate themselves, and phosphorylate cytoplasmic proteins. EGF receptor phosphorylation is attenuated in the placenta of women who smoke and who deliver IUGR infants. Transforming growth factor-α, which is 40% homologous to EGF, binds to the EGF receptor, is involved in angiogenesis, and may be the fetal ligand for this receptor, which is similar to the erbB proto-oncogene. Fetal growth is regulated by growth factors and growth factor receptors that are similar to products of nuclear proto-oncogenes. Uncontrolled or constitutive (loss of regulated inhibition) activity of oncogenes is characteristic of malignant transformation, in contrast to the controlled and regulated activity of these proto-oncogene products (growth factors or receptors) during growth. Leprechaunism, an IUGR syndrome, in addition to having insulin resistance, also demonstrates EGF resistance because of an abnormal EGF receptor.

Leptin (from Greek leptos, thin) is a 16-kDa, 167-amino-acid protein discovered in 1994 as the product of the obese (ob) gene. The human leptin gene is on chromosome 7q31 and consists of more than 15,000 base pairs and three exon sites. Leptin is primarily produced in white adipose tissue but has been shown to be

produced in the human placenta and gastric epithelium. It has been shown to regulate body weight through a negative feedback loop between adipose tissue and the hypothalamic satiety centers. Studies have shown that in children and adults, serum leptin concentrations correlate with body fat mass as well as body weight. There is also a gender difference that persists into adulthood—girls have higher serum leptin levels than boys. This gender difference has not been proven conclusively in the fetus and neonate.

Leptin has been detected in amniotic fluid and cord blood of the newborn and can be seen as early as at 29 weeks of gestational age.[Amniotic fluid leptin is derived from the mother, whereas cord blood leptin is derived from the placenta and fetal tissues. Although cord blood leptin levels appear to correlate with birthweight, maternal leptin concentration is not an accurate indicator of fetal growth. There is also a correlation between cord blood leptin level and fetal fat mass. This relationship suggests that leptin may have a role in fetal growth, but this role still needs to be defined. Cord blood leptin levels have been shown to be decreased in newborns with IUGR.This logically follows, given that increases in cord blood leptin correlate with the exponential increase in fat mass that occurs during the last trimester, and given that this fat mass is greatly reduced in fetuses or newborns with IUGR. Furthermore, in the newborn group with IUGR, there is a positive correlation between cord blood leptin levels and body mass index (which indicates fat mass) and not with body weight. The role of ghrelin in fetal growth is still under investigation.

The roles of other hormones, notably corticosteroids and thyroid hormone, have not been well defined for fetal growth. Nonetheless, repeated doses of dexamethasone to the mother may reduce birthweight and possibly brain growth. Mutations that affect the metabolism of cortisol may produce IUGR. Placental 11β-hydroxysteroid dehydrogenase (11βHSD) inactivates cortisol and thus reduces cortisol exposure to the fetus. Placental 11βHSD is reduced in pregnancies complicated by IUGR and in growth-restricted female fetuses born to women with asthma.

With thyroid hormone deficiency in the human athyrotic cretin, birthweight is not altered. These hormones, however, probably have a more significant role as regulatory signals for the initiation of maturation and differentiation in fetal tissues .

FETAL ORIGIN OF ADULT DISEASES

Reduced birthweight has been associated with certain adult morbidities that would not be obvious based on an understanding of IUGR and its immediate neonatal sequelae. Low birthweight in the fetus has been related to the subsequent risk of adult onset hypertension, non–insulin-dependent diabetes, stroke, obesity, and coronary artery disease. Recognized risks for adult morbidities include those infants born thin who demonstrate catch-up growth and who in later life become obese, as well as those with IUGR who are also born short.

The fetal organ hypothesis states that poor maternal nutrition programs the fetus and produces reduced birthweight and subsequent adult-onset diseases. This suggests that such programming occurs during a critical or sensitive period in early fetal life. Studies have confirmed a relationship between poor maternal diet and blood pressure in offspring. Potential programming or imprinting mechanisms include changes in cell-cell interaction, alterations in fetal angiogenesis or innervation, reduction in cell number, clonal selection of cell types (cells with poor availability of nutrients such as lipids may be selected to produce more endogenous lipids), metabolic differentiation (enzymes, transporters, transcription factors, gene expression), and hepatocyte polyploidization (extra chromosome copies can enhance gene expression and alter metabolism). These adaptive fetal processes may be beneficial to the fetus but may permanently alter metabolism and result in adverse metabolic diseases as adults.

Although genetic influences may have a role in postnatal and adult metabolic disorders, the fetal origin hypothesis has been demonstrated in the smaller or discordant fetus of identical twins. In addition, babies after ovum donation tend to have birthweights that correlate to the recipient mother. Furthermore, thin mothers who have poor weight gain in pregnancy have offspring with higher blood pressures than offspring of thin mothers with adequate weight gain during pregnancy. Young children or adults who were IUGR have been demonstrated to have impaired endothelial cell formation, increased carotid artery stiffness, abnormal retinal vascular morphology, and poor postnatal adaptive responses.

Various monogenic disorders also affect birthweight (see earlier).Fetal insulin resistance or poor insulin production may be one primary overriding problem and not just the poor maternal nutrition found in some offspring with postnatal insulin resistance.

EPIDEMIOLOGY OF LOW BIRTHWEIGHT

The term low birthweight refers to infants born weighing less than 2500 g. The neonatal mortality rate is directly related to the low-birthweight rate in a given population. These high-risk infants are a heterogeneous group consisting of infants born preterm (less than 37 weeks) and those born at term but of reduced weight.

IUGR is the predominant cause of low birthweight in developing areas and nations with low birthweight rates greater than 10%. Socioeconomic improvement decreases the proportion of IUGR. Between 20% and 40% of preterm infants also have decreased growth for gestational age. Although there appear to be differences in the relative incidence of IUGR and premature birth in different countries, risk factors associated with birth of an infant with low birthweight are similar .

The rate of reduced weight at term gestation is probably twice as great among black infants as among white. This may be partially independent of socioeconomic factors because black infants often have lower birthweight than infants of Hispanic or

Asian parents of similar socioeconomic status. The risk of low birthweight is related to the occupation not only of the child's parents but also of the grandparents. There is a strong familial aggregation of births of low birthweight in both white and black families. Provision of adequate nutrition to the future mother and other environmental factors may alter that future mother's growth and future reproductive capability. This intergenerational effect explains in part the observation that mothers of infants of low birthweight were themselves neonates of low birthweight.

Although medical complications of pregnancy occur equally in all socioeconomic groups, many adverse behavioral attitudes or practices contribute to the greater low-birthweight rate among women of low socioeconomic status.

MATERNAL CONTRIBUTIONS TO ABERRANT FETAL GROWTH

Physical Environment

Certain otherwise normal mothers are prone to repeated delivery of infants who are SGA; the recurrence rate may be 25% to 50%. Many of these women themselves were born SGA, raising the possibility of intergenerational transmission of a physical regulator of fetal growth. A proportion of these women also remain small throughout life and are identifiable by low prepregnancy weight and stature. These women may exert a restraint on fetal growth by some unknown regulator, possibly related to their own stature, previous nutritional status, endocrine environment, or uterine capacity. In breeding experiments using Shetland ponies and Shire horses, the offspring resulting from breeding a male Shire to a female Shetland was similar in birthweight to a Shetland pony, whereas the birthweight of offspring born to a male Shetland and a female Shire approached that of a Shire. The smaller Shetland female apparently exerts a growth restraint on the genetic potential derived from the larger Shire male. Similar observations are noted in humans. When ova are donated to a recipient mother, the fetal weight correlates best with that of the recipient mother.

Another risk for IUGR is maternal failure to expand plasma volume during pregnancy. Such women have reduced placental weights and a hematocrit level that does not reflect an expanded plasma volume.

Maternal genetic factors have a major direct effect on fetal growth. This influence depends on a transfer of maternal genes but also on the other, unexplained maternal genetic factors related in part to uteroplacental function. The observation that sisters of mothers with infants who were SGA are at higher risk of carrying fetuses who are SGA than their sisters-in-law gives further evidence of maternal genetic influences on fetal growth. The mother's genetic component to fetal growth is less than 25%.

Paternal factors have less effect on fetal growth. Paternal genes affect fetal growth directly by transfer of genetic material, which may be modified (accelerated or inhibited) by maternal factors. Paternal genotypic potential is best expressed as a

function of postnatal growth. Nonetheless, paternal patterns of imprinting of genes (IGF2) may enhance fetal growth.

Other constraints on fetal growth may be exerted during multiple gestations, because fetal growth declines when the number of fetuses increases. The onset of growth retardation in multiple gestations is also related to the number of fetuses: growth restraint begins sooner with triplets than with twins. In multiple gestations, the uterine constraint appears to occur when combined fetal size approaches 3 kg. Placental implantation site, uterine anomalies, vascular anastomoses, and nutritional factors may also interfere with growth in these pregnancies. The uterine capacity itself may also place a constraint on optimal fetal growth. Independent of the number of fetuses, the use of assisted reproductive technologies increases the risk of IUGR.

Maternal Nutrition

Prepregnancy weight and pregnancy weight gain are two important independent variables that affect fetal growth.Underweight mothers and those affected with malnutrition deliver infants with diminished birthweight. Weight gain during pregnancy in nonobese patients correlates significantly with fetal birthweight. Poor weight gain by as early as 16 weeks' gestation may predict low birthweight. The effect of prepregnancy weight in obese women is independent of pregnancy weight gain and offsets the frequently observed poor weight gain of these overweight women . Infants who are SGA are unusual for obese women, whereas macrosomia is common. This may be related to large maternal nutrient stores. Calculating the pregravid body mass index (BMI), helps the clinician determine the target for pregnancy weight gain, which may reduce the risk of IUGR. A low BMI (less than 19.8) may require a pregnancy weight gain of 12.5 to 18 kg, a normal BMI (19.8 to 26) may require a weight gain of 11.5 to 16 kg, and a high BMI (greater than 26 to 29) may require a weight gain of 7 to 11.5 kg, whereas obese women (BMI greater than 29) may need a weight gain of only 6 kg. Appropriate weight gain during pregnancy based on BMI may mitigate the risk of IUGR.

The effects of maternal nutritional status on fetal growth are minimal during the first trimester of pregnancy. This is related to the large surfeit of nutrients presented to the relatively small, undemanding embryo and early fetus. As fetal growth accelerates, the requirements for fetal growth increase and may not be sufficiently provided by an inadequate maternal diet. Earlier attempts to limit weight gain in pregnancy with a 1200-kcal diet to prevent preeclampsia resulted in a 10-fold increase in growth retardation. In an otherwise healthy population of Dutch women experiencing a short period of famine during the Hunger Winter of 1944–1945, fetal growth was most severely affected when deprivation occurred in the third trimester. Substrate deficiency during this period resulted in an overall reduction in birthweight

of 300 g. Maternal weight gain and placental weight were even more drastically reduced, demonstrating preferential use of nutrients for the fetus. Poor nutrition may also reduce uterine blood flow, placental transport, and villous surface area. Observations similar to those of the Dutch experience occurred during a more severe and prolonged famine in wartime Leningrad, where birthweight was reduced by 500 g at term.

There may even be an intergenerational effect of being in utero during maternal starvation. The daughters of women who experienced starvation during the Dutch famine of 1944–1945 have an increased risk of delivering infants of low birthweight if the daughters were exposed to starvation in utero during the first or second trimester. The reduction in the next generation's birthweight is approximately 200 to 300 g. decreased caloric uptake below critical caloric needs may result in diminished fetal growth. Increased maternal caloric expenditure can occur two ways: excessive physical activity and greater waste of calories. The nutritional aspects of cigarette smoking may be an example of the second way. Furthermore, the diminished heat expenditure that occurs among obese women may result in caloric storage and explain in part their excessively large babies. Increased maternal storage of calories may be exemplified by the "selfish mother" hypothesis. These women may not develop the usual insulin resistance during pregnancy and may direct ingested calories toward their own tissue stores. These women have fasting hypoglycemia and/or accelerated disappearance of glucose after intravenous glucose tolerance testing. The opposite occurs among women of low socioeconomic status who receive food supplementation; their skinfold thickness decreases as fetal weight increases. Decreased transport may reflect placental defects in function, nutrient supply, or blood flow. Decreased blood flow may be caused by peripheral vascular disease or failure to expand blood volume and cardiac output, as in normal pregnancy. Fetuses with insulin resistance or decreased numbers of cells may not be able to grow despite adequate nutrient supply. Examples of fetuses with diminished cell numbers include fetuses affected by rubella embryopathy, autosomal trisomies, and other genetic causes of IUGR.

Attempts at improving the low-birthweight outcome in high-risk populations (characterized by having poor nutritional histories) have demonstrated a positive effect of nutritional supplementation. Additional calories, rather than protein supplementation, correlate best with enhanced fetal weight. Caloric supplements greater than 20,000 cal per pregnancy reduced the number of infants with low birthweight; every 10,000 cal supplemented above the standard diet improved fetal weight by an average of 29 g. In Gambia, supplementation during seasonal periods of food shortage resulted in a net positive caloric intake of more than 400 kcal/day. This increased fetal weight 224 g and reduced the low-birthweight rate from 28% to less

than 5%. A threshold of 1500 kcal/day was observed, which augmented fetal weight when the mother was in positive caloric balance. In the United States, participation in the Women, Infants, and Children (WIC) program has reduced the number of births that are SGA.

Protein supplementation may even have adverse neurodevelopmental effects on the fetus. Adolescent women, in particular, are at risk because of their own growth requirements in addition to those of the fetus.

Certain maternal metabolic aberrations are associated with suboptimal fetal growth. Mothers who demonstrate excessively low fasting blood glucose values and those whose blood glucose levels are not sufficiently elevated after an oral glucose tolerance test are at risk of delivering an infant who is SGA. A "selfish mother" hypothesis has been proposed to explain the poor growth of these infants .

Chronic Disease

Of all disease mechanisms that interfere with fetal growth, those resulting in uterine ischemia or hypoxia, or both, have the most extreme effect. Chronic maternal hypertension caused by either primary renal parenchymal disease, such as nephritis, or those conditions extrinsic to parenchymal disorders, such as essential hypertension, significantly alters fetal growth and well-being. This effect is related to the duration of hypertension and to the absolute elevation of the diastolic pressure and is most severe in the presence of end-organ disorders, such as retinopathy. Well-controlled hypertension, without the development of preeclampsia, may not affect fetal growth.

Pregnancy-induced hypertension is of paramount importance to perinatologists in relation to its effect on fetal growth and well-being. This disease, which may affect uteroplacental perfusion and fetal growth long before clinical signs of edema, proteinuria, and hypertension develop, reduces uterine blood flow, as determined by Doppler flow velocity waveforms of the uterine artery. Preeclampsia is characterized by retention of the spiral arteries muscle layer, reduced perfusion of the intervillous space, necrotizing atherosis, and decreased trophoblastic invasion of the decidual spiral arteries. Such trophoblastic invasion depends on decidual laminin, fibronectin, maternal cytokines, and trophoblastic integrins and proteases. Similar arterial pathologic changes may be present in idiopathic IUGR. In pregnancies complicated by eclampsia, fetal growth deviates from the expected norm from 32 weeks onward . Treatment of hypertension in pregnancy with antihypertensive drugs may further contribute to IUGR. This is independent of the medication; with a decline of 10 mm Hg, fetal weight may be reduced 145 g. Vascular insufficiency resulting from advanced maternal diabetes mellitus, especially in the presence of end-organ disease in the kidney or retina, also produces IUGR despite the presence of maternal

hyperglycemia . Women with serious autoimmune disease associated with the lupus anticoagulant are also a high-risk population for preeclampsia and IUGR .

Another major category associated with diminished fetal weight gain is that resulting from maternal hypoxemia. Severe cyanotic congenital heart disease, such as tetralogy of Fallot or Eisenmenger complex, is the best example of this mechanism, whereas sickle cell anemia is representative of diseases that can produce local uterine hypoxia and ischemia. The maternal morbidity rate is high with cyanotic heart disease. Nutritional anemias are not usually associated with aberrant fetal growth. In sickle cell anemia, the abnormal cells may interfere with local uterine perfusion during episodes of sickling, and growth retardation is observed.

A common and nonpathologic factor related to maternal hypoxia is the diminished environmental oxygen saturation that is present at high altitudes. Infants born in the mountains of Peru demonstrate lower birthweights than do Peruvian infants born at sea level. Placental mass has hypertrophied in these newborns in an attempt to compensate for the lower circulating maternal oxygen concentration. These neonates are not born with polycythemia as a response to fetal hypoxia, as proposed for other infants who are SGA. The decline in body weight becomes manifest at an altitude of 2000 m, which corresponds to a barometric pressure of 590 mm Hg.

Drugs

The effects of maternal drug administration on the fetus are usually considered primarily in terms of teratogenicity. However, a continuum of fetal compromise may be present because many malformation syndromes are associated with diminished birthweight, whereas other agents may interfere only with fetal growth. Many of the typically abused drugs have been implicated as agents producing fetal growth retardation by reducing maternal appetite and by being associated with lower socioeconomic groups. However, at least for heroin, methadone, and ethanol, a cellular toxic effect acting directly on cell replication and growth appears to be involved. This is most evident in fetal alcohol syndrome: the prenatal onset of growth retardation persists during postnatal periods despite adequate food intake. A placental transfer block for specific amino acids has been observed in fetal alcohol syndrome.

The effects of cocaine on fetal growth may be multi-factorial and may include uterine artery vasospasm, reduced maternal prepregnancy weight, reduced weight gain during pregnancy, and, possibly, direct fetal endocrine effects. Multidrug use, poor nutrition, and poor prenatal care are common among many drug-dependent women.

Cigarette smoking during pregnancy reduces eventual fetal birthweight, which is directly related to the number of cigarettes smoked.Birthweight at term is reduced an average of 170 g if more than 10 cigarettes per day are used; smoking more than 15

per day may reduce weight by 300 g. The mechanism of fetal growth retardation is uncertain, but nicotine and subsequent catecholamine release may produce uterine vasoconstriction and fetal hypoxia. Carbon monoxide and cyanide may cause a more direct effect: after binding to hemoglobin, carbon monoxide and cyanide may diminish oxygen unloading from the mother to the fetus and from the fetus to its tissues. Nutritional supplementation does not completely eliminate the reduced fetal weight. Moreover, the effects of cigarettes may be greatest at advanced maternal age. Another mechanism producing IUGR is related to the presence of polymorphisms of the genes for glutathione S-transferase and CYP1A1, which are enzymes responsible for the metabolism of polycyclic aromatic hydrocarbons, arylamines and N-nitrosamines. Certain gene polymorphisms may reduce fetal growth by as much as 1285 g at term.

Drugs such as propranolol and other beta-blocking agents and corticosteroids probably have a direct effect on the fetus, although the confounding influence of the chronic maternal illnesses for which these agents are prescribed may also contribute to IUGR.

PLACENTAL DETERMINANTS

Optimal fetal growth depends on efficient function of the placenta as a nutrient supply line, a metabolic and endocrine unit, and an organ of gaseous exchange. Placental functional integrity requires additional energy production because placental oxidative metabolism may equal that of the fetus. This large energy requirement is essential for maintaining fetal growth-promoting roles, which include active transport of amino acids, synthesis of protein and steroid hormones, and support of placental maturation and growth. Placental growth parallels that of the fetus; however, toward term there is a greater decline in the rate of placental weight gain than in the rate of weight gain by the fetus. During this decline of placental weight, the fetus also exhibits a decrease in the rate of weight change, which suggests that placental function and the rate of weight gain have declined and led to reduced fetal growth. However, despite the change in the rate of placental weight gain, the placenta continues to mature. The placental villous surface area continues to increase with advancing gestational age ; simultaneously, the syncytial trophoblast layer continues to thin, and vascularization of the terminal villi continues to improve.Functionally, urea clearance is enhanced toward term in the ovine placenta , suggesting that permeability and diffusing distance improve as the placenta approaches term. Birthweight has been correlated with placental weight and with villous surface area , suggesting that macroscopic and microscopic events are related to optimal placental function. When placental insufficiency occurs, there may be a functional failure of the placenta as a respiratory or nutritive organ or both. Placental insufficiency associated with maternal nutritional deficiency has more than one effect on fetal

growth. In addition to diminished fetal substrate provision, placental metabolism is altered directly . Diminished placental growth adversely affects total nutrient transfer, whereas reduced placental production of chorionic somatomammotropin attenuates maternal mobilization of fuels to the fetus. Reduced placental energy production and protein synthesis limits active transport of amino acids and facilitative transport of glucose.

When placental insufficiency complicates maternal vascular disease such as preeclampsia, placental weight and volume also diminish. In addition, a decline in villous surface area and a relative increase in nonexchanging tissue occur. At the same time, these placentas demonstrate thickening of the capillary basement membrane.

Following is a list of additional findings in placental disorders associated with diminished birthweight]:

Twins (implantation site)

Twins (vascular anastomoses)

Chorioangioma

Villitis (involving toxoplasmosis, other [congenital syphilis and viruses], rubella, cytomegalovirus, and herpes simplex virus [TORCH] association)

Villitis (unknown cause)

Avascular villi

Ischemic villous necrosis

Vasculitis (decidual arteritis)

Multiple infarcts

Syncytial knots

Chronic separation (abruptio placentae)

Diffuse fibrinosis

Hydatidiform change

Abnormal insertion

Single umbilical artery (?)

Fetal vessel thrombosis

Circumvallate placenta

Reduced capillarization

Reduced terminal villus branching

Elevated vascular tone

Increased glucose utilization

Confined chromosomal mosaicism (trisomy of 2, 3, 7, 8, 9, 13, 14, 15, 16, 18, 22, or X)

Reduced spiral artery recruitment

Multiple gestations may produce significant placental disorders in suboptimal sites of implantation or, more often, related to abnormal vascular anastomoses in diamniotic monochorionic twinning . As a result of arteriovenous interconnections, one twin serves as the donor and develops IUGR, losing nutrient supplies, whereas the other is the recipient and has satisfactory growth. These anastomoses may be detectable on careful gross examination of the placenta. Ablation of vascular communications in the second trimester, by fetoscopic neodymium:yttrium-aluminum-garnet laser photocoagulation, may reduce the morbidity of the twin-twin transfusion syndrome, which develops in 5% to 17% of monozygotic twins.

Other detectable potential causes related to aberrant fetal growth include chorioangiomas, large retroplacental infarcts and hemorrhages, abnormal cord insertion patterns, and (questionably) single umbilical artery. Combined reductions of uterine and umbilical blood flow have also been detected in IUGR.Furthermore, increased vascular resistance has been demonstrated in these circulations . In addition, reduced placental prostacyclin (a potent vasodilator) production may be present in IUGR. Increased placental vascular tone may be fixed or dynamic. The latter may be due to reduced activity of placental nitric oxide synthase or increased circulating fetal levels of angiotensin II or endothelin.

Genetic, enzymatic, and endocrine abnormalities of placental tissue may reduce fetal growth. Decreased expression of enzymes involved in redox regulation (thioredoxin, glutaredoxin) may place placental vessels at risk for endothelial cell oxidative stress and is associated with IUGR. In animals, decreased expression of IGF1R and the insulin receptor produces IUGR. Furthermore, genes that may regulate nutrient transfer (connexin 2b, Esx1) are also associated with IUGR in mice.

FETAL DETERMINANTS

Optimal fetal growth depends on adequate provision of substrates, their effective placental transfer, and the inherited regulatory factors within the fetal genotype that affect nutrient utilization. In addition to substrates, oxygen must be transferred, and an appropriate hormonal milieu must be present. There must also be sufficient room within the uterus. In the absence of adverse environmental effects, the inherent growth potential of the fetus may be achieved.

Genetic determinants of fetal growth are inherited from both parents, and population norms must be established to detect aberrant fetal growth. For example, the average birthweight of Cheyenne Indians is 3800 g at term, whereas that of the New Guinea Luni tribe is 2400 g. Genetic potentials are usually determinants of early fetal growth; nutritional and environmental problems should not affect the fetus until the requirements for tissue growth increase during the third trimester. Indeed, reduced first-trimester growth as determined by crown-rump length is a risk factor for IUGR. This risk is even stronger in the presence of increased maternal α-fetoprotein levels.

Approximately 20% of birthweight variability in a given population is determined by the fetal genotype; maternal hereditary and environmental factors contribute an additional 65%; the remaining contributing factors are unknown. Birth order affects fetal size: infants born to primiparous women weigh less than subsequent siblings. The second child and each additional child weigh an average of 180 g more than the firstborn. This relationship is not true for multiparous adolescent pregnancies, in which subsequent births during adolescence produce neonates with lower term weights than that of the firstborn. Male sex of the fetus is associated with greater birthweight, beginning to become predominant after 28 weeks' gestation. At term, boys weigh approximately 150 g more than girls. A male twin, in addition to affecting its own somatic growth, can also enhance the growth of its female twin. Androgenic hormonal stimulation of fetal growth or paternal imprinting of IGF2 may contribute to these observed differences. Also, a theory states that maternal-fetal antigenic (HLA, ABO) differences are responsible for this effect. These antigenic differences result in enhanced placental trophoblastic invasion of the decidua, improving placental and subsequent fetal growth. As a corollary, interference with maternal immunologic function may inhibit this antigenic growth advantage and explain in part the diminished birthweights after maternal immunosuppressive therapy.

Alternately, chromosomes may carry growth-determining genes: genetic material on the Y chromosome may enhance the growth of the male fetus. Similarly, chromosomal deletions or imbalances result in diminished fetal growth. For example, Turner syndrome (XO) is associated with diminished birthweight. The converse is not true: additional X chromosomes beyond the norm are associated with reduced fetal growth. For each additional X chromosome (in excess of XX), birthweight may be reduced 300 g. Similarly, autosomal trisomies, such as Down syndrome, are also associated with abnormal fetal growth. Chromosomal aberrations often result in diminished fetal growth by interfering with cell division. An intrinsic defect in cultured fibroblasts from patients with trisomy 21 has been observed in tissue culture. Single-gene defects may also reduce fetal growth. The inborn errors most notably associated with diminished fetal weight are included in a list of factors that affect fetal growth, following these paragraphs. Many syndromes with autosomal-recessive, autosomal-dominant, polygenetic, or unknown inheritance are also associated with poor fetal growth and occasionally may produce marked IUGR.

Monogenic disorders that affect fetal growth often impair insulin secretion or insulin action. These include reduced fetal insulin secretion by an attenuated insulin-sensing mechanism from a loss of function mutation in the pancreatic glucose-sensing enzyme glucokinase. Reduced insulin action is noted in leprechaun syndrome, which results from a mutation in the insulin receptor. IUGR has also been

reported with deletion of the IGF1 gene. More complicated genetic mechanisms associated with IUGR include maternal uniparental disomy for chromosome 6, which probably unmasks an autosomal-recessive gene mutation. Paternal uniparental disomy of chromosome 6 is associated with transient neonatal diabetes and IUGR.

Abnormalities of the epigenetic process known as imprinting may result in reduced or excessive fetal growth. Epigenetic modification of genes by reversible modification of DNA by methylases and demethylases can suppress gene function (methylation) in a specific parent (maternal or paternal) of origin without altering the DNA sequence of that gene. Imprinted genes cluster in specific chromosome regions or domains. Imprinting is active in gametogenesis, with different genes being imprinted (methylated, suppressed) depending on the parent of origin. The fertilized egg then undergoes a series of DNA demethylations only to be followed by new patterns of methylations in the embryo.Loss of imprinting of the IGF2 gene results in excessive fetal growth and is also noted in certain malignancies (Wilms tumor, colon, ovary). The IGF2 gene, located at a highly imprinted region (11q15.5), is maternally imprinted (suppressed) but paternally expressed. The normal pattern is that only one allele is expressed (paternal). Biallelic expression predisposes to excessive growth and tumors.

Beckwith-Wiedemann syndrome (BWS) is a common overgrowth syndrome that illustrates the role of imprinting in the regulation of fetal growth. BWS is a multi-genetic disorder that may be sporadic or familial; cases may also be associated with chromosomal abnormalities in the highly imprinted region at chromosome 11p15.5. Duplication of paternally derived 11p15 and paternal uniparental isodisomy of 11p are noted. Overgrowth may result from overexpression of paternally expressed genes that enhance growth or from suppression of maternally expressed genes that inhibit growth. Many sporadic cases of BWS demonstrate biallelic expression (normal is expression of the paternally derived gene only, as the maternal gene is imprinted and suppressed) of the IGF2 gene.

Because imprinting through methylation and demethylation is quite active during gametogenesis and embryogenesis, there may be alterations in the pattern of differentially expressed genes during various assisted reproductive technologies. Indeed, children born after assisted reproductive technologies have a higher incidence of potential imprinting disorders such as BWS, Angelman syndrome, and retinoblastoma.

Additional disorders due in part to imprinting errors include uniparental disomy for chromosome 7 with IUGR, 10% of Silver-Russell syndrome, and transient neonatal diabetes.An imprintable gene possibly involved in Silver-Russell syndrome, GRB10, codes for growth-factor-receptor binding proteins that interact with the insulin and insulin-like growth factor receptors.

Infectious agents are typically sought as being responsible for early onset of IUGR. Of these, cytomegalovirus and rubella virus are the most important identifiable agents associated with marked fetal growth retardation. After maternal viremia, both agents invade the placenta, producing varying degrees of villitis, and subsequently gain access to fetal tissues. The effects of placentitis itself on fetal growth are unknown, but once congenital fetal infection has occurred, these viral agents have direct adverse effects on fetal development. Intracellular rubella virus inhibits cellular mitotic activity in addition to producing chromosomal breaks and subsequently cytolysis. In addition, this virus produces an obliterative angiopathy that further compromises cell viability. Cytomegalovirus also causes cytolysis, resulting in areas of focal tissue necrosis. These viral agents therefore reduce cell number and subsequent birthweight by simultaneously inhibiting cell division and producing cell death .

THE INFANT WITH IUGR/SGA

Definition

The infant with low birthweight (less than 2500 g) is not always premature (earlier than 37 weeks). Worldwide, more than 20 million infants are born weighing less than 2500 g. Between 30% and 40% of these infants are born at term gestation and are therefore undergrown (SGA status). Population norms need to be determined for each specific genetic group, especially those characterized by unusual inherited patterns of fetal growth. In general, these population norms established in various North American and European cities describe the usual fetal growth pattern for industrial societies and may be used as the reference norms for similar ethnic groups . Each curve defines either standard deviations or percentile units that include the normal variability or distribution of birthweights at each gestational age. By definition, infants less than two standard deviations or those at less than the third percentile (10th for Denver curves because of the lower birthweight at higher altitudes) are classified as SGA. Therefore, between 2.5% and 10% of each population has SGA status. The use of population means can be misleading. Within a sibship, fetal birthweight is less variable and more consistent than that for an entire population. Compared with family members, 80% of infants with congenital rubella infection were classified as SGA, whereas only 40% were SGA when population standards were used. Fetal growth assessment must therefore be considered in the context of prior reproductive history and clinical examination of the newborn.

Infants with IUGR may or may not be SGA. Alternatively, infants who are SGA may not have been affected by growth-restricting processes that produce IUGR. Weight parameters at birth may be insensitive in determining IUGR. The ponderal index (weight divided by length cubed) or other body proportion ratios (head circumference to weight or length, femur length to abdominal circumference, head

circumference to abdominal circumference) may be useful in detecting additional cases of IUGR during the fetal or neonatal period. IUGR resulting from placental insufficiency usually reduces birthweight more than length, and to a greater degree than head circumference, and it would be evident by a reduced ponderal index with a smaller, albeit relatively large (spared), head circumference. The greater the severity of IUGR, the greater is the deviation of weight, length, and (less so) head circumference from gestational age norms. Alterations of body proportion ratios may create a continuum rather than a dichotomous classification of birthweight status (appropriate for gestational age [AGA] versus SGA).

Deviations of fetal weight from a predetermined genetic potential produce IUGR with or without SGA status. Second-trimester fetal anthropometric and biometric ultrasonography can be used to predict an ideal weight, which may be modified by intrinsic and extrinsic growth-limiting factors. Any variation from the predicted weight would be considered IUGR. The growth potential realization index assesses deviations from norms of weight and of head, abdominal, and thigh circumferences. This index is applied to the infant after birth by calculating a neonatal growth assessment score that includes the deviation of each growth parameter from its related normative value for that gestational age. A neonatal growth assessment score of zero indicates ideal growth, and scores greater than 20 indicate IUGR but not necessarily SGA.

Aberrant Fetal Growth Patterns

Fetal growth retardation may have its origins early or late during fetal development. Infants who demonstrate reduced fetal growth early in gestation constitute approximately 20% of all infants who are SGA. They are symmetrically growth retarded: head circumference, weight, and length are proportionately affected to equivalent degrees. These fetuses and infants continue to grow, albeit with reduced net effect . In addition to inherent genetic growth constraint, other factors may produce diminished growth potential in these neonates. Congenital viral infections usually have their worst effect if infection occurs during the first trimester, when they have a significant effect on cell replication and subsequently on birthweight. Similarly, abnormal genetic factors, such as single gene deletions and chromosomal disorders, also reduce the intrauterine growth rate at an early stage of development.

Growth retardation of a later onset is usually associated with impaired uteroplacental function or nutritional deficiency during the third trimester . Nutrient supplies, oxygen, and uteroplacental perfusion are in excess of their requirements during early fetal development and should not interfere with fetal growth until the growth rate exceeds the provision of substrates or oxygen or both. During the last trimester, the fetal growth rate and net tissue accretion increase markedly; if the uteroplacental supply line is compromised, IUGR will develop. The anthropometric

findings among these infants demonstrate a relative sparing of head growth, whereas body weight and somatic organ growth are more seriously altered. Spleen, liver, adrenal, thymus, and adipose tissue growth is affected to the greatest extent in these newborns who are late-onset SGA . The relative sparing of fetal head (brain) growth is caused by preferential perfusion of the brain with well-oxygenated blood containing adequate substrates after redistribution of the cardiac output during periods of fetal distress. Infants with IUGR resulting from unknown or nutritional causes may have successfully adapted to a "hostile" in utero environment with reduced growth. After birth, in a more favorable environment, catch-up growth ensues.

Antenatal Care

DIAGNOSIS

Antenatal diagnosis of IUGR has proved difficult. Many of these infants deliver at or beyond term without prior antenatal detection. At best, when sought with careful maternal physical examination, accurate dating, and risk-assessment analysis, only 50% of these infants may be identified by clinical examination before birth. Antenatal detection is an essential component of care for these infants because they require intensive obstetric and neonatal management to reduce their excessive perinatal morbidity and mortality rates. This poor outcome is associated with unexplained antepartum or intrapartum fetal death, neonatal asphyxia, and major neonatal adaptive problems. Neonatal risks are increased at each gestational age. Antenatal identification and intensive perinatal care of the mother, the fetus, and, later, the neonate are imperative components that result in improved outcome for these infants.

Careful measurement and recording of fundal height at each antenatal visit are a reasonable clinical screening aid in the diagnosis of IUGR. When dates are confirmed by onset of quickening, audible heart tones and accurate menstrual history, size-date discrepancy (i.e., fundal height less than or lagging behind the norm for gestational age) is suggestive of IUGR. History findings that may be components of a risk assessment score for IUGR include a history of a previous infant who was SGA, vaginal bleeding, multiple gestation, low prepregnancy weight, and poor pregnancy weight gain, as noted earlier. Chronic maternal illness and preeclampsia are also high-risk situations indicating possible IUGR.

Laboratory tests, including determination of maternal serum estriol level, placental lactogen, and various pregnancy-associated proteins, have been unreliable markers for IUGR. The diagnosis of chronic fetal distress in the absence of obvious alterations of fetal heart rate patterns is now possible with cordocentesis (percutaneous umbilical blood sampling). Although not indicated for all patients with IUGR, fetal blood sampling may demonstrate hypoxia, lactic acidosis, hypoglycemia, and normoblastemia caused by chronic fetal distress. Hypoxia may precede fetal

acidosis. Fetal blood sampling may also permit rapid karyotyping of the fetus with IUGR with malformations and the identification of TORCH infections through the assessment of antibody titers, culture, or DNA diagnosis of TORCH agents.

Ultrasonographic assessment of the fetus can help detect the presence of IUGR. Either used as a routine two-step process (dating/sizing in mid-second trimester; follow-up assessment at 32 to 34 weeks) or based on risk analysis, fetal ultrasonography is the primary method for identifying fetuses with IUGR.Ultrasonography includes real-time biometric and anthropomorphic analysis of fetal growth parameters (head circumference, biparietal diameter, abdominal circumference, femur length), detection of anomalies, and identification of oligohydramnios.Oligohydramnios is a risk factor for congenital anomalies, severe IUGR with reduced urine production, pulmonary hypoplasia, variable decelerations from cord compression, and intrauterine fetal death in as many as 5% to 10% of affected fetuses. The risk of congenital anomalies with oligohydramnios increases from 1% to 9% with mild-to-severe amniotic fluid deficits; at the same time, the risk of IUGR increases from 5% to 40%. Second-trimester oligohydramnios, with elevated α-fetoprotein levels, has a particularly poor prognosis .

The degree of oligohydramnios can be determined ultrasonographically and quantitated by means of the four-quadrant amniotic fluid index (AFI). The vertical diameters of four pockets of amniotic fluid are added to determine the amniotic fluid index. Between 26 and 38 weeks of gestation, the amniotic fluid index is 12.9 ± 4.6 cm; an index of less than 5 cm signifies severe oligohydramnios.

Morphometric analysis of fetal growth parameters includes determination of serial biparietal diameters as analyzed by absolute number and rate of change . Head sparing in asymmetric IUGR may make fetal measurements of the biparietal diameter less sensitive; however, truncometry—measuring the fetal abdominal circumference (in part, liver size) at the level of the umbilical vein—may add accuracy . Using ratios of fetal growth parameters and adding the femur length and the fetal ponderal index may increase the sensitivity of fetal biometry. Three-dimensional evaluation may improve the prenatal estimate of fetal size.

Doppler flow velocity waveforms, assessed in the maternal and fetal circulations, may detect increased maternal and fetal vascular resistance before the onset of IUGR. Maternal arcuate arterial flow may reflect trophoblastic invasion of the myometrium because increased flow may be associated with increased vascular invasion and better placental perfusion. Alternatively, decreased maternal arcuate arterial waveform velocity may demonstrate increased maternal vascular resistance and decreased uteroplacental perfusion. Uterine vessel velocimetry is less accurate than waveforms in fetal vessels in predicting IUGR and fetal hypoxia.

Chronic fetal distress with hypoxia (with or without acidosis) is associated with fetal Doppler arterial waveform velocities that indicate reduced systemic (descending aorta, umbilical artery) flow and normal or increased cerebral (middle cerebral artery) flow (head sparing). The greatest risk is associated with absent or even more seriously with reversed diastolic flow in the umbilical artery Absent end-diastolic velocimetry may be stable or it may progress to reversed flow; both indicate placental insufficiency. Reversed flow greatly increases fetal risk and is usually unstable and requires consideration for delivery. If other features are otherwise normal (biophysical profile, amnionic fluid volume, reassuring cardiotocograms, minute-to-minute variation), steroids can be given and delivery temporarily delayed.

Assessment of the fetal middle cerebral artery (MCA) may show centralization in the compromised fetus, demonstrating increased flow in the MCA relative to the placenta. Preservation of MCA diastolic flow may be seen with absent or even at times reversed flow in the umbilical artery. Decreased MCA flow is associated with fetal cardiac decompensation and is an ominous sign.Umbilical venous pulsation or dilation of the ductus venosus and reversed flow in the vena cava also suggests serious cardiac compromise from hypoxia or anemia. Abnormalities on the venous side of the circulation occur later than in the umbilical arteries. Nonetheless, these Doppler waveform abnormalities may precede classic signs of fetal distress, such as abnormal results on contraction stress.

ANTENATAL MANAGEMENT

Once the diagnosis of IUGR is suspected and strengthened by ultrasonography, it is essential to institute appropriate maternal and fetal care and closely monitor the well-being of the fetus. With severe IUGR, maternal activity should be limited and bed rest initiated, with the mother assuming a left lateral recumbent position to ensure optimal uterine blood flow. Administration of oxygen (55% O2 at 8 L/min) to the mother has resulted in improved fetal oxygenation, some growth, and normalization of fetal aortic blood flow velocity in some IUGR fetuses with chronic fetal distress.

Assessment of fetal well-being should begin once the diagnosis is suspected and the fetus has approached a gestational age compatible with extrauterine survival. An inexpensive screening tool is a log of fetal activity recorded by the mother; normal activity is a reasonable sign of well-being. A specific period should be monitored, such as after a meal, and fetal activity should be recorded each day. In addition to this maternal record, a systematic approach to fetal evaluation should be performed routinely and frequently. Classically, the oxytocin challenge test (OCT) has been used to predict the potential for fetal demise or acute intrapartum death in a marginally oxygenated, compromised fetus. This test requires the intravenous administration of oxytocin, which must result in three uterine contractions within 10 minutes. Late decelerations denote relative uteroplacental insufficiency and suggest

that the oxygenation of the fetus may be impaired. A positive OCT result (three late decelerations with three contractions) also suggests that the fetus may not tolerate the contractions that occur during labor. This is not a universal observation; a significant percentage of these infants may be able to withstand spontaneous or oxytocin-induced labor without the development of fetal acidosis. Fewer decelerations than those for a positive OCT result should be considered suspect, and the test should be repeated (along with technically unsatisfactory tracings) within the next 24 to 48 hours.

Because technical and time difficulties are related to the OCT, and because contraindications exist for its use, such as a previous classic cesarean section, placenta previa, and concern about inducing premature labor, the nonstress test (NST) has been employed. This test examines fetal well-being by determining the acceleration of the fetal heart rate after spontaneous fetal movement. A healthy fetus (nonhypoxic) will respond to its own body movements with a mean acceleration of 15 beats per minute above the baseline heart rate. In addition, the frequency of fetal movements should be ascertained; at the same time, examination of beat-to-beat and long-term variability can offer additional useful information. The NST can also supplement the OCT, because fetuses with a positive OCT result but a reactive NST result and normal beat-to-beat variability are more likely to tolerate labor without untoward problems. Under stable maternal conditions and with signs of fetal well-being (negative OCT result and [or] reactive NST result), these tests may be repeated weekly.

The false-positive rate for OCT (25%) and NST (20%) is high compared with the false-negative rate for OCT (0.4 in 1000) and NST (6.8 in 1000). The rate of intrauterine fetal death is high after a positive OCT result (32%) but lower with a nonreactive NST result (12%). Therefore, the contraction stress test is more predictive of fetal death and has fewer false negative results. However, more false positive results are obtained than with the NST.

Biophysical determinants have been used successfully to assess fetal well-being. The combined analyses of fetal breathing movements, gross body movements, fetal tone, fetal heart reactivity to movement, and qualitative amniotic fluid volume have improved the antenatal management of IUGR . This biophysical profile provides a nonweighted score that can identify the fetus at risk. A biophysical profile score of 8 to 10 carries a 0.8% chance of fetal death, whereas a score of 0 predicts a fetal mortality rate of 40%. This analysis takes approximately 30 minutes and should be repeated weekly with scores of 8 to 10. If the score is less than 8, the biophysical profile should be repeated that afternoon. If the score is again less than 8, an OCT should be performed and a decision made to deliver the infant, regardless of gestational age, unless severe anomalies are determined. A low biophysical profile

correlates with fetal hypoxia determined by cordocentesis. Assessment of fetal aortic flow with the pulsatile index may also help determine optimal timing for delivery. If fetal lung maturity is present, aortic blood flow is reduced, and there is other evidence of fetal distress, the fetus may need to be delivered before term. Factors that affect the biophysical profile score include sedation, stimulants (cocaine, theophylline), indomethacin (decreases amniotic fluid), cigarette smoking (decreases fetal breathing movements), hyperglycemia (increases fetal breathing movements), and hypoglycemia (decreases all activities).

Table Biophysical Profile Scoring: Technique and Interpretation *

BIOPHYSICAL VARIABLE	NORMAL (SCORE = 2)	ABNORMAL (SCORE = 0)
Fetal breathing movements	≥1 episode of ≥30 s in 30 min	Absent or no episode of ≥30 s in 30 min
Gross body movements	≥3 discrete body or limb movements in 30 min (episodes of active continuous movement considered as single movement)	≤2 episodes of body or limb movements in 30 min
Fetal tone	≥1 episode of active extension with return to flexion of fetal limb(s) or trunk (opening and closing of hand considered normal tone)	Slow extension with return to partial flexion or movement of limb in full extension or absent fetal movement
Reactive fetal heart rate	≥2 episodes of acceleration of ≥15 beats/min and of ≥15 s associated with fetal movement in 20 min	<2 episodes of acceleration of fetal heart rate or acceleration of <15 beats/min in 20 min
Qualitative amniotic fluid volume	≥1 pocket of fluid measuring ≥1 cm in two perpendicular planes	Either no pockets or a pocket of <1 cm in two perpendicular planes

Modified from Manning FA et al: Fetal assessment based on fetal biophysical profile scoring. Am J Obstet Gynecol 151:343, 1985.

The mode of delivery is not necessarily dictated by the abnormalities recorded by biophysical or electrophysiologic surveillance of the fetus. Some patients can tolerate labor after a positive OCT result, with oxygen administration and a left lateral recumbent position. However, it would be judicious to avoid labor in those situations complicated by a nonreactive NST result, a flat baseline, absent or reversed diastolic flow, and a positive OCT result. Similarly, premature infants who are SGA, in

particular those with a breech presentation and those whose mothers have a completely unfavorable cervix, should be delivered by the abdominal route. Particular attention should be given to the asymmetrically (late-flattening) growth-retarded fetus with chronic fetal distress who tolerates labor poorly and readily develops signs of acute fetal distress, compared with the symmetrically undergrown fetus and the normal fetus. Whether labor is induced or spontaneous, continuous intrapartum fetal heart rate monitoring combined with appropriate use of fetal scalp pH determinations and fetal pulse oximetry should be employed If late decelerations become evident, scalp blood pH might be evaluated, and if fetal acidosis has developed, delivery should be expedited.

During labor, uterine contractions may further compromise marginal placental perfusion and fetal gas exchange. The myocardium of these fetuses may have diminished glycogen stores, a key energy source partially responsible for the fetal ability to withstand asphyxia. Because there is a high incidence of intrapartum birth asphyxia, it is essential that the delivery be coordinated with the neonatal team, which should be prepared to resuscitate a depressed or asphyxiated neonate. In addition, combined obstetric-pediatric management is indicated if meconium is present in the amniotic fluid. This event often follows periods of fetal hypoxia and stress, occurring with greatest frequency in the term or post-term neonate who is SGA. Obstetric management should include oropharyngeal suctioning immediately after delivery of the head. Immediately after birth, the neonatal team should further clear the oropharynx, and possibly also the trachea, of additional meconium .

Saline amnioinfusion may be beneficial in the presence of oligohydramnios and an AFI of less than 5 cm.Titration to an index of greater than 8 cm may lower the incidence of meconium-stained fluid, variable decelerations, end-stage bradycardia, fetal distress, and acute fetal acidosis.

APPROACH TO THE INFANT WHO IS SMALL FOR GESTATIONAL AGE

After birth, the infant who is SGA may develop significant neonatal problems . In the delivery room, it is essential to ensure optimal neonatal cardiopulmonary physiologic adaptation while ensuring minimal heat loss in a warm environment. Once stabilization has been established, a careful physical examination should be performed.

Table 13-7 -- Perinatal Problems of the Small-for-Gestational-Age Neonate

PROBLEM	PATHOGENESIS	ASSESSMENT/PREVENTION/TREATMENT
Fetal death	Placental insufficiency, chronic fetal	Biophysical profile
		Vessel velocimetry
		Cordocentesis

PROBLEM	PATHOGENESIS	ASSESSMENT/PREVENTION/TREATMENT
	hypoxia	Maternal O2
		Early delivery
Asphyxia	Acute fetal hypoxia superimposed on chronic fetal hypoxia, acidosis	Antepartum and intrapartum monitoring
		Efficient neonatal resuscitation
	Placental insufficiency	
	↓ Cardiac glycogen stores	
Meconium aspiration pneumonia	Hypoxic stress	Pharyngeal-tracheal aspiration
Fasting hypoglycemia	↓ Hepatic glycogen	Early oral or intravenous alimentation or both
	↓Gluconeogenesis	
	↓Counter regula-tory hormones	
	Cold stress	
	Asphyxia-hypoxia	
Alimented hyperglycemia	"Starvation diabetes"	Glucose infusion not to exceed 8 mg/kg/min except with hypoglycemia
Polycythemia/ hyperviscosity	Placental transfusion	Neonatal partial exchange transfusion
	Fetal hypoxia	
	Erythropoietin	
Temperature instability	Cold stress	Neutral thermal environment
	Poor fat stores	Early alimentation
	Catecholamine depletion	
	Hypoxia, hypoglycemia	
	Reduced fasting oxygen consumption	
Dysmorphology	TORCH	Disease-specific therapy or prevention

PROBLEM	PATHOGENESIS	ASSESSMENT/PREVENTION/TREATMENT
	Syndrome complexes	
	Chromosome disorders	
Teratogen exposure		Disease-specific therapy or prevention
Pulmonary hemorrhage (rare)	Hypothermia, polycythemia	Avoid cold stress, hypoxia
	↓ O2/DIC	Endotracheal administration of epinephrine
		PEEP
Immunodeficiency	"Malnutrition" effect	Unknown
	TORCH	Specific therapy if available
Decreased bone mineral density	Possible substrate deficiency or altered vitamin D metabolism	Appropriate postnatal oral calcium and vitamin D intake

DIC, disseminated intravascular coagulation; PEEP, positive end-expiratory pressure; TORCH, toxoplasmosis, other (e.g., congenital syphilis and viruses), rubella, cytomegalovirus, and herpes simplex virus association.

When infants with obvious anomalies and syndromes and those born to mothers with severe illness or malnutrition are excluded, there still remains a heterogeneous population of infants who are SGA. These infants have a characteristic physical appearance: the heads look relatively large for their undergrown trunks and extremities, which seem wasted. The abdomen is scaphoid, misleading one to suspect a diaphragmatic hernia. The extremities have little subcutaneous tissue or fat, which is best exemplified by a reduced skinfold thickness . In addition, the skin appears to hang; it is rough, dry, and parchment-like; and it desquamates easily. Fingernails may be long, and the hands and feet of these infants tend to look too large for the rest of the body. The facial appearance suggests the look of a "wise old person," especially compared with that of premature infants . Cranial sutures may be widened or overriding; the anterior fontanel is larger than expected, representing diminished membranous bone formation. Similarly, epiphyseal ossification at the knee (chondral bone) is also retarded. Decreased bone mineralization may also be present. When meconium is passed in utero, there is often yellow-green staining of the nails, skin, and umbilical cord, which may also appear thinner than usual. Many of these infants

have subclinical chronic fetal hypoxia, which is detectable by cordocentesis or Doppler waveform velocimetry of the umbilical arteries.

Gestational age assessment of the infant who is SGA may result in misleading data when based on physical criteria alone. Vernix caseosa is frequently reduced or absent as a result of diminished skin perfusion during periods of fetal distress or because of depressed synthesis of estriol, which enhances vernix production. In the absence of this protective covering, the skin is continuously exposed to amniotic fluid and begins to desquamate after birth. Sole creases are determined in part by exposure to amniotic fluid and therefore appear more mature. Breast tissue formation also depends on peripheral blood flow and estriol levels and become markedly reduced in infants who are SGA. In addition, the female external genitalia appear less mature because of the absence of the perineal adipose tissue covering the labia. Ear cartilage, as noted in bone ossification, may also be diminished.

Neurologic examination for gestational age assessment may be affected less by IUGR than the physical criteria. Infants with IUGR achieve appropriate neurologic maturity functionally. Peripheral nerve conduction velocity and visual- or auditory-evoked responses correlate well with gestational age in normal neonates and are not impaired after IUGR. These aspects of neurologic maturity are not sensitive to deprivation, and occasionally maturity may even become accelerated. Determinants of active or passive tone and posture may be reliable in infants who are SGA, assuming that infants with significant central nervous system disorders (anomalies, asphyxia) and metabolic disorders (hypoglycemia) are excluded.

Specific organ maturity occurs despite diminished somatic growth. Cerebral cortical convolutions, renal glomeruli, and alveolar maturation all relate to gestational age and are not retarded with IUGR. As a result of stress in utero, these infants may occasionally accelerate the maturity of specific organ systems, such as the lung, thus explaining the low incidence of respiratory distress syndrome in preterm neonates who are SGA.

When examined in closer detail, infants who are SGA demonstrate specific behavioral characteristics that suggest, despite electric neurologic maturity, that functional central nervous system maturity may be impaired.[7] In the absence of significant central nervous system disease, these neonates demonstrate abnormal sleep cycles and diminished muscle tone, reflexes, activity, and excitability. This hypoexcitability suggests an adverse effect on polysynaptic reflex propagation and implies that central nervous system functional maturity does not necessarily proceed independently of the intrauterine events that result in IUGR.

Once stabilized and assigned a gestational age, the neonate who is SGA should be examined in more detail to direct the diagnostic workup as detailed in the following outline:

Dysmorphic features, “funny-looking” facies, and abnormal hands, feet, and palmar creases, in addition to gross anomalies, suggest congenital malformation syndromes, chromosomal defects, or teratogens. Ocular disorders, such as chorioretinitis, cataracts, glaucoma, and cloudy cornea, in addition to hepatosplenomegaly, jaundice, and a blueberry-muffin rash, suggest a congenital infection . The remaining infants constitute a heterogeneous group that represents most neonates who are SGA. Multiple gestations are the most recognizable cause in this category. TORCH infections resulting in extremely low birthweight are unusual in the absence of other clinical signs of congenital infection; however, a screening determination on cord blood for IgM values and a urine culture for cytomegalovirus may be indicated. Radiographic examination of the long bones, together with ultrasonography of the head, is diagnostically useful. Careful data related to the present and past reproductive history of the mother, in addition to ongoing neonatal management and close observation, are indicated in the remaining large number of neonates who are SGA whose underlying disorders may never be determined.

NEONATAL PROBLEMS

The perinatal mortality rate among infants who have IUGR is 10 to 20 times that among infants who are AGA. Intrauterine fetal death from chronic fetal hypoxia, immediate birth asphyxia, the multisystem disorders associated with asphyxia (hypoxic-ischemic encephalopathy, persistent fetal circulation, cardiomyopathy), and lethal congenital anomalies are the main contributing factors to the high mortality rate for fetuses and neonates who have IUGR. Problems due to prematurity such as respiratory distress syndrome are also more common with IUGR . Neurologic and other morbidities are also more frequent in infants who have IUGR; they have a rate 5 to 10 times that of infants who are AGA .

ASPHYXIA

Perinatal asphyxia and its sequelae constitute the most significant immediate problem of infants who have IUGR. As discussed, uterine contractions may add an additional hypoxic stress on the chronically hypoxic fetus with a marginally functioning placenta. The ensuing acute fetal hypoxia, acidosis, and cerebral depression may result in fetal death or neonatal asphyxia. IUGR accounts for a large proportion of stillborn infants. Myocardial infarction, amniotic fluid aspiration, and signs of cerebral hypoxia are noted in the stillborn infants with IUGR. With repeated episodes of fetal asphyxia or persistent hypoxemia, myocardial glycogen reserves are depleted, further limiting the fetal cardiopulmonary adaptation to hypoxia. If inadequate resuscitation occurs at birth and Apgar scores are low, the combination of intrapartum and neonatal asphyxia places the infant in double jeopardy for a continuum of central nervous system insult. The sequelae of perinatal asphyxia include multiple organ system dysfunction potentially characterized by hypoxic

ischemic encephalopathy, ischemic heart failure, meconium aspiration pneumonia, persistent fetal circulation, gastrointestinal perforation, and acute tubular necrosis. Concomitant with these sequelae, there may be metabolic derangements such as hypoglycemia. Hypocalcemia is partly caused by excessive phosphate release from damaged cells or acidosis; it is exacerbated by sodium bicarbonate and diminished calcium intake. Hypocalcemia does not occur more often with IUGR unless these problems are present. Meconium aspiration syndrome may complicate the clinical picture and further compromise respiratory function and oxygenation with the development of pneumonitis and pneumothorax.

NEONATAL METABOLISM

Fasting hypoglycemia develops in infants who are SGA more than in any other neonatal subgroup or category. The propensity for hypoglycemia is greatest during the first 3 days of life; however, some of these infants have ketotic hypoglycemia months later. Key to the occurrence of hypoglycemia is the diminished hepatic glycogen stores . Glycogenolysis constitutes the predominant source of glucose for the neonate during the immediate hours after birth. Later in the day, when glycogen stores become depleted, fasting glucose production results from the incorporation of lactate and gluconeogenic amino acid precursors into glucose. Infants who are SGA demonstrate an inability to increase blood glucose concentration after oral or intravenous administration of alanine, the key gluconeogenic amino acid.Hypoglycemic infants who are SGA have elevated alanine and lactate levels, suggesting that substrate availability is not rate limiting for gluconeogenesis and that the enzymes or cofactors are not active. Hypoglycemic infants probably have reduced hepatic glucose production. Nonhypoglycemic infants who are SGA do demonstrate rates of gluconeogenesis from alanine that are equivalent to the rates seen in nonhypoglycemic neonates who are AGA.

Immediately after birth, fasting infants who are SGA may have lower plasma-free fatty acid levels than normally grown infants. Fasting blood glucose levels in infants who are SGA directly correlate with free fatty acid and ketone body levels in plasma. In addition, infants who are SGA have deficient use of intravenous triglycerides. After the intravenous administration of triglyceride emulsion, infants who are SGA have high free fatty acid and triglyceride levels, but ketone body formation is attenuated. This suggests that use and oxidation of free fatty acids and triglycerides are diminished in neonates who are SGA. Free fatty acid oxidation is important because it spares peripheral tissue use of glucose, whereas hepatic oxidation of free fatty acids may contribute the reducing equivalents and energy required for hepatic gluconeogenesis. Deficient provision or oxidation of fatty acids may be partly responsible for the development of fasting hypoglycemia in these infants .

Endocrine alterations have also been implicated in the pathogenesis of hypoglycemia in infants who are SGA. Hyperinsulinemia or excessive sensitivity to insulin may be one factor. Catecholamine release is deficient in these neonates during periods of hypoglycemia. Although basal glucagon levels may be elevated, exogenous administration of glucagon fails to enhance glycemia. These data suggest an abnormality of counter-regulatory hormonal mechanisms during periods of neonatal hypoglycemia in infants who are SGA.

With improved standards of care and attempts at early enteral feeding or intravenous alimentation, fasting hypoglycemia in the neonate who is SGA is a less common event. Before the start of alimentation, careful monitoring with Dextrostix reagent strips for determining blood glucose values identifies infants with asymptomatic hypoglycemia. If whole-blood glucose concentrations decline to less than 45 mg/dL during the first 3 days in term infants or preterm infants and no untoward symptoms have occurred, early feeding or glucose infusion at 4 to 8 mg/kg per minute should begin. After this initial rate, the infusion should be titrated until blood glucose values achieve normal levels. If the hypoglycemia is symptomatic, particularly when seizure activity intervenes, an intravenous minibolus of 10% dextrose in water at 200 mg/kg should be given, followed by an infusion as just described. Infants at greatest risk of having hypoglycemia are those who have been asphyxiated and those who appear most undergrown according to the ponderal index .

Temperature Regulation

After the birth of an infant whose gestation was complicated by uteroplacental insufficiency, the neonate’s initial body temperature may be elevated. When placental function fails, the neonate’s heat-eliminating capacity also becomes deficient, resulting in fetal hyperthermia. On exposure to the cold environment of the delivery room, infants who are SGA can increase their heat production (oxygen consumption) appropriately because brown adipose tissue stores are not necessarily depleted as a result of IUGR.However, the infants’ core temperature drops if the cold stress continues, implying that heat loss has exceeded heat production. Heat loss in these infants is partly caused by the large body surface area exposed to cold and the deficiency of an insulating layer of subcutaneous adipose tissue stores. Indeed, magnetic resonance imaging detection of reduced fetal fat stores is highly suggestive of IUGR that may result in fetal distress. Infants who are SGA therefore have a narrower neutral thermal environment than term infants but a broader one than premature neonates. In infants who are SGA, hypoglycemia or hypoxia, or both, interfere with heat production and may contribute to thermal instability. In all infants, particularly those who are SGA, a neutral thermal environment should be sought to prevent excessive heat loss and to promote appropriate postnatal weight gain.

When nursed in a neutral thermal environment, infants who are SGA demonstrate the usual decline of the respiratory quotient after birth, representing a shift toward free fatty acid oxidation. During the first 12 hours after birth, basal oxygen consumption may be diminished in neonates who are SGA. Similar observations have been recorded in utero among fetal lambs that are spontaneously SGA, suggesting in both situations that there is a deficiency of potentially oxidizable substrates. Supporting this hypothesis is the marked increment of oxygen consumption that occurs in well-alimented infants who are SGA. This latter observation is also analogous to the rise of energy production after the nutritional rehabilitation of infants with marasmic-kwashiorkor. The increment of oxygen consumption after fetal or infantile malnutrition represents the energy cost of growth. Infants who are SGA usually have a significantly smaller postnatal weight loss because they are maturationally capable of achieving an adequate caloric intake earlier than premature neonates. Because of this enhanced caloric intake, infants who are SGA have a higher oxygen consumption than less mature neonates. Nutritional balance studies of premature infants who are SGA demonstrated an increase of fecal fat and protein loss, despite faster rates of growth compared with premature infants who are AGA. Energy storage was lower with IUGR, suggesting less fat deposition.

A subgroup of neonates who are SGA do not demonstrate an elevation of oxygen consumption after appropriate caloric intake. These infants have had low-profile intrauterine growth and may be considered to have had “primordial” fetal growth retardation. Their growth is set and fixed at a slower rate, and their eventual growth potential is reduced. The diminished body cell number in congenitally infected infants and in those with chromosomal disorders exemplifies primordial growth retardation in these neonates.

Hyperviscosity-Polycythemia Syndrome

The plasma volume immediately after birth of infants who are SGA averages 52 mL/kg, as compared with 43 mL/kg in infants who are AGA. Once equilibrated at 12 hours of life, the plasma volume becomes equivalent in the two groups. In addition to an enhanced plasma space, the circulating red blood cell mass is expanded. Fetal hypoxia and subsequent erythropoietin synthesis induce excessive red blood cell production.Alternatively, a placental-fetal transfusion during labor or periods of fetal asphyxia may result in a shift of placental blood to the fetus. Nonetheless, the elevation of the hematocrit level potentially increases blood viscosity, which interferes with vital tissue perfusion. The altered viscosity adversely affects neonatal hemodynamics and results in an abnormal cardiopulmonary and metabolic postnatal adaptation, producing hypoxia and hypoglycemia. These infants are at increased risk of having necrotizing enterocolitis. In the event that polycythemia is present (central hematocrit level greater than 65%) with such symptoms, appropriate therapy is

directed at correcting hypoxia and hypoglycemia, and a partial exchange transfusion to reduce blood viscosity and to improve tissue perfusion should be considered.

Other Problems

IUGR is associated with a slower than normal production of long-chain polyunsaturated fatty acids. Intestinal absorption of xylose is also attenuated. At birth, cord prealbumin and bone mineral content are low in term infants who are SGA. Thrombocytopenia, neutropenia, prolonged thrombin and partial thromboplastin times, and elevated fibrin degradation products are also problems among infants who are SGA. Sudden infant death syndrome may be more common after IUGR. Inguinal hernias also typically follow preterm IUGR.

FOLLOW-UP

When infants who are SGA and have serious congenital malformations or viral infections are excluded, the remaining neonates should benefit from optimal antenatal detection, very careful management of pregnancy, and avoidance of hypoxic fetal distress. In addition, with ideal neonatal intensive care, the morbidity and mortality rates for infants who are SGA should be reduced to a minimum, and postnatal developmental handicaps should be diminished. Nonetheless, these infants continue to contribute to the excessive fetal and neonatal morbidity and mortality rates. The neonatal mortality rate is much greater than that for term neonates and for weight-matched premature neonates. The incidence of fetal death remains higher for infants who are SGA. In addition to the etiologic events that lead to the development of IUGR, these infants have additional multisystem problems that further compromise survival and future growth or development. Among these fetuses, the perinatal mortality rate is 10 times that of infants who are AGA. The incidence of intrauterine fetal death is greatest among the most severely undergrown infants. Both antepartum and intrapartum events contribute to fetal death. Lethal congenital malformations and birth asphyxia are the two leading causes of death among neonates who are SGA. Infants with very low birthweight who are SGA (less than 1500 g) are at significant risk of reduced postnatal growth and development in addition to chronic neonatal sequelae such as bronchopulmonary dysplasia or retinopathy of prematurity.

Developmental Outcome

When infants with congenital infections and severe malformations are excluded, there remains a heterogenous group of undergrown neonates. Intellectual and neurologic functions in these remaining infants depend heavily on the presence or absence of adverse perinatal events, in addition to the specific cause of IUGR. Cerebral morbidity will be worsened by hypoxic-ischemic encephalopathy subsequent to birth asphyxia, and by the postnatal problems of hypoxia and hypoglycemia. Therefore, the prognosis must consider all the potentially adverse perinatal circumstances in addition to IUGR. When these perinatal problems are

minimal or are avoided, the neonate who is SGA may still demonstrate cerebral developmental problems, especially in the presence of relative head growth retardation. If term neonates who are AGA are used as a standard, term infants who are SGA demonstrate developmental problems when they are examined at follow-up at ages 2 and 5 years and into adult years. Even when compared with premature neonates, term infants who are SGA continue to have developmental disadvantages. Follow-up of these infants reveals little difference in intelligence quotient or neurologic sequelae; however, their school performance is poor, partly because of behavioral, visuospatial, visuomotor, and learning disorders. Preterm infants who are SGA may have an even greater percentage of abnormal neurodevelopmental outcomes than term neonates who are SGA. Those infants who were SGA early, demonstrating decreased growth of the biparietal diameter before 26 weeks' gestation, and those with symmetric growth retardation have diminished developmental quotients in infancy. However, some follow-up observations in both term and preterm neonates who are SGA are favorable: these neonates compare well with their counterparts who are AGA. Cerebral palsy is uncommon after uncomplicated IUGR. Infants who are SGA are a heterogeneous group, and the populations investigated may vary in the severity of neurodevelopmental handicap; similarly, antenatal detection and perinatal management varies among high-risk centers. It therefore appears that these latter favorable reports may represent the outcome after optimal obstetric management and neonatal care. Adults who were SGA tend to have a normal IQ, but they demonstrate school difficulties, and fewer become professionals. Despite this, they report to be well adjusted and socially satisfied with their lives.

Another major determining influence on neonatal neurodevelopmental outcome in infants who are SGA is the family's socioeconomic status. Parent educational background, place of rearing, and environmental conditions all have a strong effect on outcome. Infants who are SGA born to families of higher socioeconomic status demonstrated little developmental difference on follow-up, whereas those born to poorer families had significant developmental handicaps . In addition, neurodevelopmental outcome is favorably influenced by breastfeeding.

Growth

Postnatal growth after IUGR depends in part on the cause of the growth retardation, the postnatal nutritional intake, and the social environment.Although birthweight correlates best to maternal weight, postnatal growth is related to both maternal and paternal growth characteristics. Neonates who are SGA who have primordial growth retardation related to congenital viral, chromosomal, or constitutional syndromes remain small throughout life. Those infants whose intrauterine growth was inhibited late in gestation because of uterine constraint,

placental insufficiency, or nutritional deficits will have catch-up growth after birth and approach their inherited growth potential when provided with an optimal environment. Those infants with a low ponderal index or asymmetric growth retardation have an accelerated growth phase once adequate postnatal caloric intake has been established, which suggests release of an in utero constraining factor after birth. Catch-up growth occurs in about 90% of SGA infants; it occurs usually by 2 years of age and is most likely to occur in infants who have normal birth length despite being SGA.Despite the catch-up period, some of these infants remain smaller than appropriately grown neonates , especially those who had the onset of growth retardation before 26 weeks. Growth hormone therapy in higher than usual doses for primordial IUGR and for IUGR of unknown cause has produced growth acceleration. Some infants with IUGR demonstrate abnormal postnatal growth hormone physiology, suggestive of growth hormone resistance at the receptor or IGF signal transduction pathways.

VI. Plan and organizational structure of classes.

№ п/п	Basic stages of classes, it function and maintenance	Educational aims are in the levels of mastering	Methods of control and studies	Educational materials	Distributing of time in minutes
1	Preparatory stage Organizational measures				3 min.
2	Raising of educational aims and motivation	α2		П. II «Educational aims» П. I «Actuality of theme»	12 min. 20 min.
3	Control of basic knowledges and skills level: 1.Ethiology of intrauterine growth retardation and preterm birth 2.The features of adaptational period in premature newborn children 3. Key links of intrauterine growth retardation and hyperbilirubinemia. 4. Classification	α2 α2	Individual l questioning Test control of the second level Individual questioning Individual oral questioning Typical situational task of 2 level Typical situational task of 2 level Typical situational	Second level tests Second level tests Typical situational task Typical situational task Second level tests Typical situational task	

	of intrauterine growth retardation and preterm birth 5. Clinical signs of dysadaptation period. 6. Stages of nursing for new-born children with intrauterine growth retarda-tion and hyper-bilirubinemia. 7. To establish the neurologic status of newborn children . 8.Complications of oxygenation. 9. Stages of nur-sing and treatment for premature newborn children	 α2 α2	task of 2 level Test control of 2 level Typical situational task of 2 level	 Typical situational task Second level tests Kit of medicines.	
4	Basic stage of professional skills and abilities forming: 1.To conduct the patient‘s mana-gement with intrauterine growth retarda-tion and prema-ture newborn children , to take complaints and anamnesis. 2. To conduct the patient;s exami-nation, to detect main symptoms and syndromes. 3.To formulate and substantiate the preliminary diagnosis 4.To compose the plan of patient laboratory and	 α3 α3 α3 α3	 Practical professional training Practical professional training Practical professional training Practical professional training. Tests control. Practical professional training.Tests and the third level control. Third level test control. The practical	 Patient Case history A reference chart for forming of professional abilities. Case history. A reference chart for forming of professional abilities. Situatioonal typical tasks of 3 level. The third level tests. Prescribing chart Situatio-onal typical tasks of 3 level.Third level tests. First aid algorythm for premature children.	115 min.

	instrumental investigation. 5. To interpret the results of laboratory and instrumental investigation. 6. To conduct differential diagnosis among clinical conditions accompaied by hyperbilirubinemia, respiratory distress syndrome, hypoglycemia. 7.To give the recommendations for regimen and diet for premature children depnding on degree of maturation of newborn and concomitant disease. 8. To compose the plan for premature children treatment taking into account the stage of disease and the presence of complications. 9.To be able to render the first aid in extreme situations	α3 α3 α3 α3	professional training is on solving of non standard clinical situations. The third level test control.Practical professional training. Third level test control. The third level test control. The practical professional training on salving of non typical clinical situations. Practical professional training on salving of non typical clinical situations.	The third level non typical situational tasks. First aid algorythm for premature children. The third level non typical situational tasks. The third level non typical situational tasks. The third level non typical situational tasks.	
5 6 7	Concluding stage. Control and correction of professional abilities and skills. Working out the totals of class. Home work (basic and additional literature on the topic)		Analysis of clinical work Solution of non typical tasks and the third level tests. Estimation of clinical work	Clinical work The third level non typical situational tasks. A reference chart for independent work with literature	30 min.

Methodical materials for the class basic stage supporting

The questions for the control of primary knowledge level of abilities and skills:

1. What are the main meternal factors of preterm birth?
2. The birth-weight classification of infants.
3. What are the features of respiratory system in preterm infants?
4. What are the features of temperature regulation in preterm infants?
5. What are the features of circulatory systems?
6. What are the main maternal and placental factors of intrauterine growth retardation?
7. What are the main types of intrauterine growth retardation?
8. To explain the Ballard Score.
9. To explain the method of feeding for LBW infant.
10. When should we use total perenteral nutrition for preterm infants?
11. What kind of prevention of infection for preterm infants do you know?
12. To explain the incubator care for preterm infants.

Primary tests

1. Preterm birth is
   A. less than 35 weeks
   B. less than 36 weeks
   C. less than 37 weeks
   D. less than 38 weeks
   E. less than 39 weeks

2. Normal birth weight is
   A. 4000 and more
   B**.** 2500-3999
   C. less than 2500
   D. less than 1500
   E. 1500-2500

3. The maternal factors of preterm birth
   A. maternal anemia
   B. maternal infections
   C. incompetence of cervix
   D. complications of pregnancy
   E**.** all listed above

4. The maternal causes of low birth weight:
   A. short stature of mother
   B. young mother
   C. smoking

D. prime of grand multipara
E. all listed above

5. The environmental causes of low birth weight:
A. racial
B. social status
C. nutritaional
D. geographic
E. all listed above

6. Problems of IUGR infants:
A. hypoxia
B. Meconium aspiration
C.hypotermia
D. large brain
E. all listed above

7. What are the most informative criteria of gestational age estimation after birth of child?
A. Locating of umbilical ring.
B. Interrelation between the child's body weight and height .
C. The sum of points after Dubovitz (or Ballard)score.
D. Child's weight.
E. Presence of nail plates.

8. Treatment principles of intrauterine growth retardation:
A. insulintherapy
B. antibiotic therapy
C. correction breast feeding
D. correction the function of gastrointestinal tract
E. all listed above

9. Physiological loss of body weight in infant with very low birth weight:
A. less than 2 %
B. more than 15 %
C. 10-15 %
D. 16-20 %
E. 30 %

10. Quantity of milk for premature infant with weight 2000 on 4 day of life is:
A. 200ml
B. 280ml
C. 360ml
D. 380ml
E.400 ml

11. How do you count the quantity of milk for premature infant during 10 days
A. 1/5 body weight

B. 120 kcal/kg
C. Romel's formula
D. Phinkelshtain's formula
E. all listed above

12. In the case of the 2 stage of prematurety the breast feeding start:
A. at once
B. in 2 h
C. in 3 h
D**.** in 9 h
E. in 24 h

13. Principles of feeding for 33 weeks age infants
A. nipple
B. stomach pump
C. spoon
D. breast feeding
E. syringe

14. Choose uncharacteristic syndrome for IUGR infants
A**.** meconeum aspiration
B. polycythemia
C. development delay
D. spastic syndrome
E. microcephaly

15. What is the medical treatment in the case of IUGR of the 3 degree
A. retabolil
B. fencarol
C. diazepam
D. aminocapronic acid
E. dratoverin

16. The neurologic features for preterm infants:
A. muscular hypotonia
B. poor neonatal reflexes
C. square window wrist 45-90
D.hypoglecimia
E**.**all listed above

17. The medical factors of preterm birth:
A. severe cardiac illness in the mother
B. placental dysfunction
C. isoimmunization
D. uncontrolled diabetes mellitus
E. all listed above

18. Choose predisposing factor for IUGR:

A. history of still birth
B. history of smoking
C. bleeding during the pregnancy
D. kidney disease
E. all listed above

19. Severe hypothermia leads to:
A. cold injury
B. spasms
C.acidosis
D. hypoxia
E. all listed above

20. Placental factors of IUGR:
A.implantation of placenta
B. abruption placenta
C. extensive placenta infarcts
D. single umbilical artery
E. all listed above

Answers: 1-C,2- B, 3-E, 4-E, 5-E, 6-E, 7-C, 8-C,D, 9-C, 10-B, 11-C, 12-D, 13-B, 14-A, 15-A, 16-E, 17-E, 18-E, 19-A, 20-E.

Typical situational tasks of 2 level

1. The nurse from the level II neonatal intensive care nursery calls you to evaluate a baby. The infant, born at 32 weeks' gestation, is now 1 week old and had been doing well on increasing nasogastric feedings. This afternoon, however, the nurse noted that the infant has vomitted the last two feedings and seems less active. Your examination reveals a tense and distended abdomen with decreased bowel sounds. As you are evaluating the child, he has a grossly bloody stool. Your management of this infant should include

a. Surgical consultation for an emergent exploratory laparotomy
b. Continued feeding of the infant, as gastroenteritis is usually self-limited
c. Stool culture to identify the etiology of the bloody diarrhea and an infectious diseases consultation
d. Stopping feeds, beginning intravenous fluids, ordering serial abdominal films, and initiating systemic antibiotics
e. Upper GI series and barium enema to evaluate for obstruction

2. A recovering premature infant who weighs 950 g (2 lb, 1 oz) is fed breast milk to provide 120 cal/(kg_d). Over ensuing weeks, the baby is most apt to develop

a. Hypernatremia
b. Hypocalcemia
c. Blood in the stool
d. Hyperphosphatemia
e. Vitamin D toxicity

3. An infant weighing 1400 g (3 lb) is born at 32 weeks' gestation in a delivery room that has an ambient temperature of 24□ C (75□ F). If left in an open crib for a few minutes, this child is likely to demonstrate
a. Ruddy complexion
b. Shivering
c. Hypertension
d. Increased respiratory rate
e. Metabolic alkalosis

4. Two infants are born at 36 weeks' gestation. Infant A weighs 2600 g (5 lb, 12 oz) and infant B weighs 1600 g (3 lb, 8 oz). Infant B is more likely to have which of the following problems?
a. Congenital malformations
b. Low hematocrit
c. Hyperglycemia
d. Surfactant deficiency
e. Rapid catch-up growth retardation

5. A 3-day-old infant born at 32 weeks' gestation and weighing 1700 g (3 lb, 12 oz) has three episodes of apnea, each lasting 20 to 25 s and occurring after a feeding. During these episodes, the heart rate drops from 140 to 100 beats per min, and the child remains motionless; between episodes, however, the child displays normal activity. Blood sugar is 50 mg/dL and serum calcium is normal. The child's apneic periods most likely are
a. Due to an immature respiratory center
b. A part of periodic breathing
c. Secondary to hypoglycemia
d. Manifestations of seizures
e. Evidence of underlying pulmonary disease

6. After an uneventful labor and delivery, an infant is born at 32 weeks' gestation weighing 1500 g (3 lb, 5 oz). Respiratory difficulty develops immediately after birth and increases in intensity thereafter. The child's mother (now gravida 3, para 2102) previously lost an infant because of hyaline membrane disease. At 6 h of age, the child's respiratory rate is 60 breaths per min. Examination reveals grunting, intercostal retraction, nasal flaring, and marked cyanosis in room air. Physiologic abnormalities compatible with these data include
a. Decreased lung compliance, reduced lung volume, left-to-right shunt of blood
b. Decreased lung compliance, reduced lung volume, right-to-left shunt of blood
c. Decreased lung compliance, increased lung volume, left-to-right shunt of blood
d. Normal lung compliance, reduced lung volume, left-to-right shunt of blood
e. Normal lung compliance, increased lung volume, right-to-left shunt of blood

7. In a child, delivered with weight of 1800 g, in term of 34 w,. from a woman with an extragenital pathology, the hestosis of pregnancy second half-fault, in age of 5 days the icteric of skin appeared, signs of CNS depression, in neurosonography the

signs of periventricular hemorrhage detected. What most probably could promote to it development?

A. Hestosis
B.Extragenital pathology of mother
C. Infection of mother
D. Bilirubin encepyalopathy.
E. All listed above

8. An infant is born at 36 weeks' gestation weighing 1800 g (3 lb, 5 oz). What are the most informative criteria of gestational age estimation after birth of child?

a. Locating of umbilical ring.
b. Interrelation between the child's body weight and height .
c. The sum of points after Dubovitz (or Ballard)score.
d. Child's weight.
e. Presence of nail plates.

9. A preterm newborn infant is havingpoor neonatal reflexes, uncoordinated sucking, swallowing, difficulties in feeding. The most important next step to quickly establish the diagnosis is

a. Echocardiogram
b. Ultrosonography
c. Passage of catheter into nose
d. Hemoglobin electrophoresis
e. Bronchoscopic evaluation of palate and larynx

10. An infant born at 35 weeks' gestation to a mother with intrauterine infections. This baby is proportionately smaller in all parameters including the head size. What is the type of intrauterine growt retardation?

a.hypoplastic
b.mixed
c.mainourished
d. macrosomia
e. term infant

Standard of answer

1. The answer is d. The infant presented in the question has necrotizing enterocolitis (NEC), a potentially life-threatening disease of the neonate. It is more common in premature infants, but has been described in term infants as well. Although several organisms have been isolated from NEC patients, no clear cause for this condition has been identified.

Patients present with feeding intolerance and a distended abdomen.

About a quarter have grossly bloody stool. Pneumatosis intestinalis is found on plain radiograph of the abdomen and is diagnostic for NEC in this age group. Management depends initially on perforation; if there is no evidence of free peritoneal air, the infant should be put on bowel rest with nasogastric decompression, and systemic antibiotics are initiated. Electrolytes and vital signs should be monitored closely, and

serial abdominal films should be performed to evaluate for perforation. If free air is identified on plain radiographs or if the infant clinically worsens with medical management, surgical consultation is required. An exploratory laparotomy is usually performed, and any necrotic gut is removed. Occasionally, removal of necrotic gut will result in an infant without adequate intestinal surface area to absorb nutrition, a condition known as short bowel syndrome.

2. The answer is b. It is usually impossible with any combination of parenteral and enteral nutrition to match what the infant would have accumulated in utero. The average, healthy, low-birth-weight infant of this size requires a daily intake of calcium of about 200 mg/kg. Breast milk has much less calcium (and phosphorus) than do commercial formulas. The breast milk can be supplemented with calcium, or it can be mixed with commercial formulas designed for the premature infant. Breast milk promotes gut maturation and prevents intestinal atrophy induced by lack of enteral feeding. Breast milk, however, is likely to have insufficient calcium and phosphorus for catch-up growth.

3. The answer is d. A room temperature of 24□ C (approximately 75□ F) provides a cold environment for newborn infants. Aside from the fact that these infants emerge from a warm, 37.6□ C (99.5□ F) intrauterine environment, at birth, infants (and especially preterm infants) are wet, have a relatively large surface area for their weight, and have little subcutaneous fat. Within minutes of delivery, the infants are likely to become pale or blue and their body temperatures will drop. In order to bring body temperature back to normal, they must increase their metabolic rate; ventilation, in turn, must increase proportionally to ensure an adequate oxygen supply. Because a preterm infant is likely to have respiratory problems and be unable to oxygenate adequately, lactate can accumulate and lead to a metabolic acidosis. Infants rarely shiver in response to a need to increase heat production.

4. The answer is a. Small-for-dates infants are subject to a different set of complications than preterm infants whose size is appropriate for gestational age. The small-for-dates infants have a higher incidence of major congenital anomalies and are at increased risk for future growth retardation, especially if length and head circumference as well as weight are small for gestational age. Also more common are neonatal asphyxia and the meconium aspiration syndrome, which can lead to pneumothorax, pneumomediastinum, or pulmonary hemorrhage. These, rather than hyaline membrane disease, are the major pulmonary problems in these infants. Because neonatal symptomatic hypoglycemia is more commonly found in small-for-dates infants, careful blood glucose monitoring and early feeding are appropriate precautions. Normal or elevated hematocrit is also more common in these infants.

5. The answer is a. Apneic episodes are characterized by an absence of respirations for more than 20 s and may be accompanied by bradycardia and cyanosis. A large number of conditions can cause apnea.
Periods of apnea are generally thought to be secondary to an incompletely developed respiratory center, particularly when they are seen, as is common, associated with

prematurity. Although seizures, hypoglycemia, and pulmonary disease accompanied by hypoxia can lead to apnea, these causes are less likely in the infant described, given that no unusual movements occur during the apneic spells, that the blood sugar level is more than 40 mg/dL, and that the child appears well between episodes. Periodic breathing, a common pattern of respiration in low-birth-weight babies, is characterized by recurrent breathing pauses of 3 to 10 s.

6. The answer is b. For the child described in the question, prematurity and the clinical picture presented make the diagnosis of hyaline membrane disease (infant respiratory distress syndrome) likely. In this disease, lung compliance is reduced; lung volume also is reduced, and a significant right-to-left shunt of blood can occur. Some of the shunt can result from a patent ductus arteriosus or foramen ovale, and some can be due to shunting in the lung. Minute ventilation is higher than normal, and affected infants must work harder in order to sustain adequate breathing.

7. The answer is e. Causes of preterm birth : maternal factors (medical disease during pregnancy, anemia, infections), placental factors (placenta previa, polyhydramniosis) , uterine factors (bicorneal uterus), fetal factors, medical factors.

8. The answer is c. The sum of points after Dubovitz (or Ballard)score(posture, square window wrist, arm recoil, popliteal angle,scarf sign, heel to ear, skin, lanugo, plantar surface, breast, eye, genitals)

9. The answer is b. Ultrasonography is suspected if the biparietal diameter is less than 8,5 sm at 37 weeks of gestation.

10. The answer is a. Mainourished small-for-date infants appear alert, cry lustily and have more hair. They are long and thin and usually yellow or meconium stained. Back of hands and feet appear wrinkled. Hypoplastic-these babies are proportionately smaller in all parameters including the head size. Mixed group physical characteristics of the two groups described above may be present to a variable degree.

Metodical materials for the class basic stage supporting

A professional algorythm of patients management implementation (reference chart) for the practical skills and abilities forming .

№	Task	Sequence of implementation	Remarks and warnings related to self-control
1	To conduct patient examination for preterm infants, small for gestational age infants, hyperbilirubinemia.	1. To conduct complaints and disease's anamnesis taking. 2. To take thoroughly the patient's life anamnesis.	Pay attention to the features of disease course , underlying factors, newborn, concomitant diseases etc. To establish the risk factors presence are facilitates of disease occurrence.

		3. To conduct examination of the patient. 4. To investigate cardiovascular and nervous system of the patient (palpation, percussion).	To assess patient's general condition, stage of prematurety, position in bed, color and humidity of skin and mocouse, presence of neck veins and extermities swelling. To pay regard to pulse rhythm, it tension and size on both hands, apex shove, its properties, margins of absolute and relative cardiac dullness, its changes, HR(tachi-or bradicardia, extrasystole),BP.
		5. To conduct heart and main vessels auscultation. 6. To investigate the pulmonary system (percussion, bronchophony). 7. To conduct lungs auscultation. 8. To investigate the system of digestion.	To pay regard to heart tones weakening or amplifying, appearance of murmurs and additional III, IV tones. To pay attention to features of percussion and auscultation in children of different age. Tro pay attention to features of intoxication
2	To formulate the preliminary diagnosis.	1.To formulate the preliminary diagnosis 2. To substantiate all the components of prelimi-nary diagnosis taking as a basis complaints, anamnesis, and examinations.	Basing on modern classification formulate the preliminary diagnosis of prematurety and to subtantiate each component of it.
3	To evaluate the parameters of additional laboratory investigations.	1. To evaluate the blood count data. 2. To evaluate the biochemistry data. 3.To evaluate the intrauterine infections data.	To pay attenttion to the signs of anemia, leucocytosis, changing of formula, elevation of sedimentation rate. To pay attention to the specific IG levels. To pay attention to the

			etiology of intrauterine infections and their sensitivity to the antibiotics and antiviral agents.
4	To undersrtand the data of additional and laboratory investigation.	To undersrtand the data of X-ray of thorax, ultrasonogram.	To pay special attention to the damage of brain, lungs and hepar.
5.	To conduct differential diagnosis.	1.Consistently to find the common signs in complaints, life and disease anamnesis, data of examination, data of laboratory and instrumental investiagtions in patient's and in similar states. 2.To find differences between complaints, information of life and disease anamnesis, examination data, information about the laboratory and instrumental methods of research and in similar nosology. 3. On the basis of the differences found to exclude similar diseases from the list of possible diagnoses. 4. To conduct differential diagnostics according to the above mentioned algorithm among all the nosologies having the similar signs, among prematurity, immaturity . 5. Taking into account the impossibility to exclude the diagnosis of prematurety and intrauterine growth retardation from the list of credible diagnoses to draw a conclusion about the probability of such a	Special attention must be paid to differential diagnosis among the types of intrauterine growth retardation, neonatal hypotrophy, birth trauma.

		diagnosis.	
6	To formulate the final clininical diagnosis.	1. To formulate the final clininical diagnosis 2. Taking the preliminary diagnosis, as a basis additional investtigations data, conducted differential diagnosis, substantiate all the elements of the final clininical diagnosis.	Basing on modern classification of thyroid diseases, formulate the diagnosis, complications of disease and the presence of concomitant diseases.
7	To pescribe reatment for patients.	1.To prescribe non medicinal treatment 2.To prescribe medicinal treatment.	Expressly specify the regimen and detalized diet according to a disease. Taking into account the age, severity of patient's state, the stage of disease, the presence of complications and concomitant pathology, prescribe modern medicinal treatment .

The material for the control of the secondary level of abilities and skills:

Secondary tests

1. Birth-weight in the case of macrosomia is
   A. 5000 gm or more
   B**.** 4000 gm or more
   C. 3000 gm or more
   D.less then 2 500 gm
   E. 2500-3999 gm

2. A 4-week-old infant born at 28 weeks' gestation has been feeding well but has failed to regain her birthweight while receiving a cow milk-based formula. The neonatologist suggests placing the infant on a hydrolysate formula that contains medium-chain triglycerides.

Of the following, the BEST explanation for this recommendation is that the infant has
   A. caloric insufficiency
   B. essential fatty acid deficiency
   C. fat malabsorption
   D. lactose intolerance
   E. milk protein allergy

3. The solute content of infant formulas for preterm newborns differs from that for term newborns. The solute composition of infant formulas for preterm infants compared with formulas for term infants has

A. higher osmolality
B. lower calcium content
C. lower potassium content
D. similar phosphorus content
E. similar sodium content

4. A 750-g newborn is admitted to the neonatal intensive care unit. He is receiving mechanical ventilation, intravenous fluids, and antibiotic therapy. You are asked to counsel his mother, who is anxious to breastfeed her infant.
Of the following, the MOST accurate statement about breastfeeding of a preterm infant is that

A. measurement of gastric content following a feeding provides an accurate measure of human milk intake
B. milk production of approximately 360 mL/d is a measure of successful lactation
C. nutrient composition of human milk is ideal for the nutritional needs of the preterm infant
D. risk of necrotizing enterocolitis is reduced in preterm infants fed partially or exclusively human milk
E. stress reduction interventions of acupuncture and hypnosis promote lactation

5. A 3-week-old preterm neonate, who has been receiving full enteral nutrition, develops abdominal distension, feeding residuals, and bloody stools. Physical examination reveals abdominal tenderness, hypothermia, apnea, and lethargy. An abdominal radiograph is obtained.Of the following, the radiographic finding MOST specific for the diagnosis of necrotizing enterocolitis is

A. abdominal calcification
B. bowel wall thickening
C. distended bowel loops
D. intramural gas
E. intraperitoneal fluid

6. You are caring for a 5-week-old preterm infant who was born at 31 weeks' gestation and had an uncomplicated neonatal course. He is exclusively breastfed, and his weight gain has plateaued over the past 2 weeks. He has been afebrile and well-appearing, but he is somewhat less vigorous over the past week. You are considering the need to screen him for physiologic anemia of infancy. Of the following, the MOST accurate statement about physiologic anemia of infancy is that

A. breastfed infants are protected from physiologic anemia of the newborn
B. erythropoietin levels should be monitored to predict the timing of the physiologic nadir in hemoglobin concentration in preterm infants
C. the hemoglobin concentration at birth does not correlate with the time of onset of physiologic anemia

D. the physiologic nadir in hemoglobin concentration for preterm infants is less pronounced than that in term infants

E. the physiologic nadir in hemoglobin concentration for preterm infants occurs 2 to 4 weeks earlier than in term infants

7. A preterm newborn, one of twins, is plethoric and has a central venous hematocrit of 72% (0.72).
Of the following, the MOST likely complication in this infant is

A. disseminated coagulopathy
B. hypoglycemia
C. necrotizing enterocolitis
D. renal failure
E. seizures

8. You are evaluating a 4-week-old formula-fed infant who was born at 30 weeks' gestation and weighed 1,200 g. The infant is feeding well and gaining weight appropriately. You obtain a screening hemoglobin value, which is 11.5 g/dL (115 g/L). Of the following, the MOST appropriate interpretation of this laboratory result is that the infant

A. has a normal hemoglobin value
B. requires iron supplementation
C. should be evaluated for allergic colitis
D. should be evaluated for vitamin E deficiency
E. should have further testing to rule out hemolytic disease

9. A preterm neonate has tachypnea, expiratory grunting, nasal flaring, subcostal retractions, and cyanosis shortly after birth. The mother had rupture of membranes 36 hours prior to vaginal delivery and has developed uterine tenderness and fever.
Of the following, the MOST likely chest radiographic finding in this infant is

A. diffuse reticulogranular pattern
B. displacement of the mediastinum
C. fine curvilinear lucencies
D. overinflation with coarse densities
E. prominent perihilar streaking

10. A newborn is delivered at 32 weeks' gestation by emergent cesarean section following spontaneous placental abruption. During resuscitation in the delivery room, the infant receives 100% oxygen and positive pressure ventilation through an endotracheal tube at a rate of 60 breaths/min. She has adequate chest excursions, but remains poorly perfused. Auscultation reveals a heart rate of 54 beats/min.
Of the following, the MOST appropriate next step in resuscitation is to

A. administer a bolus of albumin
B. administer intratracheal epinephrine
C. begin chest compressions
D. infuse intravenous sodium bicarbonate
E. inject intramuscular naloxone hydrochloride

11. A 1-week-old 2,000-g preterm infant required ventilation for 3 days for respiratory distress syndrome, then was weaned to oxygen hood. He is receiving total parenteral nutrition for feeding intolerance plus small volumes of human milk via a nasogastric tube. Initially, he was treated with 72 hours of intravenous ampicillin and gentamicin for maternal prolonged rupture of membranes Abruptly, he has developed hypotonia, apnea, bradycardia, and lethargy and is reintubated emergently. The serum bicarbonate level is 18 mEq/L (18 mmol/L), but sodium, potassium, chloride, glucose, creatinine, and blood urea nitrogen concentrations are normal. Head ultrasonography at this time shows no evidence of intracranial hemorrhage. Lumbar puncture demonstrates 3 white blood cells/mm^3, negative Gram stain, protein of 30 mg/dL (300 g/L), and glucose of 50 mg/dL (2.8 mmol/L).
Of the following, the MOST likely cause of the patient's symptoms is

A. apnea of prematurity
B. carnitine deficiency
C. epidural hematoma
D. hypermagnesemia
E. Listeria meningitis

12. You are caring for a 2-month-old infant who was born at 30 weeks' gestation and weighed 1,000 g at birth. At 2 weeks after birth, the infant developed severe necrotizing enterocolitis and underwent a resection of the ileum and ileocecal valve. She is estimated to have approximately 70 cm of remaining jejunum connected to a stoma. Most of the colon remains, but it is not in continuity with the small intestine. The infant has been maintained exclusively on parenteral nutrition, but you are planning to transition her to enteral feedings. Of the following, a TRUE statement about feeding this child who has short bowel syndrome is that

A. a stool-reducing substance of 1% or greater suggests good tolerance of enteral feedings
B. bolus feedings are preferred over continuous feedings
C. cow milk protein formulas are preferred because of their decreased osmolarity
D. rectal bleeding in this patient suggests intolerance of enteral feeding
E. small bowel bacterial overgrowth is a frequent cause of feeding intolerance

13. During resuscitation of a 1.5-kg preterm newborn who has apnea, you notice that inflation pressures of 15 to 20 cm H2O for the first three breaths do not result in good chest wall excursion, and the infant's color remains poor. The heart rate is 90 beats/min. Of the following, the BEST next course of action is

A. administration of intravenous epinephrine
B. administration of intravenous naloxone
C. chest compressions
D. endotracheal intubation
E. increase in inflation pressure

14. A 975-g preterm infant develops a nosocomial infection with coagulase-negative staphylococci. Of the following, the MOST likely predisposing risk factor for this infection is

A. endotracheal intubation
B. enteral feedings
C. nasogastric tube
D. previous antibiotic therapy
E. umbilical catheterization

15. A 15-year-old primigravid woman presents to the labor and delivery area at 34 weeks' gestation and reports that her membranes ruptured 4 days ago. She has rare uterine contractions, only fingertip cervical dilation, and no history of fever. There is no fetal heart rate evidence of distress. Her physician starts oxytocin induction. Ten hours later, she delivers a 3.0-kg female infant whose Apgar scores are 6 at 1 minute and 9 at 5 minutes.
Of the following, the MOST important risk factor for infection is this infant's
A. female gender
B. mother's age
C. 1-minute Apgar score
D. premature rupture of membranes
E. preterm gestation

16. You are called to the newborn nursery to evaluate a 1-day-old baby who is irritable, tremulous, and has been feeding poorly. On physical examination, you note that the term baby weighs 2,200 g (<5th percentile), and her head circumference is 31 cm (<5th percentile). She is hirsute, has fifth finger clinodactyly, and has hypoplastic nails on her hands and feet. Her facial features are swollen, and her eyelids are edematous due to face presentation at delivery.
Of the following, the baby's features are MOST likely due to prenatal exposure to
A. alcohol
B. lithium
C. retinoic acid
D. tobacco
E. valproic acid

17. A newborn delivered at 34 weeks' gestation has excessive oral secretions and choking spells. The maternal history is notable for polyhydramnios. The infant's abdomen is somewhat distended and tympanitic.
Of the following, the BEST procedure to evaluate this infant's symptoms is
A. attempt to pass a catheter through the posterior nose
B. attempt to pass a nasogastric tube into the stomach
C. barium swallow
D. fiberoptic endoscopy
E. transillumination of the chest

18. Very low birth weight is
A. less than 2500
B. les than 2000
C.less than 1500

D. less than 1000
E. less than 900

19. A preterm black male infant was found to be jaundiced 12 h after birth. At 36 h of age, his serum bilirubin was 220 mmol/L, hemoglobin concentrationwas 125 g/L, and reticulocyte count 9%. Many nucleated red cells and some spherocytes were seen in the peripheral blood smear. The differential diagnosis should include which of the following?

A. Pyruvate kinase deficiency
B. Hereditary spherocytosis
C. Sickle cell anemia
D. Rh incompatibility
E. Polycythemia

20. Post term infants are

A. 37 weeks and more
B. 38 weeks and more
C. 39 weeks and more
D. 40 weeks and more
E. 42 weeks and more

Answers : 1-B, 2-C, 3-B, 4-C, 5-C, 6-, 7-C, 8-A, 9-E, 10-C, 11-E, 12-D,13-E, 14-A, 15-E, 16-A, 17-B, 18-C, 19-B, 20-E

Materials of the medical support for the students independent training: a reference chart for organization of students independent work with educational literature.

Tasks	Instructions
To study the etiology of intrauterine growth retardation and preterm birth. Be able to detect the degrees of preterm birth.	To select the key links of intrauterine growth retardation and preterm birth.
To study anatomic and physiologic features of premature children ; the features of adaptational period in premature newborn children	To establish the symptoms and gather it to clinical syndromes of premature newborn children
To study the additional methods of research (laboratory, instrumental)	To work out a plan of patient examination.
To conduct differential diagnostics, to establish a final diagnosis	To substantiate the basic components of diagnosis in accordance with modern classification, and to conduct a differential diagnosis.
To prescribe the individual holiatry to	To make the prescribing chart speci-

patient with the intrauterine growth retardation and preterm birth. Principles of feeding Able to render the first aid in the case of hypoglycemia, respiratory failure, enteroparesis, hyperbilirubinemia.	fying the regimen, diet, medicinal treatment, taking into account the age, severity of patient's state, stage of disease, presence of complications and concomitant diseases.

Basic literature:

1.Nelson Textbook of Pediatrics, ed 16.2000.

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4.Аряєв М.Л. Неонатологія . Київ, «Адеф-Україна», 2003. – С. 515-550.

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6.Госпітальна педіатрія / за ред. І.С.Сміяна, В.Г. Майданика - Тернопіль-Київ, 1997. - С. 4-75.

Additional literature:

1.Шабалов Н.П. Неонатология. Т.П. - Санкт-Петербург, «Специальная Литература»., 1997. - U.110-123., 65-81.

2. Неонатология:Руководство / под ред. В.В. Гаврюшова, К.А.Сотниковой'. - Л. Медицина, 19а5. - С. 112-124.

3. Неонатология:Пер.с англ./Под ред.Т.Л.Гомелла, М.Д.Каннигам.- М.:Медицина,1995. - С.328-350.

Theme: **ASPHYXIA**.

Etiology, pathogenesis of asphyxia in newborn period. Classification of asphyxia, clinical presentation, diagnostics, differential diagnostics, treatment, prophylaxis. Emergency in asphyxia in newborn period.
Neonatal Resuscitation. Prognosis.

Amount of educational hours – 4 academic hours.

I. ACTUALITY OF THEME

The knowledge of asphyxia manifestations in neonates allows to conduct in due time diagnostics, differential diagnostics, medical treatment and prophylaxis. Recent studies have reported that 2 % of all newborns required assisted ventilation directly after the delivery. Asphyxia: means to be pulseless, but more useful is a definition of impaired or interrupted gas exchange. In the human, the transition from fetus to neonate represents a series of rapid and dramatic physiologic changes. This transition goes smoothly most of the time; however, approximately 10% of the time the active intervention of a skilled individual or team is necessary to assist in that transition to ensure that it occurs with the least possible damage. Although certain episodes of fetal asphyxia cannot be prevented, there are many circumstances in which, in the immediate neonatal period, a prompt and skilled resuscitation may prevent lifelong adverse sequelae. This, along with the fact that the need for intervention cannot always be predicted, has prompted the International Guidelines for Neonatal Resuscitation to state: "At least one person skilled in initiating neonatal resuscitation should be present at every delivery. An additional person capable of performing a complete resuscitation should be immediately available. Although many elements of a resuscitation sequence have been agreed on, debate and discussion regarding the process continue. Research has yet to answer many questions. For the present, guidelines such as those published by the American Academy of Pediatrics and the American Heart Association as well as those of the International Liaison Committee on Resuscitation (ILCOR) represent a middle ground for various contending views. During a period of asphyxia, the resulting hypoxemia, acidosis, and poor perfusion can damage a neonate's brain, heart, kidney, liver, and lungs. The resulting clinical abnormalities include cerebral edema, irritability, seizures, cardiomegaly, heart failure, renal failure, poor liver function, disseminated intravascular coagulopathy, and respiratory distress syndrome Therefore a prophylaxis, treatment and rehabilitation of this state, is not only medical but also social, problem

Concrete purposes:

1. To determine the etiologic and pathogenetics factors in intrauterine hypoxia and asphyxia in newborn period.

2. To classify and analyse the typical clinical manifestation of asphyxia in newborn period.
3. To determine the features of asphyxia for newborns and put a preliminary clinical diagnosis.
4. To make the plan of examination and analyse the information about laboratory and instrumental data in the classic course of asphyxia in newborn period.
5. To demonstrate skills of treatment, rehabilitation and prophylaxis of asphyxia in children.
6. To diagnose complications of asphyxia and to diagnose and render an urgent help in emergency in asphyxia.
7. To conduct differential diagnostics of asphyxia and other nervous system diseases in newborn period.
8. To determine nearest and remote prognosis in patients with asphyxia in newborn period.
9. To demonstrate the skills of medical specialist's moral and deontological principles and principles of professional subordination in pediatrics.

II. Classes (pointing of planned mastering level)

1. A student must have a conception (familiarize): α1

- The place of asphyxia in the structure of nervous system diseases in children;
- Statistical information in relation to morbidity, frequency of complications, lethality, the nearest and remote prognosis in patients with asphyxia ;
- About the history of scientific studying and the contribution of domestic scientists;

2. A student must know (master): α2

-causes of asphyxia in newborn period;
-key links of asphyxia in newborn period;
-key links of the nervous system diseases pathogenesis in newborn period ;
-classification of asphyxia ;
-classical clinical manifestation of asphyxia in newborn period ;
-clinical syndromes in dependence of asphyxia period ;
-laboratory and instrumental diagnosis of asphyxia ;
- complications of asphyxia ;
- treatment principles of asphyxia in newborn period.

3. A student must master: α3

Skills:

- Collection of complaints and anamnesis of disease;
- Examination of newborn with asphyxia and revealing the main symptoms and syndromes;
-To formulate and substantiate the preliminary diagnosis;

-Determination of laboratory and instrumental inspection plan of patient's examination (according to diagnostics' standards);

Abilities:

-To interpret the results of laboratory and instrumental tests.

-To conduct differential diagnosis among asphyxia and other nervous system diseases in newborn period.

-To give recommendations in relation to the patient's regimen and diet with the asphyxia, taking into account the stage of the disease, severity of the state and concomitant pathology;

-To complete the treatment plan in asphyxia according to standards taking into account the stage of the disease, complications and concomitant pathology.

-To assign the treatment for newborn child in dependence of asphyxia severity

-To render first aid in extreme situations in newborn child in dependence of asphyxia severity

-To render primary resuscitation of newborn.

III. Aims of personality development (educative aims):

- A student must learn to adhere rules of behaviour and principles of medical etiquette and deontology, to develop bedside manner;
- Be able to set a psychological contact with a patient and his family;
- To master the sense of professional responsibility for a timely and adequate medicare.

IV. Interdisciplinary integration:

Subject	To know	To be able
1. Basic		
1. General anatomy	Structure of nervous system of baby and children of the first months of life.	To determine the neurological state of the child with the signs of asphyxia
2. Normal physiology	Normal physiology of nervous system of baby and children of the first months of life, normative indices of laboratory and instrumental methods of examination and their assessment.	To assess the data of laboratory and instrumental methods of examination of patients
3. Physiopathology	The key links in pathogenesis of neurologic diseases of baby and children of the first months of life.	To determine the function of nervous system of baby and children of the first months of life.
4. Pathologic anatomy	Morphological changes of nervous system, that develop during the disease, depend on	To analyze and interpret the data of clinical examination and accessory methods of

	the stage of the disease .	examination
5. Pharmacology	Pharmacokinetics and pharmacodynamics and side effects of preparations used in the treatment of asphyxia in newborn period.	To prescribe age- dependent treatment of patient, taking into account individual features and period of disease, to establish the individual regimen of preparations taking and dosage. To be able to make a prescription.
6. Propedeutics of pediatrics.	Basic stages and methods of patient clinical examination	To collect complaints, anamnesis vitae et morbi, to find out the basic risk factors of thyroid diseases, conduct patient examination, to reveal the clinical signs of thyroid gland diseases, to interpret the data of additional methods of examination
7. Radiology	Normal parameters of ultrasound, X-ray and MRI diagnostics in diseases in newborn period.	To interpret the data of ultrasound, X-ray and MRI diagnostics
2. Interdisciplinary integration		
1. Intrauterine hypoxia and asphyxia in newborn period	Clinical signs of intrauterine hypoxia and asphyxia in neonates	To determine specific clinical signs of intrauterine hypoxia and asphyxia in neonates and to conduct differential diagnostics with the birth trauma
2. Birth trauma	Clinical signs of birth trauma	To determine specific clinical signs of birth trauma manifestations (CNS and spinal) and to conduct differential diagnostics to other neurologic diseases in newborn period.
3. Intrauterine infections and neonatal infections	Clinical signs of intrauterine infections in neonates subject to the time of transplacental passage.	To determine the clinical signs of intrauterine infections and neonatal infections and conduct differential diagnostics with the birth trauma

V. Contents of theme:

ASPHYXIA

DEFINITION

Asphyxia: means to be pulseless, but more useful is a definition of **impaired or interrupted gas exchange.** These situations can take place:

a.*Intrauterine:* the gas exchange depends on the function of placenta, and the blood-flow in the umbilical vessels.

b. *Intrapartum*

c.*Postnatal:* after delivery the gas exchange take place in the pulmonary vesicles or alveoli and depends on the function of the heart, lungs and brain.

The asphyxia can be acute or chronic. The chronic asphyxia can be complicated by an acute asphyxia.

. FREQUENCY

The frequency of asphyxia depends on which assessment you use to define asphyxia.

The Apgar score define asphyxia as < 7 p at one minute/ The majority of these infants are mostly in very good condition some minutes later and few of them suffer a severe asphyxia.

A National survey in Sweden gave an incidence of 1,7 % with a low Apgar score (3 or less at 1 minute or 6 or less at 5 minutes).

The biochemical definition of asphyxia is pH< 7,10 in the umbilical artery.

The electrophysiological definition of (intrauterine) asphyxia is prolonged bradycardia assessed by FHR.

Recent studies have reported that 2 % of all newborns required assisted ventilation directly after the delivery.

CAUSES

I. Intrauterine asphyxia a. *Chronic:*

- Impaired placental function: This is common when pregnancy is complicated with pre-ecclampsia (hypertension, high levels of protein in urine, and edema). Regular controls of blood pressure is necessary.

Values from the measurement of the growing fetus can be plotted in a special growing curve. In that way the examiner can detect a declining growth, which indicate a growth-retarded child. First you will find a weight-retardation, later the length will be involved and finally the head-circumference will be pathological indicating a severe growth-retardation.

- Fetal anemia: this can happen when there is a severe immunization, mostly an immunization between the Rhesus factors.

If the mother is Rh -and the fetus is Rh + it will cause an incompatibility. The fetal erythrocytes will be destroyed, so the result is an increasing anemia. It

is important to check the blood group early in the pregnancy and follow the Rh-mother with immunization tests.

It is possible to prevent this type of immunization with injection anti-D-antibodies to the mother during the first days after delivery.

- Fetal anemia: due to twin transfusion. One twin is anaemic and the other has a high haemoglobin. This condition is often associated with a wide difference in growth between the twins.

- Fetal hypoxia: due to a heavy smoking mother. During pregnancy it is important to assess the frequency of smoking and tell the mother the danger of smoking for the fetus. Mostly you can find a diminished birth weight but a normal or often high hemoglobin.

Unknown factors.

b. *Acute:*

- Complication with the umbilical cord such as a real knot. This diagnosis will be clear after delivery when you examine the umbilical cord. The condition is sometimes connected with intrauterine death.

Placental separation: this situation is associated with both interruption of gas exchange and loss of blood. The ablatio can be of different grades. The total ablation is lifethreating for both mother and child and must lead to an acute Caesarean section.

- Sepsis: this condition can be associated with premature rupture of the membranes and fever. The child can be critical ill with insufficient cardiac output and respiratory problems. Both the chock and the infection must be treated.

II. Intrapartum asphyxia

- Prolapse of the umbilical cord with cessation of the blood flow to the child.
- Breech presentation or other malpresentations.
- Trauma: narrow pelvis and/or prolonged labour.
- Duplex/Triplex: greater risk for number two (or three).
- Drugs depressing the CNS: sedatives, analgesics or general anaesthetics like opiates.

III. Postnatal asphyxia

- Congenital malformations:
- obstructing the airway or preventing lung expansion (Choanal atresia. Congenital diaphragmatic hernia, Meconium aspiration syndrome).
- Prematurity: surfactant
- **Hypercapnia,** blood flow to the brain is increased. The result is a stable delivery of oxygen to the brain to meet metabolic demands and maintenance of a normal intracellular pH. These flow changes are operational unless the infant is extremely hypotensive.

1. During periods of mild asphyxia, adaptive changes in blood flow allow adequate oxygen delivery to the brain, heart, and adrenal gland. This is accomplished through an increase in and a redistribution of the cardiac output. Blood flow to the skin, muscle, kidney, and gastrointestinal tract is sacrificed to maintain perfusion of the vital organs.

2. During periods of severe or prolonged asphyxia, the underperfused (sacrificed) tissues and organs gradually become acidotic because of anaerobic metabolism and lactic acid production. This leads to myocardial depression and a gradual decrease in blood pressure so that blood fails to perfuse the vital organs, with resultant permanent tissue damage in such organs. The extent of the tissue damage depends on the amount of time that has elapsed between the failure of blood flow (i.e., tissue hypoxia) and the institution of resuscitation (i.e., reoxygenation of the tissues).

A. CLINICAL FEATURES

The ability to recognize the clinical signs and symptoms of perinatal asphyxia requires knowledge of the predisposing risk factors for asphyxia, as well as the prenatal and postnatal symptoms of asphyxia.

1. Prenatal risk factors for asphyxia are listed in Table 1.

2. Events that occur with the onset of asphyxia. **a.**

Sequence:

- A clear understanding of the sequence of events that occur with the onset of asphyxia is of utmost importance in determining the condition of the asphyxiated infant and in initiating therapy.

- Respiratory effort ceases abruptly, and the fetus (infant) experiences primary apnoea. This is followed by a phase of gasping, and, if resuscitation is not initiated, progression to terminal apnea.

Prenatal Risk Factors for Asphyxia

Extremes in maternal age	Fetal bradycardia
(i.e., < 20 years or > 35 years)	Malpresentation
Placenta abruption	Multiple gestation
Placenta previa	Prolonged rupture of the fetal Membranes
Preeclampsia	
Preterm gestation	Maternal diabetes
Postterm gestation	Maternal use of illicit drugs
Meconium-stained amniotic fluid	

1)A rapid decrease in the oxygenation of blood occurs, with resultant respiratory acidosis followed by combined respirator)' and metabolic acidosis.

2)The onset of hypoxia results in a rapid decrease in heart rate.

3)Blood pressure rises initially but,, with progression to terminal apnoea, falls to hypotensive levels.

4)The fall in blood pressure causes a decrease in the flow of blood to the organs and consequent tissue damage.

b. **Recovery.**

These events can be reversed with appropriate resuscitative measures [i.e., reoxygenation of the central nervous system (CNS); see III E].

(1) As a result of such intervention, heart rate and blood pressure improve; gasping then occurs, followed by regular breathing. Last to recover are body functions that are controlled by the higher regions of the brain.

(2) The longer the episode of asphyxia, the longer it takes for heart rate, breathing, and other body functions to recover.

3. Postnatal symptoms of asphyxia vary with the degree of asphyxia It is not clear why 3me infants exhibit multiorgan involvement, whereas others have only one or two organ systems involved. Some specific effects of asphyxia are listed by organ system.

a. **Brain**

(1)Mild asphyxia. The infant who experiences mild asphyxia initially will be depressed. This is followed by a period of hyperalertness, which resolves within 1 or 2 days. There are no focal signs, and the prognosis is excellent for a normal outcome.

(2)Moderate asphyxia. The infant who experiences moderate asphvxia will be very depressed. This is followed by a prolonged period of hyperalertness ■and hyperreflexia. Generalized seizures often occur 12-24 hours after the

episode of asphyxia but are controlled easily, resolving in a few days regardless of therapy. The prognosis is variable; negative results on electroencephalogram (EEG) are predictive of a normal outcome.

C. ASSESSMENT

I. Intrauterine assessment

A. Ultrasound and Doppler technique:

- Ultrasound: to measure the growth of the fetus. For this reason it is important to have a reliable gestational age. Early during pregnancy an ultrasound will be done to date the fetus. This method is more safe than common clinical methods. A growth-retarded fetus is in a great risk of developing asphyxia.
- Doppler techniques: to measure the blood flow in the umbilical vessels or aorta. A low flow or decreasing flow indicates a fetus in risk of asphyxia.

B.Electrofysiological:

Severe pathological FHR will lead to cessation of the delivery with Caesarean section.

Fetal Heart Rate (FHR): Episodes of bradycardia can be dangerous and lead to brain damage. The problem is to do this type of measurement during long periods and on every pregnant woman.

II. Extrauterine assessment

***C.* Biochemical**

- C blood sample drawn from the umbilical artery is an ideal way to evaluate whether an intrapartum asphyxia exist or not. Low pH (< 7,10) indicates an intrapartum asphyxia.

PC02 and P02 will also be deranged as you have a diminished gas exchange. The low pH is the result of an increased level of H+ and lactate.

D. Clinical

- **Apgar Score:** This is the most common way of assessing the newborn baby. It is a clinical method and can be used without any equipment.

In general there is a poor relationship between pH in the umbilical artery and Apgar score. That means that the baby may have been asphyxiated thus clinical symptoms are not evident.

Several studies have shown that Apgar score is a poor index of asphyxia and also has little prognostic **value.**

But remember: if the baby has a poor Apgar score he has a problem

The score system grades five clinical features from 0 to 2 at 1,5 and 10 minutes of age.

After 1-2 minutes the baby starts to gasp (this is no real breathing-movements), but if gas exchange does not start heart rate continue to fall and

blood pressure will decrease. Some minutes later the gasps ceased. This period between last gasp and cardiac arrest is known as terminal apnea. During this period an acidaemia develops. The neonatal primate is capable of surviving at least twenty minutes of complete oxygen deprivation. This is because of the existence of large stores of glycogen in brain, liver and myocardium, which can produce energy by anaerobic glycolysis during asphyxia: When the baby is in terminal apnoea you had to resuscitate the baby with positive pressure ventilation. In primary apnoea the baby may start to breathe after cutaneous stimulation. Episodes of- acute total asphyxia creating total anoxia are comparatively rare. More common are events, which lead to gradual development of hypoxic and chronic partial asphyxia. This can occur before or rearing labour.

If. Later symptoms

a. Lung effects

It is common with respiratory problems after acute 'asphyxia. In the tissues damaged by asphyxia there is a reactive hyperaemia, which causes fluid transudation

and edema. This can be more or less extended. In severe forms this develops into shock lung with high mortality risk.

In term babies there is a great risk of developing meconium aspiration syndrome.

Respiratory support is often necessary.

b. Renal effects

. Whenever a neonate develops severe hypoxia or hypotension damage in the kidneys may result. This can be a great clinical problem with anuria or oliguria.

Renal function must be investigated and taken into consideration in the treatment the first days after the asphyxial period.

c. Cardiovascular effects

After severe birth asphyxia heart failure follows with low blood pressure and low cardiac output. The effect will be decreased blood perfusion in all organ tissues.

d. Other effects

Mostly there will be a lot of biochemical changes like hypoglycaemia and hypocalciaemia due to metabolic derangement.

e. CNS effects

Infants who are exposed to hypoxic periods intrauterine may not exhibit major neurological abnormalities during the newborn period. The absence of clinical encephalopathy in the term newborn precludes the occurrence of significant hypoxic-ischaemic cerebral injury during the intrapartum period.

The clinical encephalopathy may be classified as mild, moderate or severe

Severity of encephalopathy.			
Clinical features	Mild	Moderate	Severe
Level of consciousness	Hyperalert	Lethargic	Stuporous, comatose
Muscle tone	Normal	Mild hypotonia	Flaccid
Seizures	None	Common	Intractable
EEG findings	Normal	Pathologic	Severe pathology suppression -burst
Duration	< 24 hours	2-14 days	Weeks

Diagnosis:

1. Clinical symptoms
2. Metabolic derangement
3. Renal and/or cardiac failure
4. Assessment of the brain:

a.EEG: EEG is useful particulary in the asphyxiated term newborn. Serial recordings are almost necessary.

Low voltage. Burst-suppression patterns or electrical inactivity are associated with bad prognosis.

Rapid resolution of EEG abnormalities and/or normal interictal EEG are associated with a good prognosis.

b.Ultrasonography: Ultrasound can be useful in premature newborns but is of more limited value in the term newborn.

*c.**Computed** tomography:* CT is of major value both acutely during the neonatal period and later in childhood. The optimal timing of CT scanning is between 2 and 4 days.

Decreased tissue attenuation corresponds to irreversible brain swelling associated with necrosis.

Later in childhood CT is useful for diagnosis of atrophy of the brain.

TREATMENT

1. **General principles.** The primary objective in treating perinatal asphyxia is to restore an oxygen supply to the body tissues, especially the brain.

This requires ventilation with oxygen and ensuring an adequate cardiac output. The secondary objective is evaluate the degree of hypoxic injury and to plan treatment.

2. Specific therapy. Problems commonly associated with asphyxia are listed in Table 2. These conditions should be anticipated or considered and treated if present. When the heart rate is less than 100 beats/min ventilation is necessary. In 450 % ventilation with bag and mask is satisfactorily and the other 20 % had to be intubated.

Management of the severely asphyxiated newborn:

Prevention of intrauterine asphyxia:

- recognition of risk factors
- fetal monitoring during labour
- appropriate intervention Supportive care:
- adequate ventilation
- prevention of hypoxemia, hyperoxaemia, hypercapnia
- optimal perfusion

Maintenance of adequate blood glucose levels Control of seizures Avoidance of fluid overload

Ethical aspects of resuscitation: Recommendation from the Swedish Pediatric Association.

No further resuscitation:

- Cardiac arrest in 20 minutes

Normal' heart rate but no spontaneous breathing after 45 minutes of resuscitation.

G. PROGNOSIS

Prognosis is difficult because of the inability to establish the precise extent and duration of cerebral insult and injury. At the time of delivery low delayed Apgar scores between 0 and 3 at 10, 15 and 20 minutes of age are associated with significantly increased mortality and morbidity, e.g. cerebral palsy. The single most useful prognostic factor is the severity of the neonatal neurological syndrome.

There are generally no long - term abnormalities reported following mild encephalopathy, whereas essentially all infants with severe encephalopathy have either died or developed multiple neurological sequel.

The overall prevalence of neurological sequel following hypoxic-ischaemic encephalopathy observed at 3 *'A* years of age is approximately 17%. Prolonged duration of encephalopathy with an abnormal neurological examination after 7 days of age is associated with an increased incidence of long-term sequel.

D. PROGNOSIS

Outcome is related to the severity and duration of the asphyxial insult and to the adequacy of compensatory mechanisms, resuscitation procedures, and specific treatment of multiorgan system involvement. Neurologic outcome is the most difficult to predict but is best related to the degree of hypoxic encephalopathy and EEC activity in the neonatal period, and to findings on physical examination of the infant at 9 -12 months of age.

HYPOXIC-ISCHEMIC ENCEPHALOPATHY (HIE)

The neuropathologic lesions that follow hypoxic ischemic injury in the perinatal period most commonly follows perinatal asphyxia.

Selective necrosis of the neurons of the deeper cerebral cortical layers is the hallmark of hypoxic injury to the perinatal brain, hi full-term babies, parasagittal cerebral injury occurs as a result of the generalized reduction in the cerebral blood flow, seen in perinatal asphyxia. In preterm babies, the areas of infarction involve the deeper periventricular white matter. Neuronal necrosis may also entail basal ganglia.

Clinical features The clinical state following asphyxia correlates better with the five and ten minute Apgar scores, than with the one minute Apgar score. Several asphyxiated babies fall into two groups,; the quick or rapid responders and slow responders. Slow responders are more likely to develop altered sensorium and seizures due to anoxicischemic insult. Babies, who- are mildly or moderately asphyxiated, seldom develop any neurologic symptoms in the early postnatal period. Premature babies may not show features of frank neonatal encephalopathy except when they have intraventricular bleeding. Preterm infants who survive neonatal asphyxia may develop cerebral palsy, hearing or visual defects.

Term infants usually present with features suggestive of cerebral cortical involvement. They may present either with (i) normal, (ii) increased or (iii) diminished muscle tone. Eighty percent of those with normal tone develop normally

without neurological sequel. Hypertonic infants are generally hyperalert. These infants have extensor posture, brisk stretch reflexes and strong Moro reflex with low threshold. Most of these develop normally but may develope seizures Hypotonic babies are markedly depressed with weak Moro reflex and poor spontaneous movements. They suck poorly. Seizures, generally subtle, are unusual at birth but may appear a few hours after birth. Brain stem encephalopathy is less common. The latter present with stupor, respiratory disturbances and hypotonia. They may have pooling of secretions and difficulty in swallowing. There may be intermittent decerebration.

Some of the ischemic infants with encephalopathy gradually improve while others deteriorate. If not treated promptly, 20 to 30 percent of infants with severe ischemia die.

Diagnosis A thorough neurologic examination combined with a careful history are helpful for the diagnosis. Ultrasound examination of the brain, EEC. intracranial pressure measurement and CT scanning arc also valuable.

Treatment Prevention of asphyxia remains the most important mode of treatment. Careful monitoring of the fetus during labour and prompt appropriate intervention at the earliest signs of fetal compromise is important in preventing perinatal asphyxia.

The rapid responders from anoxia need observation in the nursery for only 12 to 24 hours. These babies become active, and start accepting feeds within a few hours. The slow responders need more aggressive management. Both hypoxemia and hyperoxemia, as well as hypercapnia should be circumvented, since they affect cerebral blood flow. These babies should be kept in ward, with a minimal noise level or in the nursery. Intravenous fluids should be restricted to two-third of the maintenance requirements and blood glucose levels must be maintained at 75-100 mg/dL. Acidosis, hypocalcemia and hypoglycemia need correction. Seizures should be controlled with phenobarbitone but not in preterm babies who are severely disturbed and in those with decerebratibn.

Complications Associated With Perinatal Asphyxia

Hypotension	Adrenal hemorrhage and necrosis
Hypoxic encephalopathy and seizures	Hypoglycemia
Persistent pulmonary hypertension	Polycythemia
Hypoxic cardiomyopathy	Hypocalcemia
Ileus and necrotizing enterocolitis	Disseminated intravascular coagulation (DIC)
Acute tubular necrosis	

Prognosis. Prognosis of neonatal seizures due to birth injury and anoxia is poor; 40 percent die in the neonatal period and 25 percent are left with neurodevelopmental handicaps and recurrence of seizures in later life. Hypocaldgmic seizures carry better prognosis. Twenty-percent cases of idiopathic neonatal seizures are associated with permanent motor and developmental handicaps.

Management. Infant should be evaluated for the cause and treated appropriately. Diazepam 1 to 2 mg given controls the spasm immediately. For severe recurrent and persisting seizures, beyond 24 hours it is destable to give 20 mg/kg of phenobarbitone intravenously. This may be repeated after 30 to 60 minutes if considered necessary.

Neonatal seizures

(1)Developmental defects of the brain e.g. Microcephaly, hydrocephalus, porencephaly, polymicrogyria, heterotropia, hydrocephalic, corpus callosum.
(2) Perinatal complications. Intracranial birth injuries and perinatal anoxia. Intraventricular hemorrhage (more often in near term babies with history of difficult labor).
(3) Perinatal infections. Intrauterine infections, neonatal septicemia and meningitis.
(4) Metabolic causes. Hypoglycemia (blood glucose level below 40 mg/DI), hypocalcemia (serum calcium level below 7 mg/dL), hypomagnesemia, hyperbilirubinemia (kemicterus), hypo or hyper-natremia, alkalosis, pyridoxine dependency and inborn errors of metabolism.
(5) Narcotic withdrawal syndrome. Babies born to mothers addicted to narcotics may suffer from convulsions.

NEONATAL HYPOGLYCEMIA

Hypoglycemia is seen in 1-3 per 1000 newborn infants. Current definition of hypoglycemia is based on plasma glucose of less than 40 mg/dL or blood glucose of less than 3 5mg/dL irrespective of gestational age.

Pathogenesis. Neonatal hypoglycemia results from:

(a) Lack of substrate for the production of glucose such as (i) glycogen in the liver and (ii) alanine in the muscles for gluconeogenesis.

b) In the early post-neonatal period, the enzyme glycogen synthetase decreases and phosphorylase increases. Inappropriate changes in the hormones, their receptors and enzymes regulating glucose metabolism cause neonatal hypoglycemia.

Clinical features. Neonatal hypoglycemia may be. asymptomatic. Early transitional adaptive hypoglycemia occurs in low birth weight infants and babies of

diabetic mothers. It manifests soon after birth. Hypoglycemia may be secondary to perinatal stresses, such as asphyxia, infection, respiratory distress and neurological disturbances. Classical transient neonatal hypoglycemia is observed in infants with fetal under nutrition, twins and babies born to mothers with toxemia of pregnancy. Recurrent, severe hypoglycemia is caused by enzymatic or metabolic defects.

Causes of hypoglycemia are given below:

Transient Hypoglycemia	
1.	Inadequate substrate
2.	Premature and SGA infants
3.	Smaller or the twins
4.	Infants of diabetic mother
5.	Relative hyperinsulinism as in infants of diabetic mothers
Persistent Hypoglycemia	
1.	Hyperinsulinemia states
2.	Beta cell hyperplasia (Nesidioblastosis)
3.	Adenoma of beta cells
4.	Leucine sensitivity
5.	Deficiency of hormones such as glucagon, HGH, epinephrine, adrenal and ACTH
6.	Deficiency of substrate such as in ketonic hypoglycemia and Maple syrup urine disease
7.	Disorders of carbohydrate metabolism such as glycogen storage disease and fructose intolerance

Clinical features of hypoglycemia are related to (a) release of epinephrine and activation of autonomic nervous system. Symptoms include sweating, shakiness, tremors and tachycardia. Diminished utilization of glucose in the cerebrum manifests as lethargy or irritability, restlessness, disturbance in sensorium, twitching and convulsions.

Prognosis. Prolonged symptomatic hypoglycemia especially in low birth weight infants and infants of diabetic mother carries guarded prognosis, with regard to subsequent intellectual and neurological development.

Treatment. Hypoglycemia can be prevented by introduction of breastfeeding within four hours of birth. The symptomatic infants are treated with a bolus of 2-4 ml of 10 percent dextrose and then with 5 to 10 mg/kg of glucose per minute till the blood sugar rises above 40 mg/dL. If this is not achieved within 24 hours, prednisolone should be administered orally in a dose of 1 to 2 mg/kg/day for three to five days. Alternatively hydrocortisone acetate is given 1M in a dose of 5 mg/kg/day in divided doses.

Ephedrin 0.5mg/kg/3hr orally for two days may be used for treatment of hypoglycemia in infants of diabetic mothers. This releases liver glycogen and should not be used in cases of fetal malnutrition.

HYPOCALCEMIA

In the neonatal period, there is transient hypoparathyroidism. As a result, less phosphate is excreted in urine. Extra phosphate load also occurs because of tissue breakdown due to perinatal asphyxia. Human milk is low in phosphate, but cow's milk is rich in phosphate. Immature parathyroid in the neonate cannot easily cope with excess phosphate in cow's milk leading to hypocalcemia. Hypocalcemia may be observed in the first one or two days in the premature infants. Delayed oral feeding and rapid correction of metabolic acidosis arc other precipitating factors.

Exchange transfusion with citrate blood reduces level of ionized calcium. Maternal hyperparathyroidism and high maternal blood calcium level may suppress fetal parathyroid. Congenital absence of thymus and parathyroid is observed in Di - George syndrome.

Clinical features. Infants with hypocalcemia show tremors. Frank convulsions usually occur by about the seventh day. Spasm of the larynx and carpopedal spasms are unusual. Chvostek sign is not diagnostic, as it may be present even in the normal newborns.

Diagnosis. Serum calcium is less than 7 mg/dL. Serum phosphate level is elevated. In ECG, QT interval is prolonged. Chest X-ray may be useful for diagnosis of congenital absence of thymus and parathyroid gland.

Treatment. Calcium gluconate, 2 ml/kg of 10 percent solution is administered JV to control the seizure. Electrocardiographic monitoring of treatment with calcium is desirable. Later 5 ml/kg/day of 10 percent calcium gluconate solution is given IV or orally for several days. Calcium gluconate should not be mixed with sodium bicarbonate solution, as it precipitates calcium carbonate. Calcium should never be given along with digitalis. Diet should be low in phosphates.

INTRACRANIAL HEMORRHAGE

Intracranial hemorrhage may occur in the subdural, subarachnoid, intraventricular or intracerebral regions. Subdural and subarachnoid hemorrhage follow head trauma e.g., in breech, difficult and prolonged labour and after forceps delivery. Other forms of intracranial bleeding are associated with immaturity and hypoxia. With better obstetric care intracranial bleeding has become rare.

Pathogenesis. Hypoxic stress in premature infants leads to periventricular venous infarction, Intraventricular bleeding and subependymal hemorrhage. Rise in blood pressure in hypoxic state may rupture capillaries on the arterial end.

Clinical features. Clinical features of both perinatal hypoxia and intracranial hemorrhage are similar. Subdural hematoma follows birth injury. In intraventricular

hemorrhage, features of cerebral depression or excitation along with asymmetric cerebral signs appear on the second or third day. Convulsions may occur in most cases. Muscle tone and neurological reflexes are either

depressed or exaggerated. Sucking or swallowing are poor, and the infant stares vacantly. Anterior fontanel becomes prominent; breathing is slow, gasping, or irregular with apnoea Supervening in severe cases.

Clinical Diagnosis. Clinical diagnosis of ICH is based on the history of severe asphyxial insult, shock conditions and drop-in hematocrit associated with bulging fontanel and neurologic symptoms of seizure. It can be confirmed with lumbar puncture, although ultrasonographic evaluation of the head has become a routine in established nurseries. CT scan is more helpful in localizing parenchymal bleed and associated ischemic changes in the brain.

Subdural hematoma follows traumatic birth. High intensity transillumination of head is useful in the absence of availability of ultrasound or CT Scan.

Ultrasonic findings of the head are graded according to the presence of blood in the ventricle and parenchyma. Grade 1 & 11 are less consequential in the long term. Grade III & IV hemorrhages have poor neurologic outcome.

Management. ICH is best managed by preventive measures. Improved prenatal and obstetric care has brought down the incidence of 40% (in < 1500 gm infants) in 1975 to <15 % in 1995. The severity of ICH has also decreased.

The treatment consists of underlying problems *i. e.,* RDS, hypoxia, hypotension and supportive therapy. Grade III & IV hemorrhages may result in obstructive hydrocephalus and subsequent neurologic deficits.

Infants with ICH should be followed closely by friquent documentation of head circumference. If the growth is rapid (more than 1 cm/wk) or clinical signs of increased intracranial pressure are noted, relief of pressure by ventriculoperitoneal shunt is indicated.

THE APGAR SCORE

Clinical feature	Score		
	0	1	2
Heart Rate	0	<100	>100
Respiration	Absent	Gasping/irregular	Regular/crying
Muscle tone	Limp	Diminished/normal with no movements	Normal with normal movements
Color of trunk	White	Blue	Pink
Response to pharyngeal catheter	No	Grimace	Cough

ROLE OF THE APGAR SCORE The Apgar score is a tool that can be used objectively to define the state of an infant at given times after birth, traditionally at 1 minute and 5 minutes. Clearly, if the 1-minute Apgar score is very low, a resuscitation is necessary and in most circumstances should have already been started by 1 minute. The Apgar score should not be used as the primary indicator for resuscitation because it is not normally assigned until 1 minute of age. As noted earlier, an asphyxial process may begin in utero and continue into the neonatal period. Thus, to minimize the chances of brain damage, one should begin resuscitation as soon as there is evidence that the infant is not able to establish ventilation sufficient to maintain an adequate heart rate. Waiting until a 1-minute Apgar score is assigned before initiating resuscitation only increases the chance of permanent damage in a severely asphyxiated infant.

Apgar Score

SIGN	0	1	2
Heart rate	Absent	Less than 100 beats per minute	More than 100 beats per minute
Respiratory effort	Absent	Slow, irregular	Good, crying
Muscle tone	Flaccid	Some flexion of extremities	Active motion
Reflex irritability	No response	Grimace	Vigorous cry
Color	Pale	Cyanotic	Completely pink

Complications of Endotracheal Intubation

COMPLICATION	CAUSE
Hypoxia	Procedure taking too long; incorrect placement of tube
Bradycardia/apnea	Hypoxia
Vagal response	Stimulation of posterior pharynx by laryngoscope blade, endotracheal tube, or suction catheter
Pneumothorax	Overventilation of one lung caused by placement of tube in main bronchus (usually the right)
Contusions or lacerations of tongue, gums,	Rough handling of laryngoscope or

COMPLICATION	CAUSE
pharynx, epiglottis, trachea, vocal cords, or esophagus	endotracheal tube; laryngoscope blade that is too long or too short
Perforation of trachea or esophagus	Insertion of tube or stylet was too vigorous, or stylet protrudes beyond end of tube
Infection	Introduction of organisms by equipment or hands

VI. Plan and organizational structure of classes.

№	Basic stages of classes, their function and content	Educational aims are in the levels of mastering	Methods of control and studies	Educational materials	Distributing of time in minutes
1	Preparatory stage Organizational measures	α2		«Actuality of theme»	3 min
2	Raising of educational aims and motivation	α2		«Educational aims»	12 min
3	Control of basic knowledges and skills level: • Etiology of intrauterine hypoxia and asphyxia in newborn period • The main of asphyxia pathogenesis • Classification of asphyxia • Typical manifestation of asphyxia, stages of disease, features of clinic and diagnostics • Laboratory and instrumental diagnosis of asphyxia • Clinical syndromes of asphyxia • Treatment principles of asphyxia	α2	Individual oral questioning Test control of the second level Individual oral questioning Typical situational task of 2 level Typical situational task of 2 level Typical situational task of 2 level Test control of 2 level Typical situational task of 2 level	The second level tests. The table «Classification of natal injuries in newborn period» Structurally logical chart of natal injuries Typical situational task of 2 level Tests of 2 level Typical situational tasks of 2 level Kit of medicines.	20 min
4	Basic stage of professional skills and abilities forming:				115 min

	• To conduct the patient management with asphyxia, to take complaints and anamnesis. • To conduct the patient examination, to detect main symptoms and syndromes of asphyxia. • To formulate and substantiate the preliminary diagnosis • To compose the plan of patient laboratory and instrumental examination • To interpret the results of laboratory and instrumental examination • To conduct differential diagnostics among asphyxia and other neurologic diseases in newborn period • To give the recommendations for regimen and diet of patient • To compose the plan of asphyxia patient treatment taking into account the stage of disease and presence of complications • To be able to render the first aid in extreme situations	α3 α3 α3 α3 α3 α3 α3	Practical professional training Practical professional training Practical professional training Practical professional training Practical professional training, tests and the third level control. The practical professional training in solving of non typical clinical situations. The third level test control. Practical professional training. The practical professional training in solving of non typical clinical situations. The third level test control.	Patient Patient Case history A reference chart for forming of professional abilities. Case history. A reference chart for forming of professional abilities. Case history. A reference chart for forming of professional abilities. Situational typical tasks of 3 level. The third level tests. Prescribing chart The third level non typical situational tasks. Treatment algorithm for the patients with asphyxia The third level non typical situational tasks. Treatment algorithm for the patients with asphyxia	
5	**Concluding stage.** Control and correction of professional abilities and skills		Analysis of clinical work	Clinical work	25 min

6	Working out the totals of class		The practical professional training in solving of non typical clinical situations.	The third level non typical situational tasks.	
7	Home work (basic and additional literature on the topic)		Estimation of clinical work.	A reference chart for independent work with literature	

Questions for self-control

1. Name the main causes of asphyxia.
2. Point out the classification of asphyxia.
3. What the main clinical manifestations of asphyxia and ultrasound findings?
4. Define diagnostic and differential diagnostic measures in asphyxia.
5. What is the common treatment tactics in asphyxia?
6. What are the main consequences of asphyxiain later periods of childhood and their prophylaxis ?

The primary control tests

1. A mother delivers a neonate with meconium staining and Apgar scores of 3 at 1 and 5 min of life. She had no prenatal care and the delivery was by emergency cesarean section for severe fetal bradycardia. Which of the following sequelae could be expected to develop in this intubated neonate with respiratory distress?

a. Sustained rise in pulmonary arterial pressure
b. Hyperactive bowel sounds
c. Microcephaly with micrognathia
d. Cataracts
e. Thrombocytosis

2. Child was born after third pregnancy and second labors, 42 w. of gestational age , body weight 4200 g, length 58 cm. In the labors there is meconium in amniotic fluid. Aspiration of amniotic fluid suspected. Independent respiration is absent. What tactics indicated in this case?

A. A tactile stimulation
B. Closed cardiac massage
C. Suction of respiratory ways
D. Oxygen therapy.
E. Treatment of oligemia

3. At 43 weeks' gestation, a long, thin infant is delivered. The infant is apneic, limp, pale, and covered with "pea soup" amniotic fluid. The first step in the resuscitation of this infant at delivery should be

a. Suction of the trachea under direct vision
b. Artificial ventilation with bag and mask
c. Artificial ventilation with endotracheal tube
d. Administration of 100% oxygen by mask
e. Catheterization of the umbilical vein

4. An infant who appears to be of normal size is noted to be lethargic and somewhat limp after birth. The mother is 28 years old, and this is her fourth delivery. The pregnancy was uncomplicated, with normal fetal monitoring prior to delivery. Labor was rapid, with local anesthesia and intravenous meperidine administered for maternal pain control. Which of the following therapeutic maneuvers is likely to improve this infant's condition most rapidly?

a. Intravenous infusion of 10% dextrose in water
b. Administration of naloxone
c. Administration of vitamin K
d. Measurement of electrolytes and magnesium levels
e. Neurologic consult

5. You are called to the delivery room. A newborn infant seems lethargic and has poor tone with only marginal respiratory effort, but his heart rate is above 100 beats per min. The mother had an uncomplicated pregnancy, and delivery was uncomplicated and vaginal 10 min after spontaneous rupture of membranes. The mother received only pain medications while in labor.The most important aspect of the management is (SELECT 1 TREATMENT)

a. Atropine
b. *N*-acetylcysteine
c. Meso-2,3-dimercaptosuccimic acid (DMSA succimer)
d. Naloxone
e. Sodium bicarbonate

6. What cause of asphyxia is wrong

A. Knotting of cord
B. maternal staphylococcus
C. maternal acute bleeding
D. Diabetes in mother
E. preterm gestation

7. A 3-day-old infant born at 32 weeks' gestation and weighing 1700 g (3 lb, 12 oz) has three episodes of apnea, each lasting 20 to 25 s and occurring after a feeding. During these episodes, the heart rate drops from 140 to 100 beats per min, and the child remains motionless; between episodes, however, the child displays normal activity. Blood sugar is 50 mg/dL and serum calcium is normal. The child's apneic periods most likely are

a. Due to an immature respiratory center
b. A part of periodic breathing
c. Secondary to hypoglycemia
d. Manifestations of seizures
e. Evidence of underlying pulmonary disease

8. A newborn infant develops respiratory distress immediately after birth. His abdomen is scaphoid. No breath sounds are heard on the left side of his chest, but they are

audible on the right. Immediate intubation is successful with little or no improvement in clinical status. The most likely explanation for this infant's condition is

a. Pneumonia
b. Cyanotic heart disease
c. Diaphragmatic hernia
d. Choanal atresia
e. Pneumothorax

9. Asphyxia is severe if Apgar scores are during first minute

A. 0-3
B. 0-6
C. 6-8
D. 3-7
E. 4-6

10. Assesment of newborn by Apgar should be performed at the

A. 1 and 5 minutes of life
B. 1 and 10 minutes of life
C. 5 and 10 minutes of life
D. 10 and 15 minutes of life
E. 1 and 20 minutes of life

11. A newborn infant is having poor neonatal reflexes, uncoordinated sucking, swallowing, difficulties in feeding. The most important next step to quickly establish the diagnosis is

a. Echocardiogram
b. Ultrosonography
c. Passage of catheter into nose
d. Hemoglobin electrophoresis
e. Bronchoscopic evaluation of palate and larynx

12. Child was born after third pregnancy and second labors, 40 w. of gestational age, body weight 4200 g, length 55 cm. Aspiration of amniotic fluid suspected. Independent respiration is absent,heart rate is 50 beats/min. What tactics indicated in this case?

A. A tactile stimulation
B. Closed cardiac massage
C. Suction of respiratory ways
D. Oxygen therapy.
E. Treatment of oligemia

13. Child was born after second labors, 38 w. of gestational age , body weight 3200 g, length 52 cm. Independent respiration is absent,heart rate is 110 beats/min. What tactics indicated in this case?

A. A tactile stimulation
B. Closed cardiac massage
C. Suction of respiratory ways

D. Oxygen therapy.
E. Passage of catheter into nose

14. Child was born after second labors, 38 w. of gestational age , body weight 3200 g, length 52 cm. Suction of respiratory ways suspected.Independent respiration is absent,heart rate is 110 beats/min. What tactics indicated in this case?
A. A tactile stimulation
B. Closed cardiac massage
C. Suction of respiratory ways
D. Oxygen therapy.
E. Passage of catheter into nose

15. Step A resuscitation includs
A. A tactile stimulation
B. Closed cardiac massage
C. Suction of respiratory ways
D. Oxygen therapy.
E. Passage of catheter into nose

16. Step B resuscitation includs
A. Mechanical ventilation whis mask and bag
B. Closed cardiac massage
C. Suction of respiratory ways
D. Oxygen therapy.
E. Passage of catheter into nose

17. Step C resuscitation includs
A. Mechanical ventilation whis mask and bag
B. Closed cardiac massage and ventilation
C. Suction of respiratory ways
D. Oxygen therapy.
E. Passage of catheter into nose

18. Diagnosis of neonatal hypoglycemia if a blood glucose level is less then
A.1,7 mmol/L
B. 5,5 mmol/L
C. 2,2 mmol/L
D. 3,3 mmol/L
E. 0,7 mmol/L

19. A newborn infant has no respiration and neonatal reflexes. What is necessary in first step
A. Mechanical ventilation whis mask and bag
B. Closed cardiac massage and ventilation
C. Suction of respiratory ways
D. Oxygen therapy.
E. Apgar assessment

20. For assessment of asphyxia severity following scale should be used

A. Silverman
B. Downess
C. Ballard
D. Apgar
E. Glasgo

Answers to the primary control tests
1-A, 2-C, 3-A, 4-B, 5-D, 6-B, 7-A, 8-C, 9-A, 10-A, 11-C, 12-D
13-C, 14-A, 15-C, 16-A, 17-B, 18-C, 19-C, 20-D.

Situational tasks

Situational Task 1

A mother delivers a neonate with meconium staining and Apgar scores of 3 at 1 and 5 min of life. She had no prenatal care and the delivery was by emergency cesarean section for severe fetal bradycardia.

1. Which pulmonary sequele could be expected to develop in this intubated neonate with respiratory distress?

2. Which other sequelae could be expected to develop in this intubated neonate with respiratory distress?

The answers are

1. Sustained rise in pulmonary arterial pressure

2. The low Apgar scores, meconium staining, and ensuing respiratory distress suggest that asphyxia has occurred. During a period of asphyxia, the resulting hypoxemia, acidosis, and poor perfusion can damage a neonate's brain, heart, kidney, liver, and lungs. The resulting clinical abnormalities include cerebral edema, irritability, seizures, cardiomegaly, heart failure, renal failure, poor liver function, disseminated intravascular coagulopathy, and respiratory distress syndrome. There can be excessively high pulmonary arterial pressure at the same time systemic blood pressure begins to fall, resulting in a persistent right-to-left shunt across a patent ductus arteriosus or foramen ovale

Situational Task 2

A 2-day-old infant with meconium aspiration syndrome is worsening. The delivered FiO2 is 100%, and yet his arterial PaO2 is 40 mmHg on the most recent arterial blood-gas analysis. You have increased his ventilator pressures without success.

1. What is the next step in this patient's management?

The answers are

1. Extracorporeal membrane oxygenation

Infants in severe respiratory failure from any number of illnesses— such as meconium aspiration, severe pneumonia, persistant fetal circulation, and diaphragmatic hernia—may fail conventional ventilation. Extracorporeal membrane oxygenation (ECMO) is an alternative to conventional ventilation. Essentially the ECMO takes deoxygenated blood, oxygenates it, and sends it back into the infant's circulation. With reversible disease, ECMO can be extremely effective.

Situational Task 3

A 19-year-old primiparous woman develops toxemia in her last trimester of pregnancy and during the course of her labor is treated with magnesium sulfate. At 38 weeks' gestation, she delivers a 2100-g infant with Apgar scores of 1 at 1 min and at 5 at 5 min. Laboratory studies at 18 h of age reveal a hematocrit of 79%, platelet count of 100,000/□L, glucose 38 mg/dL, magnesium 2.5 meq/L, and calcium 8.7 mg/dL. Soon after, this the infant has a generalized convulsion.

1. What is most likely cause of the infant's seizure?
2. Conduct differential diagnostics.
3. What therapy is nessecery?

The answers are

1. Polycythemia
2. a. Hypoglycemia b. Hypermagnesemia c. Hypocalcemia

An infant of 2100 g at 38 weeks would be considered small for gestational age (SGA), a not uncommon consequence of maternal toxemia. Pregnancy-induced hypertension can produce a decrease in uteroplacental blood flow and areas of placental infarction. This can result in fetal nutritional deprivation and intermittent fetal hypoxemia, with a decrease in glycogen storage and a relative erythrocytosis, respectively. Hence, neonatal hypoglycemia and polycythemia are common clinical findings in these infants. A blood glucose level of 30 mg/dL in a full-term infant, however, is probably normal during the first postnatal day, and an infant is very unlikely to have a convulsion as a result of a level of 38 mg. Serum calcium levels usually decline during the first 2 to 3 postnatal days, but will only be considered abnormally low in a term infant when they fall below 7.5 to 8 mg/dL. Neonatal hypermagnesemia is common in an infant whose mother has received MgSO4 therapy, but is usually asymptomatic or produces decreased muscle tone or floppiness. A persistent venous hematocrit of greater than 65% in a neonate is regarded as polycythemia and will be accompanied by an increase in blood viscosity. Manifestations of the "hyperviscosity syndrome" include tremulousness or jitteriness that can progress to seizure activity because of sludging of blood in the cerebral microcirculation or frank thrombus formation, renal vein thrombosis, necrotizing enterocolitis, and tachypnea.

3. Therapy by partial exchange transfusion with albumin is probably more likely to be useful if performed prophylactically before significant symptoms have developed.

Situational Task 4

An infant who appears to be of normal size is noted to be lethargic and somewhat limp after birth. The mother is 28 years old, and this is her fourth delivery. The pregnancy was uncomplicated, with normal fetal monitoring prior to delivery. Labor was rapid, with local anesthesia and intravenous meperidine administered for maternal pain control.

1. What are first steps in the management of this infant?
2. Which of the following therapeutic maneuvers is likely to improve this infant's condition most rapidly?

The answers are

1. First steps are managing the ABCs of airway, breathing, and circulation.

2. Administration of naloxone.

In the description provided, the most likely cause of the neonatal depression is maternal analgesic narcotic drug administration. While controlling the pain of the delivery in the mother, use of narcotics can result in depression of the newborn via crossing of the placenta. Appropriate first steps in the management of this infant (after managing the ABCs of airway, breathing, and circulation) is the administration of naloxone, 0.1 mg/kg, IM, IV, or intratracheal. The other possibilities are unlikely, given the clinical information provided.

Situational Task 5

At 43 weeks' gestation, a long, thin infant is delivered. The infant is apneic, limp, pale, and covered with "pea soup" amniotic fluid.

1. What should be first step in the resuscitation of this infant at delivery?

2. What are the steps in the management of this infant?

The answers are

1. To prevent or minimize meconium aspiration risk, these infants should have immediate nasopharyngeal suction as their heads are delivered and suction of the trachea under direct vision after delivery and before initiation of respiration.

2. Infants who are postmature (more than 42 weeks' gestation) and show evidence of chronic placental insufficiency (low birth weight for gestational age and wasted appearance) have a higher-than-average chance of being asphyxiated, and passage of meconium into the amniotic fluid thus places these infants at risk for meconium aspiration. To prevent or minimize this risk, these infants should have immediate nasopharyngeal suction as their heads are delivered. Immediately after delivery and before initiation of respiration, their tracheas should be carefully and thoroughly suctioned through an endotracheal tube under direct vision with a laryngoscope. Afterward, appropriate resuscitative measures should be undertaken to establish adequate ventilation and circulation. Artificial ventilation performed before tracheal suction could force meconium into smaller airways.

Situational Task 6

You are called to a delivery of a term infant, about to be born via cesarean section to a mother with multiple medical problems including a 1-month history of a seizure disorder, for which she takes phenytoin; rheumatic heart disease, for which she must take penicillin daily for life; hypertension, for which she takes propanolol; acid reflux, for which she takes aluminum hydroxide; and a deep venous thrombosis in her left calf diagnosed two days ago, for which she was started on a heparin infusion. The obstetrician is concerned about the possible effects of the mother's multiple medications on the newborn infant.

1. You correctly note that the one medication most likely to cause harm in this newborn infant at delivery is

a. Propanolol b. Penicillin c. Aluminum hydroxide

d. Phenytoin e. Heparin

2. Describe effects of other medications.

The answers are

1. Propanolol..

Propranolol, which may cause growth retardation when given throughout pregnancy, diminishes the ability of an asphyxiated infant to increase heart rate and cardiac output. It has also been associated with hypoglycemia and apnea.

2. The effect of a drug on the fetus is determined by the nature of the drug and by the timing and degree of exposure. Heparin does not cross the placental barrier and does not appear to directly affect the fetus once pregnancy is well established. Phenytoin may cause birth defects when given during the first trimester. Penicillin and aluminum hydroxide have not been found to affect the fetus.

Situational Task 7

A 26-year-old gravida 3 woman has a history of gestational diabetes and a delivery of two previous infants at term that were greater than 4000 grams, each of whom had severe hypoglycemia.

1. Which of the following maneuvers is least likely to reduce the chance of the next child's having hypoglycemia?

2. What other steps to reduce the chance of the next child's having hypoglycemia?

The answers are

1. Maternal intravenous loading with 10% glucose beginning 2 to 4 h prior to the

expected time of delivery

2. a. Careful control of the maternal blood glucose levels during pregnancy

b. Careful glucose monitoring of the infant

c. Early feedings of the infant

d. Maintenance of the infant in a neutral thermal environment

Glucose loading of the mother will result in fetal hyperglycemia, which causes insulin release and reactive hypoglycemia. Careful medical support of the antepartum woman diminishes the hypertrophy of the fetal islet cells. Careful monitoring of the infant with early feeding or intravenous infusion of glucose can prevent hypoglycemia. A neutral thermal environment diminishes glucose consumption and, therefore, helps with glucose homeostasis.

Situational Task 8

You are called to the delivery room. A newborn infant seems lethargic and has poor tone with only marginal respiratory effort, but his heart rate is above 100 beats per min. The mother had an uncomplicated pregnancy, and delivery was uncomplicated and vaginal 10 min after spontaneous rupture of membranes. The mother received only pain medications while in labor.

1. What should be first step in the resuscitation of this infant at delivery?

2. What are the steps in the management of this infant?

The answers are

1. Naloxone

2. Ventilatory support

Morphine and other narcotics produce their major toxic effect by suppression of ventilation. Ventilatory support can be necessary initially, but naloxone is a specific antidote and can be very rapidly effective. The effect of naloxone can wear off more quickly than the effects of the drug for which it was given, so careful observation and repeated doses may be necessary.

Situational Task 9

A newborn infant develops respiratory distress immediately after birth. His abdomen is scaphoid. No breath sounds are heard on the left side of his chest, but they are audible on the right and bowel sounds are heard in the chest. Immediate intubation is successful with little or no improvement in clinical status.

1. The is most likely explanation forthis infant's condition?
2. What procedure is most likely to provide a specific etiologic diagnosis ?
3. Conduct differential diagnostics.

The answers are

1. Diaphragmatic hernia occurs with the transmittal of abdominal contents across a congenital or traumatic defect in the diaphragm. In the newborn, this condition results in profound respiratory distress with significant mortality. Prenatal diagnosis is common and, when found, necessitates that the birth take place at a tertiary level center. In the neonate, respiratory failure in the first hours of life, a scaphoid abdomen, and presence of bowel sounds in the chest are common findings. Intensive respiratory support including mechanical ventilation and extracorporeal membrane oxygenation (ECMO) has increased survival. Mortality can be as high as 50% despite aggressive treatment.
2. Emergency chest x-ray.
3. a. Pneumonia b. Cyanotic heart disease c. Choanal atresia d.Pneumothorax

Situational Task 10

A postterm infant is born at home after a prolonged and difficult labor. The maternal grandmother brings the infant to the hospital at 1 h of life because of fast breathing. Grandmother notes that the child spit up some dark brown particulate fluid shortly after birth. Physical examination reveals an infant in marked respiratory distress. Other findings include both an umbilical cord and flaking skin with a yellow-green hue. Chest radiograph reveals patchy infiltrates bilaterally.

1. What is the diagnosis?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.

The answers are

1. Meconium aspiration.
2. Infants who are under perinatal stress will occasionally pass meconium in utero. The aspiration of this meconium into the lungs can cause a chemical pneumonitis and subsequent respiratory distress. These infants are also at risk for developing primary pulmonary hypertension (persistent fetal circulation); some become quite ill and require extracorporeal membrane oxygenation (ECMO). Meconium stains skin and umbilical cords.

3. a. Primary pulmonary hypertension b. Respiratory distress syndrome (hyaline membrane disease) c. Bacterial pneumonia

Methodical materials for the class basic stage supporting.
A professional algorithm of patients management implementation (reference chart) for the practical skills and abilities forming .

№	Task	Sequence of implementation	Remarks and warnings related to self-control
1	To conduct examination of the patient with intrauterine hypoxia and asphyxia in newborn period.	1. To conduct the complaints and disease anamnesis. 2. To gather thoroughly the patient's life anamnesis. 3. To conduct examination of the patient. 4. To investigate cardiovascular system of the patient (palpation, percussion). 5. To conduct auscultation of the heart and of the main vessels. 6. To investigate the pulmonary system (percussion, bronchophony). 7. To conduct lungs auscultation. 8.To investigate the system of digestion.	To pay attention to features of disease course, underlying factors, concomitant diseases etc. To establish the risk factors which can cause the development of disease. To assess patient general condition, position in bed, color and humidity of skin and mucose, presence of neck veins and extremities' swelling. To pay regard to rhythm of pulse, it tension and size on both hands, apex shove, it properties, margins of absolute and relative cardiac dullness, it changes, HR(tachi-or bradicardia, extrasystole),BP. To pay regard to heart tones weakening or amplifying, appearance of murmurs and additional III, IV tones. Pay attention to features of percussion and auscultation in neonates with asphyxia Pay attention to changes in neonates
2	To formulate the preliminary diagnosis.	1. To formulate the preliminary diagnosis 2. To substantiate all components of preliminary diagnosis based on complaints, anamnesis, and examinations.	To formulate the based on modern classification preliminary diagnosis of asphyxia and to substantiate each component of it.

3	To evaluate the parameters of additional laboratory investigations.	1.To evaluate the blood count data. 2. To evaluate the biochemistry data. 3.To evaluate the screening of sera for all components of the TORCH-complex	To pay attention to signs of anemia, leucocytosis, changing of formula, elevation of sedimentation rate. Pay attention to cholesterol, lipids, bilirubin, calcium and glucose levels, detection of pathogen-specific IgM and IgG.
4	To understand the data of additional and laboratory investigation.	To understand the data of ultrasound, X-ray and MRI diagnostics.	To pay special attention to the normal parameters of ultrasound, X-ray and MRI diagnostics in diseases in newborn period.
5	To conduct differential diagnosis.	1.Consistently to find the common signs in complaints, life and disease anamnesis, data of examination, data of laboratory and instrumental investigations in patient and in similar states. 2.To find differences between complaints, information of life and disease anamnesis, examination data, information about the laboratory and instrumental methods of research and in similar nosology. 3. On the basis of found out differences to exclude similar diseases from the list of credible diagnoses. 4. To conduct differential diagnostics according to the above mentioned algorithm among all of nosologies are having the similar signs, among other nervous system diseases in newborn period. 5. Taking into account the impossibility to exclude the	Special attention must be paid to differential diagnosis among the intrauterine hypoxia and asphyxia in newborn period, intrauterine infections and neonatal infections, congenital thyreoid deficiency.

		diagnosis of natal injuries from the list of credible diagnoses to draw a conclusion about most probability of such diagnosis.	
6	To formulate the concluding clinical diagnosis.	1. To formulate the concluding clinical diagnosis. 2. Basing on preliminary diagnosis, additional investigations data, conducted differential diagnosis to substantiate all elements of concluding clinical diagnosis.	Being based on modern classification of natal injuries to formulate a diagnosis, complications of disease and presence of concomitant diseases
7	To prescribe treatment for patients.	1. To prescribe non medicinal treatment 2. To prescribe the medicinal treatment.	To specify the regimen and detailed diet according to the disease. Taking into account age, severity of patient state, the stage of disease, the presence of complications and concomitant pathology, to prescribe modern medicinal treatment in accordance to the standards of intrauterine hypoxia and asphyxia in newborn period therapy.

Materials of control for conclusive classes stage:
The secondary control tests

1. You are called to the delivery room to evaluate a newborn. The pregnancy was complicated by maternal lupus. The infant is pink, vigorous, and in no distress. He has clear breath sounds and is well perfused. His heart rate is 50 beats/min. You obtain an electrocardiogram. Of the following, the MOST likely diagnosis for this infant is

A. atrial fibrillation
B. first-degree heart block
C. second-degree (Wenckebach) heart block
D. third-degree (complete) heart block
E. Wolff-Parkinson-White syndrome

2. In newborn child the cramps and tetany have developed in the first day of life. Ca concentration is 6,2 g/l (N - 8,5-10,5). What from following diagnoses are the least probable?

A. Acute hypoxia of fetus.

B. Big amount of intaked phosphorus
C. Diabetes in mother
D. Hyperparathyropdism in mother
E. Prematurity

3. A 19-year-old primiparous woman develops toxemia in her last trimester of pregnancy and during the course of her labor is treated with magnesium sulfate. At 38 weeks' gestation, she delivers a 2100-g infant with Apgar scores of 1 at 1 min and at 5 at 5 min. Laboratory studies at 18 h of age reveal a hematocrit of 79%, platelet count of 300,000x 10 9/l, glucose 3,8 mmol/l, magnesium 1.5 mmol/l,(normal- 0,7-1.0), and calcium 1.5 mmol/l. Soon after, this the infant has a generalized convulsion. The most likely cause of the infant's seizure is

a. Polycythemia
b. Hypoglycemia
c. Hypocalcemia
d. Hypermagnesemia
e. Thrombocytopenia

4. At 43 weeks' gestation, a long, thin infant is delivered. The infant is apneic, limp, pale, and covered with "pea soup" amniotic fluid. The first step in the resuscitation of this infant at delivery should be

a. Suction of the trachea under direct vision
b. Artificial ventilation with bag and mask
c. Artificial ventilation with endotracheal tube
d. Administration of 100% oxygen by mask
e. Catheterization of the umbilical vein

5. The infant in the preceding question immediately develops tachypnea with cyanosis. She improves somewhat on oxygen but has predominantly thoracic breathing movements, and the chest x-ray, which appears to have been taken inadvertently at expiration, seems normal. The procedure most likely to provide a specific etiologic diagnosis is

a. Venous blood gas
b. CT scan of the head
c. Ultrasound or fluoroscopy of the chest
d. Bronchoalveolar lavage
e. Blood culture

6. A 3-day-old infant born at 32 weeks' gestation and weighing 1700 g (3 lb, 12 oz) has three episodes of apnea, each lasting 20 to 25 s and occurring after a feeding. During these episodes, the heart rate drops from 140 to 100 beats per min, and the child remains motionless; between episodes, however, the child displays normal activity. Blood sugar is 50 mg/dL and serum calcium is normal. The child's apneic periods most likely are

a. Due to an immature respiratory center
b. A part of periodic breathing

c. Secondary to hypoglycemia
d. Manifestations of seizures
e. Evidence of underlying pulmonary disease

7. . A preterm newborn infant is having poor neonatal reflexes, uncoordinated sucking, swallowing, difficulties in feeding. The most important next step to quickly establish the diagnosis is

a. Echocardiogram
b. Ultrosonography
c. Passage of catheter into nose
d. Hemoglobin electrophoresis
e. Bronchoscopic evaluation of palate and larynx

8. A preterm neonate has tachypnea, expiratory grunting, nasal flaring, subcostal retractions, and cyanosis shortly after birth. The mother had rupture of membranes 36 hours prior to vaginal delivery and has developed uterine tenderness and fever.
Of the following, the MOST likely chest radiographic finding in this infant is

A. diffuse reticulogranular pattern
B. displacement of the mediastinum
C. fine curvilinear lucencies
D. overinflation with coarse densities
E. prominent perihilar streaking

9. A newborn is delivered at 32 weeks' gestation by emergent cesarean section following spontaneous placental abruption. During resuscitation in the delivery room, the infant receives 100% oxygen and positive pressure ventilation through an endotracheal tube at a rate of 60 breaths/min. She has adequate chest excursions, but remains poorly perfused. Auscultation reveals a heart rate of 54 beats/min.
Of the following, the MOST appropriate next step in resuscitation is to

A. administer a bolus of albumin
B. administer intratracheal epinephrine
C. begin chest compressions
D. infuse intravenous sodium bicarbonate
E. inject intramuscular naloxone hydrochloride

10. A 1-week-old 2,000-g preterm infant required ventilation for 3 days for respiratory distress syndrome, then was weaned to oxygen hood. He is receiving total parenteral nutrition for feeding intolerance plus small volumes of human milk via a nasogastric tube. Initially, he was treated with 72 hours of intravenous ampicillin and gentamicin for maternal prolonged rupture of membranes Abruptly, he has developed hypotonia, apnea, bradycardia, and lethargy and is reintubated emergently. The serum bicarbonate level is 18 mEq/L (18 mmol/L), but sodium, potassium, chloride, glucose, creatinine, and blood urea nitrogen concentrations are normal. Head ultrasonography at this time shows no evidence of intracranial hemorrhage. Lumbar puncture demonstrates 3 white blood cells/mm^3, negative Gram stain, protein of 30 mg/dL (300 g/L), and glucose of 50 mg/dL (2.8 mmol/L).

Of the following, the MOST likely cause of the patient's symptoms is

A. apnea of prematurity
B. carnitine deficiency
C. epidural hematoma
D. hypermagnesemia
E. Listeria meningitis

11. During resuscitation of a 1.5-kg preterm newborn who has apnea, you notice that inflation pressures of 15 to 20 cm H2O for the first three breaths do not result in good chest wall excursion, and the infant's color remains poor. The heart rate is 90 beats/min. Of the following, the BEST next course of action is

A. administration of intravenous epinephrine
B. administration of intravenous naloxone
C. chest compressions
D. endotracheal intubation
E. increase in inflation pressure

12. A 15-year-old primigravid woman presents to the labor and delivery area at 36 weeks' gestation and reports that her membranes ruptured 4 days ago. She has rare uterine contractions, only fingertip cervical dilation, and no history of fever. Her physician starts oxytocin induction. Ten hours later, she delivers a 3.0-kg female infant whose Apgar scores are 3 at 1 minute and 6 at 5 minutes.

Of the following, the MOST important risk factor for infection is this infant's

A. female gender
B. mother's age
C. 1-minute Apgar score
D. premature rupture of membranes
E. preterm gestation

13. During resuscitation of a 3,5 -kg full-term newborn who has apnea, you notice that inflation pressures of 15 to 20 cm H2O for the first three breaths do not result in good chest wall excursion, and the infant's color remains poor. The heart rate is 60 beats/min. Of the following, the BEST next course of action is

A. administration of intravenous epinephrine
B. administration of intravenous naloxone
C. chest compressions
D. infuse intravenous sodium bicarbonate
E. increase in inflation pressure

14. An infant is delivered by emergent cesarean section because of fetal distress from acute placental abruption. The Apgar scores are 1 and 3 at 1 and 5 minutes, respectively. The cord pH is 6.98, and the base deficit is 20 mEq/L. The infant is resuscitated and admitted to the neonatal intensive care unit for observation of potential injury to the brain and other organs.

Of the following, the MOST frequent complication of perinatal asphyxia is

A. hepatic cholestasis

B. myocardial dysfunction
C. necrotizing enterocolitis
D. pulmonary hemorrhage
E. renal failure

15. A 6-hour-old infant delivered at 41 weeks' estimated gestational age has respiratory distress. The clinical history is significant for meconium-stained amniotic fluid. Chest radiography shows bilateral, diffuse, and coarse infiltrates. The infant is receiving mechanical ventilation with a fraction of inspired oxygen of 1.0 and a high mean airway pressure. An arterial blood gas measurement reveals a partial pressure of oxygen of 36 mm Hg. Of the following, the manifestation MOST helpful for the diagnosis of persistent pulmonary hypertension is

A. differential oxygen saturations between right arm and leg
B. elevated partial pressure of carbon dioxide
C. high-velocity murmur of tricuspid regurgitation
D. precordial hyperactivity
E. response to inhaled nitric oxide

16. . A term newborn has rhythmic, multifocal, clonic seizures lasting 3 minutes on the second day after birth. The intrapartum history is significant for a difficult vertex vaginal delivery assisted with forceps. Apgar scores were 3 and 6 at 1 and 5 minutes, respectively. The infant had appeared well until the onset of seizures. The serum glucose, calcium, and electrolyte concentrations are normal.
Of the following, the MOST useful test for confirmation of the diagnosis is

A. cerebrospinal fluid examination
B. computed tomography
C. cranial ultrasonography
D. electroencephalography
E. fiberoptic transillumination

17. A 4-hour-old term infant has blue hands and feet. His extremities are slightly cold to touch, and chest auscultation reveals normal heart and breath sounds.
Of the following, the MOST appropriate plan of action is to

A. measure blood viscosity
B. measure methemoglobin concentration
C. observe the infant
D. obtain chest radiography
E. order echocardiography

18. A near-term newborn was delivered by emergent cesarean section following placental abruption. Because of respiratory depression, she required resuscitation. The Apgar scores were 1, 4, and 7 at 1, 5, and 10 minutes, respectively. The cord blood pH was 6.9, and the base deficit 18 mEq/L. At 6 hours of age, the infant has clonic seizures, which are controlled with phenobarbital. She is obtunded but arousable and shows proximal muscle hypotonia. Her mother asks about the long-term prognosis for her child.

Of the following, the MOST likely long-term outcome in this infant is

A. cerebral palsy
B. hearing loss
C. normal development
D. seizure disorder
E. visual impairment

19. A 3.7-kg male infant is delivered at 38 weeks' gestation by scheduled repeat cesarean section to a 24-year-old multigravid woman who has intact fetal membranes. The Apgar score is 8 at both 1 and 5 minutes. Physical examination of the infant at 10 minutes after birth reveals mild intercostal retractions and a respiratory rate of 80 breaths/min. He is acyanotic and has a peripheral oxygen saturation of 88% on room air. There is no heart murmur. A chest radiograph reveals expansion of the lungs to nine anterior ribs, perihilar streaking, and a fluid density in the right horizontal fissure. Of the following, the BEST therapy for this infant is

A. intravenous ampicillin and gentamicin
B. intravenous furosemide
C. intravenous prostaglandin E1
D. supplemental oxygen by hood
E. tracheal intubation and surfactant

20. A term infant is delivered following abruptio placenta. He has flaccid tone, gasping respiration, and cyanosis. He does not respond to positioning, drying, warming, suctioning, tactile stimulation, and free-flowing oxygen. His 1-minute Apgar score is 1 (heart rate of 80 beats/min). Of the following, this infant's MOST urgent need is

A. chest compressions
B. intravenous antibiotics
C. intravenous bicarbonate
D. intravenous fluid bolus
E. positive-pressure ventilation

Answers to the secondary control tests
1-D, 2-A, 3-C, 4-A, 5-C, 6-A, 7-C, 8-A, 9-C, 10-C, 11-D, 12-D, 13-C, 14-D, 15-B, 16-C, 17-C, 18-C, 19-D, 20-E.

Materials of the medical support for the students' self training: a reference chart for organization of students independent work with educational literature.

Tasks	Instructions
To study the etiology and pathogenesis of intrauterine hypoxia and asphyxia in newborn period	To enumerate basic etiologic factors, to select the key links of hypoxia and asphyxia in newborn period pathogenesis.
To study clinical manifestations hypoxia and asphyxia in newborn period.	To establish the symptoms and to gather it in the clinical syndromes to put the probable diagnosis of asphyxia

To study diagnostic criteria of hypoxia and asphyxia in newborn period	To make the flow diagram of disease
To study the additional methods of research (laboratory, instrumental)	To work out a plan of patient investigation.
To study the changes in additional investigational methods which are pathognomonic for hypoxia and asphyxia in newborn period.	To enumerate the basic diagnostic criteria of asphyxia according to the data of additional investigational methods.
To conduct differential diagnostics, s to establish a concluding diagnosis	To substantiate the basic components of diagnosis in accordance with the modern classification, and to conduct a differential diagnosis.
To prescribe the individual holiatry to patient with the hypoxia and asphyxia in newborn period. To be able to render the first aid in emergency in asphyxia.	To make the prescribing chart specifying the regimen, diet, medicinal treatment, taking into account the age, severity of patient state, the stage of disease, the presence of complications and concomitant diseases.

THE RECOMMENDED LITERATURE

Basic:

1. Nelson Essentials of Pediatrics, fifth edition, Copyright © 2007 / edited by Richard E. Behrman, Robert M. Kliegman, Ann M. Arvin; senior editor, Waldo E. - Section XII.

2. Rudolph's Pediatrics, 21st Edition. Chapter 2.

3. Key Topics in Neonatology. Richard H. Mupanemunda, Michael Watkinson, BIOS Scientific Publishers Limited, 1999, p.16 -19.

Additional:

1. Martin: Fanaroff and Martin's Neonatal-Perinatal Medicine, 8th ed., Copyright © 2006 Chapters 25, 26, 28 , 42, 43 .

2. Аряєв М.Л. Неонатологія. - Київ: «АДЕФ-Україна.», 2006. - 754 с

3. Шабалов Н.П. Неонатология. Том I - Санкт-Петербург, 2006г.

4. Неонатологія. Навчальний посібник для практичних занять зі студентами медичних факультетів вищих навчальних медичних закладів / Волосовець О.П., Безруков Л.О. та інш. - Чернівці, 2000. - С. 203 - 214.

Theme: **BIRTH TRAUMA.**

Classification of birth trauma. Etiology, pathogenesis, clinical presentation, diagnostics, differential diagnostics, treatment, prophylaxis. Emergency in birth trauma. Prognosis.

Amount of educational hours – 4 academic hours.

I. ACTUALITY OF THEME

The knowledge of birth trauma manifestations (CNS and spinal) in neonates allows to conduct in due time diagnostics, differential diagnostics, medical treatment and prophylaxis.

The continuing advances in antenatal and perinatal care have led to a progressive fall in fetal deaths due to trauma during delivery. However, birth injuries still cause a significant neonatal morbidity of which neonatal staff should be aware. Difficult delivery by any methods is a prime risk factor but so is a very rapid delivery. An increased risk is also attached to preterm delivery, Caesarean delivery and multiple pregnancy. Birth trauma (CNS and spinal) may lead to the mental and physical development retardation and psychical inability of children, that is why the early diagnosis, treatment, rehabilitation and prophylaxis are very important.

Concrete purposes:

1. To determine the etiologic and pathogenesis factors in natal injuries in newborn period.
2. To classify and analyse the typical clinical manifestation of natal injuries in newborn period.
3. To determine the features of natal injuries for newborns and put a preliminary clinical diagnosis.
4. To make the plan of examination and analyse the information about laboratory and instrumental data in the classic course of natal injuries in newborn period.
5. To demonstrate skills of treatment, rehabilitation and prophylaxis in natal trauma in children.
6. To diagnose complications of natal trauma and to diagnose and render an urgent help in emergency in birth trauma.
7. To conduct differential diagnostics of natal injuries and other nervous system diseases in newborn period.
8. To determine nearest and remote prognosis in patients with birth trauma in children.
9. To demonstrate the skills of medical specialist's moral and deontological principles and principles of professional subordination in pediatrics.

II. Classes (pointing of planned mastering level)

1. A student must have a conception (familiarize): α1

- The place of birth trauma in the structure of nervous system diseases in children;
- Statistical information in relation to morbidity, frequency of complications, lethality, the nearest and remote prognosis in patients with birth trauma;
- The history of scientific studying and the contribution of domestic scientists;

2. A student must know (master): α2

- causes of natal injuries in newborn period;
- key links of natal injuries in newborn period;
- key links of the nervous system diseases pathogenesis in newborn period ;
- classification of birth trauma;
- classical clinical manifestation of natal injuries in newborn period ;
- clinical syndromes in dependence of natal trauma period ;
- laboratory and instrumental diagnosis of natal trauma ;
- complications of natal trauma;
- treatment principles of natal injuries in children.

3. A student must master: α3

Skills:

- Collection of complaints and anamnesis of disease;
- Examination of patient with natal injuries and revealing the main symptoms and syndromes;.
- To formulate and substantiate the preliminary diagnosis;
- Determination of laboratory and instrumental inspection plan of patient's examination (according to diagnostics' standards);

Abilities:

-To interpret the results of laboratory and instrumental tests.

- To conduct differential diagnosis among natal injuries and other nervous system diseases in newborn period.
- To give recommendations in relation to the patient's regimen and diet with the natal injuries , taking into account the stage of the disease, severity of the state and concomitant pathology;
- To complete the treatment plan in natal injuries according to standards taking into account the stage of the disease, complications and concomitant pathology.
- To give the first aid in extreme situations in newborn with natal injuries .
- To realize the life prognosis of patients with natal injuries

III. Aims of personality development (educative aims):

- A student must learn to adhere rules of behaviour and principles of medical etiquette and deontology, to develop bedside manner;
- Be able to set a psychological contact with a patient and his family;

- To master the sense of professional responsibility for a timely and adequate medicare.

IV. Interdisciplinary integration:

Subject	To know	Be able
1. Basic		
Human anatomy	Structure of nervous system in baby and children in the first months of life.	To estimate the neurological state in child with the signs of natal injuries
Normal physiology	Normal physiology of nervous system in baby and children in the first months of life, normative indices of laboratory and instrumental investigational methods and their assessment.	To assess the data of laboratory and instrumental investigational methods
Physiopathology	Key links of pathogenesis of nervous system diseases in baby and children in the first months of life.	To estimate the function of nervous system in baby and children in the first months of life.
Pathologic anatomy	Morphological features of nervous system diseases development depending of the stage of the disease .	To analyse and interpret the information about clinical examination and about additional methods of investigation
Pharmacology	Pharmacokinetics and pharmacodynamics, the side effects of preparations used in the treatment of natal injuries	To prescribe age- dependent treatment of patient, taking into account individual features and period of disease, to establish the individual regimen of preparations taking and dosage. To be able to make a prescription..
Propedeutical pediatrics.	Basic stages and methods of patient clinical examination	To collect complaints, anamnesis vitae et morbi, to find out the basic risk factors of nervous system diseases, conduct patient examination, to reveal the clinical signs of nervous system diseases, to interpret the data about additional methods of investigation.
Radiology	Normal parameters of ultrasound, X-ray and magnetic resonance	To interpret the data of ultrasound, X-ray and MRI diagnostics

	imaging (MRI) in diseases in newborn period.	
2. Interdisciplinary integration		
Birth trauma	Clinical signs of birth trauma	To establish specific clinical signs of birth trauma manife-stations (CNS and spinal) and to conduct differential diagnosis to other nervous system diseases in newborn period.
Intrauterine hypoxia and asphyxia in newborn period	Clinical signs of intrauterine hypoxia and asphyxia in neonates	To establish specific clinical signs of intrauterine hypoxia and asphyxia in neonates and to conduct differential diagnosis with the birth trauma
Intrauterine infections and neonatal infections	Clinical signs of intrauterine infections in neonates in dependence on time of transplacental transmission.	To determine the clinical signs of intrauterine infections and neonatal infections and conduct differential diagnosis with the birth trauma

V. Contents of theme:

NATAL TRAUMA

Cranial Injuries

Caput succedaneum is a diffuse, sometimes ecchymotic, edematous swelling of the soft tissues of the scalp involving the portion presenting during vertex delivery. It may extend across the midline and across suture lines. The edema disappears within the first few days of life. Analogous swelling, discoloration, and distortion of the face are seen in face presentations. No specific treatment is needed, but if there are extensive ecchymoses, phototherapy for hyperbilirubinemia may be indicated. Molding of the head and overriding of the parietal bones are frequently associated with caput succedaneum and become more evident after the caput has receded but disappear during the first weeks of life. Rarely, a hemorrhagic caput may result in shock and require blood transfusion.

Erythema, abrasions, ecchymoses and subcutaneous fat necrosis of facial or scalp soft tissues may be seen after forceps deliveries. Their location depends on the area of application of the forceps. Ecchymoses may be seen after manipulative deliveries and occasionally in premature infants for no discernible reason.

Subconjunctival and retinal hemorrhages are frequent, and petechiae of the skin of the head and neck are common. All are probably secondary to a sudden increase in intrathoracic pressure during passage of the chest through the birth canal. Parents should be assured that they are temporary and the result of normal hazards of delivery.

Cephalohematoma is a subperiosteal hemorrhage, hence always limited to the surface of 1 cranial bone. There is no discoloration of the overlying scalp, and swelling is usually not visible until several hours after birth, since subperiosteal bleeding is a slow process. An underlying skull fracture, usually linear and not depressed, is occasionally associated with cephalohematoma. Cranial meningocele may be differentiated from cephalohematoma by pulsation, increased pressure on crying, and the roentgenographic evidence of bony defect. Most cephalohematomas are resorbed within 2 wk –3 mo, depending on their size. They may begin to calcify by the end of the 2nd wk. A sensation of central depression suggesting but not indicative of an underlying fracture or bony defect is usually encountered on palpation of the organized rim of a cephalohematoma. A few remain for years as bony protuberances and are detectable roentgenographically as widening of the diploic space; cystlike defects may persist for months or years. Despite these residuals, cephalohematomas require no treatment, although phototherapy may be necessary to ameliorate hyperbilirubinemia. Incision and drainage are contraindicated because of the risk of introducing infection in a benign condition. A massive cephalohematoma may rarely result in blood loss severe enough to require transfusion. It may also be associated with a skull fracture, coagulopathy, and intracranial hemorrhage.

Fractures of the skull may occur as a result of pressure from forceps or from the maternal symphysis pubis, sacral promontory, or ischial spines. Linear fractures, the most common, cause no symptoms and require no treatment. Depressed fractures are usually indentations of the calvarium similar to a dent in a ping-pong ball; usually they are a complication of forceps delivery or fetal compression. The infant may be asymptomatic unless there is associated intracranial injury; it is advisable to elevate severe depressions to prevent cortical injury from sustained pressure. Fracture of the occipital bone with separation of the basal and squamous portions almost invariably causes fatal hemorrhage owing to disruption of the underlying sinuses. It may result during breech deliveries from traction on the hyperextended spine of the infant with the head fixed in the maternal pelvis.

Intracranial (Intraventricular) Hemorrhage

ETIOLOGY AND EPIDEMIOLOGY. Intracranial hemorrhage may result from trauma or asphyxia and, rarely, from a primary hemorrhagic disturbance or congenital vascular anomaly. Traumatic epidural, subdural, or subarachnoid hemorrhage is especially likely when the fetal head is large in proportion to the size of the mother's pelvic outlet; when for other reasons the labor is prolonged; when there are breech or precipitate deliveries; or when there is injudicious mechanical interference with delivery. Massive subdural hemorrhages, often associated with tears in the tentorium cerebelli or, less frequently, in the falx cerebri, are rare but are encountered more

often in full-term than in premature infants. Primary hemorrhagic disturbances and vascular malformations are rare and usually give rise to subarachnoid or intracerebral hemorrhage. Intracranial bleeding may be associated with disseminated intravascular coagulopathy, isoimmune thrombocytopenia, and neonatal vitamin K deficiency (especially in infants born to mothers receiving phenobarbital or phenytoin). Intracranial hemorrhages often involve the ventricles (intraventricular hemorrhage) of premature infants delivered spontaneously without apparent trauma.

PATHOGENESIS OF INTRAVENTRICULAR HEMORRHAGE (IVH). IVH in the premature infant occurs in the gelatinous subependymal germinal matrix. This periventricular area is the site of embryonal neurons and fetal glial cells, which migrate to the cortex. Immature blood vessels in this highly vascular area may be subjected to various forces that, together with poor tissue vascular support, predispose the premature infant to IVH. By term, the germinal matrix has become attenuated and the tissue's vascular support has strengthened. Predisposing factors or events for IVH include prematurity, respiratory distress syndrome, hypoxic ischemic or hypotensive injury, reperfusion of damaged vessels, increased or decreased cerebral blood flow, reduced vascular integrity, increased venous pressure, pneumothorax, hypervolemia, and hypertension. These factors result in rupture of the germinal matrix blood vessels. Similar injurious factors (hypoxic-ischemic-hypotensive) may produce cortical intraparenchymal echodensities (IPE) due to hemorrhagic infarction and later development of periventricular leukomalacia (PVL). PVL with or without severe IVH is the result of necrosis of the periventricular white matter and damage to the corticospinal fibers in the internal capsule.

CLINICAL MANIFESTATIONS. The incidence of IVH increases with decreasing birth weight: 60–70% of 500- to 750-g infants and 10–20% of 1,000- to 1,500-g infants. IVH is rarely present at birth; however, 80–90% of cases occur between birth and the 3rd day of life. Twenty to forty per cent of cases progress during the 1st wk of life. Delayed hemorrhage may occur in 10–15% of patients after the 1st wk of life. New-onset IVH is rare after the 1st mo of life regardless of birthweight. The most common symptoms are diminished or absent Moro reflex, poor muscle tone, lethargy, apnea, and somnolence. In premature infants with intraventricular hemorrhage there is often a precipitous deterioration on the 2nd or 3rd day of life. Periods of apnea, pallor, or cyanosis, failure to suck well, abnormal eye signs, a high-pitched shrill cry, muscular twitchings, convulsions, decreased muscle tone, paralyses, metabolic acidosis, shock, and a decreased hematocrit or its failure to increase after transfusion may be the first indications. The fontanel may be tense and bulging. Severe neurologic depression progresses to coma after more severe intraventricular hemorrhages, with associated hemorrhage in the cerebral cortex and ventricular dilation. In a small percentage of cases there may be no clinical manifestations.

PVL is usually asymptomatic until the neurologic sequelae of white matter necrosis becomes manifest in later infancy as spastic diplegia. As a result of nonhemorrhagic ischemic injury, PVL often coexists with IVH. PVL may be present at birth but usually occurs later as an early echo-dense phase–10 days of life) followed by the typical echo-lucent (cystic) phase 20 days of life).

DIAGNOSIS. Intracranial hemorrhage is diagnosed on the basis of the history, clinical manifestations, transfontanel cranial ultrasonography or computed tomography (CT), and knowledge of the birthweight-specific risks of the type of hemorrhage. The diagnosis of subdural hemorrhage in a LGA term infant with cephalopelvic disproportion may be delayed 1 mo until the chronic subdural fluid volume expands, producing megalocephaly, frontal bossing, bulging fontanel, seizures, and anemia. Alternatively, the well neonate with a seizure of short duration may have a benign subarachnoid hemorrhage.

Although preterm infants with IVH manifest rapid shock, mottling, anemia, coma, or a bulging fontanel, many signs of IVH are nonspecific or absent. Therefore, it is recommended that the premature infant be evaluated with real-time cerebral ultrasonography through the anterior fontanel to detect IVH. Infants weighing under 1,000 g are at high risk for IVH and should be examined within the first 3{endash}–5 days of life and again the following week. The ultrasound examination will also detect the precystic and cystic symmetric lesions of PVL and the asymmetric intraparenchymal echogenic lesions of cortical hemorrhagic infarction. Furthermore, the delayed development of cortical atrophy, or porencephaly, and the severity, progression, or regression of posthemorrhagic hydrocephalus can be determined with ultrasonography.

Four levels of increasing severity of IVH are defined by ultrasound for LBW infants: Grade I is bleeding confined to the germinal matrix{endash}–subependymal region or to less than 10% of the ventricle; grade II is intraventricular bleeding with 10–50% filling of the ventricle; grade III is more than 50% involvement with dilated ventricles; grade IV includes grade III, with corticoperiventricular intraparenchymal lesions that are not necessarily a direct extension of the IVH. Seventy-five per cent of infants with IVH are grade I–II. Severe IVH is independently associated with immaturity and the severity of respiratory distress syndrome (RDS). Immature infants without RDS are at risk for IVH, whereas infants with severe RDS are at greater risk than those with mild or no RDS at the same gestational age.

CT scan is indicated for term infants in whom the diagnosis is suspected, since ultrasound may not reveal intraparenchymal hemorrhage or infarction. Lumbar puncture is indicated in the presence of signs of increased intracranial pressure or deteriorating clinical condition to identify gross subarachnoid hemorrhage or to rule out the possibility of bacterial meningitis; the cerebrospinal fluid usually has elevated

protein levels with many red blood cells. Not infrequently there is hypoglycorrhachia and a mild lymphocytosis. Since a small amount of bleeding into the cerebrospinal fluid often occurs in the course of normal and even cesarean deliveries, small numbers of red blood cells or slight xanthochromia in subarachnoid fluid does not necessarily indicate significant intracranial hemorrhage. Conversely, the subarachnoid fluid may be absolutely clear in the presence of severe subdural or intracerebral hemorrhage when there is no communication with the subarachnoid space.

PROGNOSIS. Patients with massive hemorrhage associated with tears of the tentorium or falx cerebri rapidly deteriorate and may die after birth. In utero hemorrhage associated with maternal idiopathic or, more often, fetal alloimmune thrombocytopenia may occur as severe cerebral hemorrhage or a porencephalic cyst after resolution of a fetal cortical hemorrhage.

Most infants with IVH and acute ventricular distention do not develop posthemorrhagic hydrocephalus. Ten to fifteen per cent of LBW neonates with IVH have hydrocephalus, which initially may be present without clinical signs such as enlarging head circumference, apnea, bradycardia, lethargy, bulging fontanel, or widely split sutures. In infants who develop symptomatic hydrocephalus, clinical signs may be delayed 2{endash}–4 wk despite progressive ventricular distention and compression (thinning) of the cerebral cortex. Posthemorrhagic hydrocephalus is arrested or regresses in 65% of affected infants.

Progressive hydrocephalus requiring ventricular-peritoneal shunting, gestational age of less than 30 wk, prolonged mechanical ventilation (> 28 days), intraparenchymal hemorrhage, and extensive PVL are associated with a poor prognosis. Because PVL and intraparenchymal bleeding represent hypoxic ischemic injury, they are independent risk factors for spastic diplegia and other motor deficits. IVH with intraparenchymal echo-densities greater than 1 cm are associated with a high mortality and a high incidence of motor and cognitive deficits. Grade I{endash}–II IVH may be due to factors other than severe hypoxia-ischemia, and in such a case it has a lower risk of long-term neurologic sequelae if it is unassociated with PVL or intraparenchymal hemorrhage.

PREVENTION. The incidence of traumatic intracranial hemorrhage may be reduced by judicious management of cephalopelvic disproportion and operative (forceps, cesarean section) delivery. Fetal or neonatal hemorrhage due to maternal idiopathic thrombocytopenic purpura (ITP) or alloimmune thrombocytopenia may be prevented by maternal treatment with steroids, intravenous immunoglobulin, or fetal platelet transfusion. The incidence of IVH may possibly be reduced by neonatal administration of low-dose indomethacin and vitamin E. Wide fluctuations of blood pressure should be avoided. Vitamin K should be given prior to delivery to all women receiving phenobarbital or phenytoin during the pregnancy.

TREATMENT. IVH associated with hypoxic-ischemic encephalopathy is frequently associated with multiple organ system dysfunction. Seizures are treated with anticonvulsant drugs, anemia-shock requires transfusion with packed red blood cells or fresh frozen plasma, and acidosis is treated with judicious and slow administration of 1{endash}–2 mEq/kg sodium bicarbonate. Serial lumbar punctures have no role during the acute hemorrhage; however, repeated lumbar punctures may reduce the symptoms of posthemorrhagic hydrocephalus. Repeat lumbar punctures may increase the risk of nosocomial meningitis. Neurosurgical placement of an external ventriculostomy catheter may be needed in the early stage of uncontrolled symptomatic hydrocephalus. After the protein content of the ventricular fluid declines, a permanent ventricular-peritoneal shunt is put in place.

Symptomatic subdural hemorrhage in large term infants should be treated by removing the subdural fluid collection by means of a spinal needle placed through the lateral margin of the anterior fontanel. In addition to birth trauma, child abuse should be suspected in all infants with subdural effusions.

Spine and Spinal Cord

Strong traction exerted when the spine is hyperextended or when the direction of pull is lateral, or forceful longitudinal traction on the trunk while the head is still firmly engaged in the pelvis, especially when combined with flexion and torsion of the vertical axis, may produce fracture and separation of the vertebrae. Such injuries, rarely diagnosed clinically, are most likely to occur when difficulty is encountered in delivering the shoulders in cephalic presentations and the head in breech presentations. The injury occurs most commonly at the level of the 4th cervical vertebra with cephalic presentations and the lower cervical{endash}–upper thoracic vertebrae with breech presentations. Transection of the cord may occur with or without vertebral fractures; hemorrhage and edema may produce neurologic signs that are indistinguishable from those of transection except that they are not permanent. There is areflexia, loss of sensation, and complete paralysis of voluntary motion below the level of injury, although the persistence of a withdrawal reflex mediated through spinal centers distal to the area of injury is frequently misinterpreted as representing voluntary motion. If the injury is severe, the infant, who from birth may be in poor condition owing to respiratory depression, shock, or hypothermia, may deteriorate rapidly to death within several hours before neurologic signs are obvious. Alternatively, the course may be protracted with symptoms and signs appearing at birth or later in the 1st wk; immobility, flaccidity, and associated brachial plexus injuries may not be recognized for several days. Constipation may also be present. Some infants survive for prolonged periods, their initial flaccidity, immobility, and areflexia being replaced after several weeks or months by rigid

flexion of extremities, increased muscle tone, and spasms. Apnea on day 1 and poor motor recovery by 3 mo are poor prognostic signs.

The differential diagnosis includes amyotonia congenita and myelodysplasia associated with spina bifida occulta. The diagnosis is confirmed by ultrasonography or magnetic resonance imaging (MRI). Treatment of the survivors is supportive, and they often remain permanently injured. When there is compression from a fracture or dislocation, the prognosis is related to the time elapsing before the compression is relieved.

Peripheral Nerve Injuries

BRACHIAL PALSY. Injury to the brachial plexus may cause paralysis of the upper arm with or without paralysis of the forearm or hand or, more commonly, paralysis of the entire arm. These injuries occur in macrosomic infants and when lateral traction is exerted on the head and neck during delivery of the shoulder in a vertex presentation, when the arms are extended over the head in a breech presentation, or when there is excessive traction on the shoulders. Approximately 45% are associated with shoulder dystocia.

In **Erb-Duchenne paralysis** the injury is limited to the 5th and 6th cervical nerves. The infant loses the power to abduct the arm from the shoulder, to rotate the arm externally, and to supinate the forearm. The characteristic position consists of adduction and internal rotation of the arm with pronation of the forearm. The power of extension of the forearm is retained, but the biceps reflex is absent; the Moro reflex is absent on the affected side . There may be some sensory impairment on the outer aspect of the arm. The power in the forearm and the hand grasp are preserved unless the lower part of the plexus is also injured; the presence of the hand grasp is a favorable prognostic sign. When the injury includes the phrenic nerve, alteration of the diaphragmatic excursion may be observed fluoroscopically.

Klumpke paralysis is a rarer form of brachial palsy; injury to the 7th and 8th cervical nerves and the 1st thoracic nerve produces a paralyzed hand, and ipsilateral ptosis and miosis (Horner syndrome) if the sympathetic fibers of the 1st thoracic root are also injured.

The mild cases may not be detected immediately after birth. Differentiation must be made from cerebral injury; from fracture, dislocation, or epiphyseal separation of the humerus; and from fracture of the clavicle. MRI will demonstrate nerve root rupture or avulsion.

The prognosis depends on whether the nerve was merely injured or was lacerated. If the paralysis was due to edema and hemorrhage about the nerve fibers, there should be a return of function within a few months; if due to laceration, permanent damage may result. The involvement of the deltoid is usually the most serious

problem and may result in a shoulder drop secondary to muscular atrophy. In general, paralysis of the upper arm has a better prognosis than paralysis of the lower arm.

Treatment consists of partial immobilization and appropriate positioning to prevent development of contractures. In upper arm paralysis, the arm should be abducted 90 degrees, with external rotation at the shoulder and with full supination of the forearm and slight extension at the wrist with the palm turned toward the face. This may be done with a brace or splint during the first 1–2 wk. Immobilization should be intermittent through the day while the infant is asleep and between feedings. In lower arm or hand paralysis, the wrist should be splinted in a neutral position and padding placed in the fist. When the entire arm is paralyzed, the same treatment principles should be followed. Gentle massage and range of motion exercises may be started by 7–10 days of age. Infants should be followed closely with active and passive corrective exercises. If the paralysis persists without improvement for 3–6 mo, neuroplasty, neurolysis, end-to-end anastomosis, or nerve grafting offer hope for partial recovery.

PHRENIC NERVE PARALYSIS. Phrenic nerve injury (3rd, 4th, 5th cervical nerves) with diaphragmatic paralysis must be considered when cyanosis and irregular and labored respirations develop. Such injuries, usually unilateral, are associated with ipsilateral upper brachial palsy. Because breathing is thoracic in type, the abdomen does not bulge with inspiration. Breath sounds are diminished on the affected side. The thrust of the diaphragm, which often may be felt just under the costal margin on the normal side, is absent on the affected side. The diagnosis is established by ultrasonography or fluoroscopic examination, which reveals the elevation of the diaphragm on the paralyzed side and seesaw movements of the two sides of the diaphragm during respiration.

There is no specific treatment; the infant should be placed on the involved side and given oxygen if necessary. Initially, intravenous feedings may be needed; later, progressive gavage or oral feedings may be started depending on the infant's condition. Pulmonary infections are a serious complication. Recovery usually occurs spontaneously by 1–3 mo; rarely, surgical plication of the diaphragm may be indicated.

FACIAL NERVE PALSY. Usually, facial palsy is a peripheral paralysis that results from pressure over the facial nerve in utero, from efforts during labor, or from forceps during delivery. Rarely nonobstetric, it may result from nuclear agenesis of the facial nerve. Peripheral paralysis is flaccid and, when complete, involves the entire side of the face, including the forehead. When the infant cries, there is movement only on the nonparalyzed side of the face, and the mouth is drawn to that side. On the affected side the forehead is smooth, the eye cannot be closed, the nasolabial fold is absent, and the corner of the mouth droops. The forehead will wrinkle on the affected

side with central paralysis, since only the lower two thirds of the face is involved. Usually there are also other manifestations of intracranial injury, most commonly a 6th nerve palsy. The prognosis depends upon whether the nerve was injured by pressure or whether the nerve fibers were torn. Improvement occurs within a few weeks in the former instance. Care of the exposed eye is essential. Neuroplasty may be indicated when the paralysis is persistent. Facial palsy may be confused with the absence of the depressor muscles of the mouth, which is a benign problem.

Other peripheral nerves are seldom injured in utero or at birth except when they are involved in fractures or hemorrhages.

Viscera

The liver is the only internal organ other than the brain that is injured with any frequency during birth. The damage usually results from pressure on the liver during delivery of the head in breech presentations. Large infant size, intrauterine asphyxia, coagulation disorders, extreme prematurity, and hepatomegaly are contributing factors. Incorrect cardiac massage is a less frequent cause. The liver is ruptured when there is formation of a subcapsular hematoma, which may tamponade further bleeding. The infant usually appears normal for the first 1–3 days. Nonspecific signs related to loss of blood into the hematoma may appear early and include poor feeding, listlessness, pallor, jaundice, tachypnea, and tachycardia. A mass may be palpable in the right upper quadrant; the abdomen may appear blue. The hematoma may be large enough to cause anemia. Shock and death may occur if the hematoma breaks through the capsule into the peritoneal cavity, reducing pressure and allowing fresh hemorrhage. Early suspicion by means of ultrasonographic diagnosis and prompt supportive therapy can decrease the mortality of this disorder. Surgical repair of a laceration may be required.

Rupture of the spleen may occur alone or in association with rupture of the liver. The causes, complications, treatment, and prevention are similar.

Although adrenal hemorrhage occurs with some frequency, especially after breech delivery in LGA or infants of diabetic mothers, its cause is undetermined; it may be due to trauma, anoxia, or severe stress, as in overwhelming infections. Ninety per cent are unilateral; 75% are right-sided. Calcified central hematomas of the adrenal have been identified roentgenographically or at autopsy in older infants and children, suggesting that not all adrenal hemorrhages are immediately fatal. In severe cases the diagnosis is usually made at postmortem examination. The symptoms are profound shock and cyanosis. There may be a mass in the flank with overlying skin discoloration; jaundice may also develop. If adrenal hemorrhage is suspected, abdominal ultrasonography may be helpful, and treatment for acute adrenal failure may be indicated

Fractures

CLAVICLE. This bone is fractured during labor and delivery more frequently than any other bone; it is particularly vulnerable when there is difficulty in delivery of the shoulder in vertex presentations and of the extended arms in breech deliveries. The infant characteristically does not move the arm freely on the affected side; crepitus and bony irregularity may be palpated, and occasionally discoloration is visible over the fracture site. The Moro reflex is absent on the affected side, and there is spasm of the sternocleidomastoid muscle with obliteration of the supraclavicular depression at the site of the fracture. In greenstick fractures there may be no limitation of movement, and the Moro reflex may be present. Fracture of the humerus or brachial palsy may also be responsible for limitation of movement of an arm and absence of a Moro reflex on the affected side. The prognosis is excellent. Treatment, if any, consists of immobilization of the arm and shoulder on the affected side. A remarkable degree of callus develops at the site within a week and may be the first evidence of the fracture.

EXTREMITIES

In fractures of the long bones spontaneous movement of the extremity is usually absent. The Moro reflex is also absent from the involved extremity. There may be associated nerve involvement. Satisfactory results of treatment for a fractured humerus are obtained with 2–4 wk of immobilization during which the arm is strapped to the chest, a triangular splint and a Velpeau bandage are applied, or a cast is applied. For fracture of the femur, good results are obtained with traction-suspension of both lower extremities, even if the fracture is unilateral; the legs, immobilized in a spica cast, are attached to an overhead frame. Splints are effective for treatment of fractures of the forearm or leg. Healing is usually accompanied by excess callus formation.The prognosis is excellent for fractures of the extremities. Fractures in preterm infants are related to osteopenia .

Dislocations and epiphyseal separations rarely result from birth trauma. The upper femoral epiphysis may be separated by forcible manipulation of the infant's leg as, for example, in breech extraction or after version. There is swelling, slight shortening, limitation of active motion, painful passive motion, and external rotation of the leg. The diagnosis is established roentgenographically. The prognosis is good for the milder injuries, but coxa vara frequently results from extensive displacement.

NOSE. The most prevalent injury of the nose is a dislocation of the cartilaginous portion of the septum from the vomerine groove and the columella. The infant may have difficulty in nursing and some impairment in nasal respiration. On physical examination, the nares appear asymmetric and the nose flattened. An oral airway rarely is needed, and surgical consultation should be obtained for definitive treatment.

VI. Plan and organizational structure of classes.

№	Basic stages of classes, their function and maintenance	Educational aims are in the levels of mastering	Methods of control and studies	Educational materials	Distributing of time in minutes
1 2 3	Preparatory stage Organizational measures Raising of educational aims and motivation Control of basic knowledges and skills level: 1.Etiology of birth trauma . 2 Key links of birth trauma pathogenesis 3. Classification of birth trauma. 4. Typical manifestation of birth trauma ,stages of disease, feature of clinic and diagnostics 5. Laboratory and instrumental diagnosis of birth trauma. 6.Clinical syndromes of birth trauma . 7.Treatment principles of birth trauma .	 α2	 Individual oral questioning Test control of the second level Individual oral questioning Typical situational task of 2 level	I. «Actuality of theme» II. «Educational aims» The second level tests The table «classification of natal injuries in newborn period» Structurally logical chart of natal injuries Typical situational task of 2 level Tests of 2 level Typical situational tasks of 2 level Kit of medicines.	3 min. 12 min. 20 min
4	Basic stage of professional skills and abilities forming: 1.To conduct the patient management with birth trauma, to take complaints and anamnesis. 2.To conduct the patient examination, to detect main symptoms and syndromes of birth trauma . 3.To formulate and substantiate the preliminary diagnosis 4.To compose the plan of patient laboratory and instrumental investigation. 5.Interpret the results of laboratory and instrumental investigation. 6.To conduct differential diagnosis among natal injuries and other nervous system diseases in newborn period.	α3 α3 α3 α3 α3 α3	 Practical professional training Practical professional training Practical professional training Practical professional training The practical professional training.Tests and third level control The practical professional	 Patient Patient Case history A reference chart for forming of professional abilities. Case history. A reference chart for forming of	 115 min

	7.To give the recommendations for regimen and diet of patient. 8.To compose the plan of natal injuries patient treatment taking into account the stage of disease and presence of complications. 9.To be able to render the first aid in extreme situations	α3	training in solving of non typical clinical situations. Third level test control. Practical professional training. The practical professional training in solving of non typical clinical situations. Third level test control.	professional abilities. Case history. A reference chart for forming of professional abilities. Situational typical tasks of 3 level.Third level tests. Prescribing chart The third level non typical situational tasks. Treatment algorithm for the patients with natal injuries The First aid algo-rithm in natal injuries	
5 6 7	**Concluding stage**. Control and correction of professional abilities and skills. Working out the totals of class. Home work (basic and additional literature on the topic)		Analysis of clinical work. The practical pro-fessional training in solving of non typical clinical situations. Estimation of clinical work.	Clinical work. The third level non typical situational tasks. A reference chart for independent work with literature	30 min

Questions for elementary level of knowledge control

1. Name the main causes of birth injuries?.
2. Point out the classification of birth trauma.
3. What the main clinical manifestations of natal trauma in intracranial and spinal injuries?
4. Define diagnostic and differential diagnostic measures in natal injuries.
5. What is the common treatment tactics in CNS and spinal injuries?
6. What are the main consequences of natal trauma in later periods of childhood and their prophylaxis ?

The primary control tests

1. In a child there is formation on his head is soft with consistency, spreads outside the cranial bone. In examination after 2 day this formation was not detected.
What is the diagnosis?
A.Subdural hematoma
B.Cephalohematoma
C.Cerebral hernia
D. Epidural hematoma
E. Caput succedaneum

2. In a child has delivered with a severe natal trauma of CNS in age of 5 days take place an anxiety, periodically there are short-term clonic and tonic cramps. What period of natal trauma in a child?

A. Subacute
B. Acute
C. The period of the residual phenomena
D. The early regenerative period
E. The late regenerative period

3.In a prematurely born child has delivered with a severe natal trauma of CNS, in age of 25 days take place an anxiety, periodically there are short-term clonic and tonic cramps. What period of natal trauma in a child?

A. Subacute
B. Acute
C. The period of the residual phenomena
D. The early regenerative period
E. The late regenerative period

4. In a child has delivered with a severe natal trauma of CNS, in the age of 1,5 year there is psychomotor retardation, pallor of skin, rapid fatigueability.,
What period of natal trauma takes place in this case?

A. Subacute
B. Acute
C. The period of the residual phenomena
D. The early regenerative period
E. The late regenerative period

5. In a baby to the day of excerption remains a cephalohematoma of considerable dimensions. What is the tactic?

A Introduction to the hematoma of sclerosing solutions.
B. Not to treat
C. To direct after the excerption to neuro-surgeon.
D.CT of cerebrum
E. LP in a maternity hospital.

6. In a child has delivered with a severe natal trauma of CNS in age of 5 month take place an anxiety, moderate developmental retardation, periodically there is infringement of microcirculation, marble of skin, motive disturbances . What period of natal trauma in a child?

A. Subacute
B.The period of the residual phenomena
C.Acute
D. The early regenerative period
E. The late regenerative period

7. In a child has delivered with natal trauma of CNS in age of 4 month the head dimensions are correspond to age, take place the mild hyperesthesia, anxiety. Lumbar

puncture: the liquor follows a jet. What syndrome of natal trauma takes place in this case?

A. Convulsive
B. Hydrocephalic
C. Asthenoneurotic
D. Hypertensive
E. Depression of CNS.

8. In a child on a 3 day after delivery a severe vomit appeared ,anxiety , strain of the big fontanel, divergence of cranial seams, Grefe symptom, positive Lessage symptom, in lumbar puncture in a liquor the blood is revealed. What type of intracranial hemorrhage it is needed to diagnose in this case?

A. In brain parenchyma
B.Intraventricular
C.Subdural
D.Subarachnoidal
E.Epidural

9. In prematured child on 2 day after birth there were tonic cramps with the subsequent development of opistotonus, has stopped to suck independently, anisocoria, oppression of reflexes were admit An intraventricular hemorrhage is suspected. What test will allow confirming a diagnosis?

A. X-ray of skull.
B. Diafanoscopy.
C. Neurosonografy.
D. Reovasography of cerebral vessels
E. All listed above.

10. In newborn child to the end of 1 day of life on the basis of clinic survey and according to the data of neurosonogaphy an intraventricular hemorrhage suspected. What preparations are listed below pathogenically indicated in this case?

A. Magnesias sulfas
B. Cephasolinum
C. Dicinonum
D. Calcium gluconat
E. ATP
F. All listed above

11. A 1-month-old comatose infant with multiple broken bones in various stages of healing, bulging anterior fontanelle, and retinal hemorrhages. (SELECT 1 ABNORMALITY)

a. Intraventricular hemorrhage
b. Caput succedaneum
c. Subdural hemorrhage
d. Subarachnoid hemorrhage
e. Cephalohematoma

12. A 13-day-old female infant delivered by midforceps after occiput-posterior presentation has massive, persistently enlarging cephalhematoma. Indicate therapy

A. Therapy is not indicated
B. Surgical drainage
C. Introduction to the hematoma of sclerosing solutions.
D. Bronchoalveolar lavage
E. Phototherapy

13. A term newborn has rhythmic, multifocal, clonic seizures lasting 3 minutes on the second day after birth. The intrapartum history is significant for a difficult vertex vaginal delivery assisted with forceps. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The infant had appeared well until the onset of seizures. The serum glucose, calcium, and electrolyte concentrations are normal.
Of the following, the MOST useful test for confirmation of the diagnosis is

A. cerebrospinal fluid examination
B. computed tomography
C. cranial ultrasonography
D. electroencephalography
E. fiberoptic transillumination

14. A term newborn has multifocal, rhythmic, migratory clonic seizures at 6 hours after birth. The infant is lethargic, hypotonic, and hyperreflexic. She has a weak suck and constricted but reactive pupils.
Of the following, the MOST likely cause of seizures in this infant is

A. bacterial meningitis
B. benign familial seizures
C. hypocalcemia
D. perinatal asphyxia
E. subarachnoid hemorrhage

15. A near-term newborn was delivered by emergent cesarean section following placental abruption. Because of respiratory depression, she required resuscitation. The Apgar scores were 1, 4, and 7 at 1, 5, and 10 minutes, respectively. The cord blood pH was 6.9, and the base deficit 18 mEq/L. At 6 hours of age, the infant has clonic seizures, which are controlled with phenobarbital. She is obtunded but arousable and shows proximal muscle hypotonia. Her mother asks about the long-term prognosis for her child. Of the following, the MOST likely long-term outcome in this infant is

A. cerebral palsy
B. hearing loss
C. normal development
D. seizure disorder
E. visual impairment

16. A term newborn, one of twins, is plethoric and has a central venous hematocrit of 72% (0.72). Of the following, the MOST likely complication in this infant is

A. disseminated coagulopathy
B. hypoglycemia
C. necrotizing enterocolitis
D. renal failure
E. seizures

17. A 1-day-old term newborn during crying face assimmetriya is marked – the left angle of the mought is lowered. What natal trauma takes place in this case?
a. Intraventricular hemorrhage
b. Caput succedaneum
c. Natal injuri of facial nerve
d. Subarachnoid hemorrhage
e. Cephalohematoma

18. In a child has delivered with a severe natal trauma of CNS in age of 5 days take place an anxiety, periodically there are short-term clonic and tonic cramps. What syndrome of natal trauma has the child?
A. Convulsive
B. Hydrocephalic
C. Asthenoneurotic
D. Hypertensive
E. Depression of CNS.

19. A 1-day-old healthy infant with a superficial swelling over the right parietotemporal region that does not cross the suture lines. What is the diagnosis?
A.Subdural hematoma
B.Cephalohematoma
C.Cerebral hernia
D. Epidural hematoma
E. Caput succedaneum

20. The examination of a newborn's back reveals a quarter-size "lump" of soft tissue overlying the lower spine. Evaluation with ultrasound of this lesion may demonstrate
a. Ebstein pearl
b. Mongolian spot
c. Cephalohematoma
d. Omphalocele
e. Occult spina bifida

Answers to the primary control tests
1-E, 2-B, 3-A, 4-C, 5-C, 6-D, 7-D, 8-D, 9-C, 10-C, 11- C, 12- B, 13-C, 14- E, 15-C, 16-E, 17-C, 18-A, 19-B, 20-E.

Situational tasks
Situational Task 1
A 1-day-old infant who was born by a difficult forceps delivery isalert and active. She does not move her left arm, however, which she keepsinternally rotated by her

side with the forearm extended and pronated; shealso does not move it during a Moro reflex. The rest of her physical examinationis normal.
1. What diagnosis is most likely indicates?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.
4. What tests are confirmed the suspected diagnosis injury to the phrenic nerve ?

The answers are

1. Left-sided Erb-Duchenne paralysis
2. In a difficult delivery in which traction is applied to the head and neck, several injuries, including all those listed in the question, may occur. Erb-Duchenne paralysis affects the fifth and sixth cervical nerves; the affected arm cannot be abducted or externally rotated at the shoulder, and the forearm cannot be supinated. Injury to the seventh and eighth cervical and first thoracic nerves (Klumpke paralysis) results in palsy of the hand and also can produce Horner's syndrome. Fractures in the upper limb are not associated with a characteristic posture, andpassive movement usually elicits pain. Spinal injury causes complete paralysisbelow the level of injury.
3. a. Fracture of the left clavicle b. Left-sided Klumpke paralysis c. Spinal injury with left hemiparesis
4. When paralysis of an upper extremity from injury to the brachial plexus is found in a neonate, injury to the phrenic nerve should also besuspected because the nerve roots are close together and can be injured concurrently. The paralyzed diaphragm can be noted to remain elevated on a chest x-ray taken during deep inspiration when it will contrast with the opposite normal diaphragm in its lower normal position; on expiration, this asymmetry cannot be seen. On inspiration, not only is breathing impaired since the paralyzed diaphragm does not contract, but the negative pressure generated by the intact diaphragm pulls the mediastinum toward the normal side, impairing ventilation further. The diagnosis can easily be made by fluoroscopy, where these characteristic movements on inspiration and expiration can be seen. Rarely, both diaphragms can be paralyzed, producing much more severe ventilatory impairment. Fortunately, these injuries frequently improve spontaneously.

Situational Task 2

1-day-old infant who was born by a difficult forceps delivery is alert and active and immediately develops tachypnea with cyanosis. She improves somewhat on oxygen but has predominantly thoracic breathing movements, and the chest x-ray, which appears to have been taken inadvertently at expiration, seems normal.
1. What procedure is most likely to provide a specific etiologic diagnosis?
2. What tests are confirmed the suspected diagnosis injury to the phrenic nerve ?
3. What tests are confirmed the suspected diagnosis injury of the fifth and sixth cervical nerves?

The answers are

1. Ultrasound or fluoroscopy of the chest
2. The paralyzed diaphragm can be noted to remain elevated on a chest x-ray taken during deep inspiration when it will with the opposite normal diaphragm in its lower normal position; on expiration, this asymmetry cannot be seen. On inspiration, not

only is breathing impaired since the paralyzed diaphragm does not contract, but the negative pressure generated by the intact diaphragm pulls the mediastinum toward the normal side, impairing ventilation further. The diagnosis can easily be made by fluoroscopy, where these characteristic movements on inspiration and expiration can be seen. Rarely, both diaphragms can be paralyzed, producing much more severe ventilatory impairment. Fortunately, these injuries frequently improve spontaneously.
3. Erb-Duchenne paralysis affects the fifth and sixth cervical nerves; the affected arm cannot be abducted or externally rotated at the shoulder, and the forearm cannot be supinated.

Situational Task 3

A 19-year-old primiparous woman develops toxemia in her last trimester of pregnancy and during the course of her labor is treated with magnesium sulfate. At 38 weeks' gestation, she delivers a 2100-g infant with Apgar scores of 1 at 1 min and at 5 at 5 min. Laboratory studies at 18 h of age reveal a hematocrit of 79%, platelet count of 100,000/□L, glucose 38 mg/dL, magnesium 2.5 meq/L, and calcium 8.7 mg/dL. Soon after, this the infant has a generalized convulsion.
1. What is the most likely cause of the infant's seizure
2. Conduct differential diagnostics.

The answers are

1. Polycythemia.

An infant of 2100 g at 38 weeks would be considered small for gestational age (SGA), a not uncommon consequence of maternal toxemia. Pregnancy-induced hypertension can produce a decrease in uteroplacental blood flow and areas of placental infarction. This can result in fetal nutritional deprivation and intermittent fetal hypoxemia, with a decrease in glycogen storage and a relative erythrocytosis, respectively. Hence, neonatal hypoglycemia and polycythemia are common clinical findings in these infants. A blood glucose level of 30 mg/dL in a full-term infant, however, is probably normal during the first postnatal day, and an infant is very unlikely to have a convulsion as a result of a level of 38 mg. Serum calcium levels usually decline during the first 2 to 3 postnatal days, but will only be considered abnormally low in a term infant when they fall below 7.5 to 8 mg/dL. Neonatal hypermagnesemia is common in an infant whose mother has received MgSO4 therapy, but is usually asymptomatic or produces decreased muscle tone or floppiness. A persistent venous hematocrit of greater than 65% in a neonate is regarded as polycythemia and will be accompanied by an increase in blood viscosity. Manifestations of the "hyperviscosity syndrome" include tremulousness or jitteriness that can progress to seizure activity because of sludging of blood in the cerebral microcirculation or frank thrombus formation, renal vein thrombosis, necrotizing enterocolitis, and tachypnea. Therapy by partial exchange transfusion with albumin is probably more likely to be useful if performed prophylactically before significant symptoms have developed

2. Hypoglycemia, Hypocalcemia, Hypermagnesemia, Thrombocytopenia.

Situational Task 4

The signs and symptoms of meningitis in an infant can be different than those in an adult.

1. What signs and symptoms of meningitis in an infant do you know

2. Which of the signs and symptoms of meningitis is more helpful in an adult patient than in a 1-month-old?

The answers are

1. a. Lethargy b. Jaundice c. Vomiting d. Brudzinski's sign e. Hypothermia

2. Brudzinski's sign . Neonatal sepsis,a clinical syndrome of systemic illness accompanied by bacteremia, often results in spread of infection to the meninges and other distant sites.

The diagnosis of serious infection, including meningitis, in a neonate is difficult because the signs and symptoms are subtle and nonspecific. They include lethargy; feeding problems including abdominal distention, vomiting, and diarrhea; temperature instability; respiratory distress or apnea; and jaundice. Nuchal rigidity and Kernig and Brudzinski signs are frequently not present in the neonate with meningitis.

Situational Task 5

A 1-day-old healthy infant with a superficial swelling over the right parietotemporal region that does not cross the suture lines.

1. What diagnosis is most likely indicates? Why this diagnosis is most likely indicates?

2. Conduct differential diagnostics.

The answers are

1. Cephalohematoma. Cephalhematomas do not cross the suture line since they are subperiostealhemorrhages. No discoloration of the scalp is seen, and the swelling usually progresses over the first few hours of life. Occasionally, skull fractures are present as well. Most cephalhematomas resolve within the first few weeks or months of life without residual findings

2. Caput succedaneum. Caput succedaneum is soft-tissue swelling of the scalp involving the presenting delivery portion of the head. This lesion is sometimes ecchymotic and can extend across the suture lines. The edema resolves in the first few days of life.

Situational Task 6

A 1-day-old comatose infant with cephalohematoma, bulging anterior fontanelle, and retinal hemorrhages.

1. What diagnosis is most likely indicates? Why this diagnosis is most likely indicates?

2. Conduct differential diagnostics.

The answers are

1. Subdural hemorrhage.

Subdural hematomas are commonly seen as part of the shaken baby syndrome. This lesion occurs when the bridging cortical veins that drain the cerebral cortex have been ruptured, leading to a collection of blood between the dura and the cerebral mantle. Repeated trauma can lead to additional collections of blood. In many children,

additional findings of abuse such as broken bones, bruises, and retinal hemorrhages are found

2. Intraventricular hemorrhage (IVH) is commonly seen in very small, preterm infants. The incidence of IVH increases with smaller-size infants and in those with perinatal complications. It occurs in the gelatinous subependymal germinal matrix of the brain and can lead to progressive posthemorrhagic hydrocephalus. Hydrocephalus in these children can present with enlarging head circumference, apnea and bradycardia, lethargy, bulging fontanelle, widely split sutures, or no signs at all. Therapy can include ventricular-peritoneal shunting.

Situational Task 7

Previous premature infant born at 27 weeks' gestation and now 1 months of age presenting with macrocephaly and hydrocephalus on ultrasonogram.

1. What diagnosis is most likely indicates? Why this diagnosis is most likely indicates?
2. What can therapy can include
3. Conduct differential diagnostics.

The answers are

1. Intraventricular hemorrhage.

Intraventricular hemorrhage (IVH) is commonly seen in very small, preterm infants. The incidence of IVH increases with smaller-size infants andin those with perinatal complications. It occurs in the gelatinous subependymal germinal matrix of the brain and can lead to progressive posthemorrhagic hydrocephalus. Hydrocephalus in these children can present with enlarging head circumference, apnea and bradycardia, lethargy, bulging fontanelle, widely split sutures, or no signs at all.

2. Therapy can include ventricular-peritoneal shunting.

3. Subdural hematomas are commonly seen as part of the shaken baby syndrome.

This lesion occurs when the bridging cortical veins that drain the cerebral cortex have been ruptured, leading to a collection of blood between the dura and the cerebral mantle. Repeated trauma can lead to additional collections of blood. In many children, additional findings of abuse such as broken bones, bruises, and retinal hemorrhages are found.

Situational Task 8

The examination of a newborn's back reveals a quarter-size "lump" of soft tissue overlying the lower spine.

1. What diagnosis is most likely indicates? Why this diagnosis is most likely indicates?
2. What examination is indicate?
3. Conduct differential diagnostics.

The answers are

1. Occult spina bifida.

Virtually any abnormality (except Mongolian spots) over the lower spine points to the possibility of occult spinal dysraphism. This designation includes a number of spinal cord and vertebral anomalies that frequently produce severe loss of neurologic function, particularly in the region of the back, the lower extremities, and the urinary

system. Examples of these abnormalities are subcutaneous lipomeningomyelocele, diastematomyelia,hamartoma, lipoma, tight filum terminale, tethered cord, dermal and epidermal cysts, dermal sinuses, neurenteric canals, and angiomas. Occasionally, the loss of neurologic function from such anomalies is mild and, as a result, easily overlooked. Prompt evaluation of these lesions via CT, MRI, or ultrasound is indicated.

2. Evaluation with ultrasound of this lesion

3. Subcutaneous lipomeningomyelocele, diastematomyelia,hamartoma, lipoma, tight filum terminale, tethered cord, dermal and epidermal cysts, dermal sinuses, neurenteric canals, and angiomas

Situational Task 9

In worn child after the first pregnancy, difficult confinements, there was cephalohematoma An icterus appeared on 2 day of life, on 3 day-admitted the changing in neurological state: nystagmus, Grefe. Symptom. Urine is yellow, excrements yellow.. Blood type of mother (II)Rh-, child's (II)Rh+. On the third day Hb 200 g/l, RBC.-6,1x10, bilirubin –in the blood-58 mcmol/l due to unbinding fraction, Ht-0,57.

1. What diagnosis is most likely indicates?
2. How to explain the jaundice in child?
3 What are The most common associated with cephalohematoma complications ?
4. Conduct differential diagnostics.

The answers are

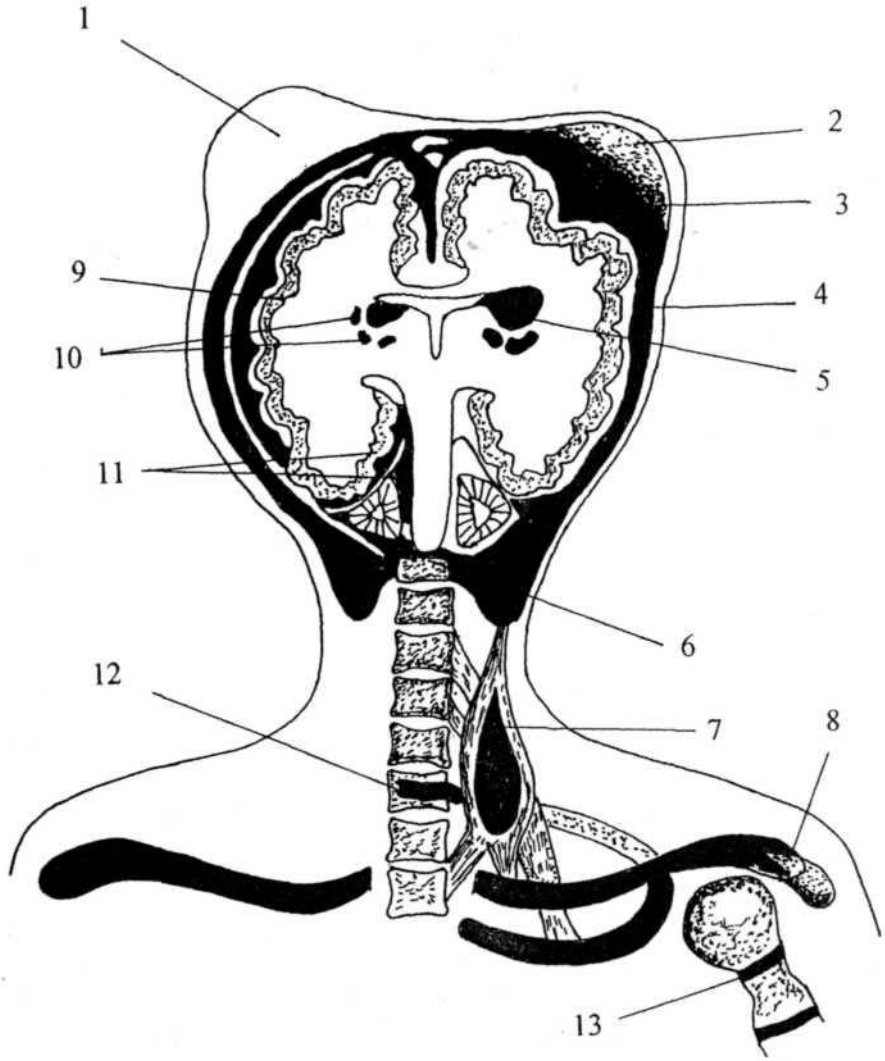
1. Cranial natal trauma
2. Cephalohematoma and intracranial hemorrhage
3. Skull fracture and intracranial hemorrhage.
4. Biliary atresia, Fetal hepatitis, Hemolytic disease of newborns, Physiologic icterus

Situational Task 10

Figure 1: Indicate right answers

Answers to Situational Task 10 (Figure 1):

1 - Caput succedaneum; 2 - Cephalhematoma; 3 - Epidural haematoma;Subgaleal hemorrhage; 4 - Subdural haematoma; 5 – intraventricular hemorrhage; 6 - Subarachnoidal hemorrhage; 7 – Injury to the sternocleidomastoid muscle; 8 - Clavicle fracture ; 9 – Leptomeningeal hemorrhage; 10 - Periventricular hemorrhage; 11 – Tentorium cerebelli hemorrhage with its rupture; 12 - C VI fracture; 13 – epiphyseal separation



VII. Metohodical materials for the class basic stage supporting.

A professional algorithm of patients management implementation (reference chart) for the practical skills and abilities forming .

№	Task	Sequence of implementation	Remarks and warnings related to self-control
1	To conduct examination of the patients with natal injuries .	1.To conduct the complaints and disease anamnesis. 2.To gather thoroughly the patient's life anamnesis. 3.To conduct examination of the patient. 4.To investigate cardiovascular	To pay attention to features of disease course, underlying factors, concomitant diseases etc. To establish the risk factors which can cause the development of disease. To assess patient general condition, position in bed, color and humidity of skin and mucose, presence of neck veins and extremities' swelling. To pay regard to rhythm

		system of the patient (palpation, percussion).	of pulse, it tension and size on both hands, apex shove, it properties, margins of absolute and relative cardiac dullness, it changes, HR (tachy- or bradycardia, extra systole), BP.
		5.To conduct of the heart and of the main vessels auscultation. 6.To investigate the pulmonary system (percussion, bronchophony). 7.To conduct lungs auscultation. 8.To investigate the system of digestion.	To pay regard to heart tones weakening or amplifying, appearance of murmurs and additional III, IV tones. To pay attention on features of percussion and auscultation in neonates Pay attention to changes in neonates
2	To formulate the preliminary diagnosis.	1.To formulate the preliminary diagnosis 2.To substantiate all components of preliminary diagnosis based on complaints, anamnesis, and examinations.	To formulate the based on modern classification preliminary diagnosis of natal injuries and to substantiate each component of it.
3	To evaluate the parameters of additional laboratory investigations.	1.To evaluate the blood count data. 2. To evaluate the biochemistry data. 3.To evaluate the screening of sera for all components of the TORCH-complex	To pay attention to signs of anemia, leucocytosis, changing of formula, elevation of sedimentation rate. Pay attention to cholesterol, lipids, bilirubin, calcium and glucose levels, detection of pathogen-specific IgM and IgG.
4	To understand the data of additional and laboratory investigation.	To understand the data of ultrasound, X-ray and MRI diagnostics.	To pay special attention to the normal parameters of ultrasound, X-ray and MRI diagnostics in diseases in newborn period.
5.	To conduct differential diagnosis.	1.Consistently to find the common signs in complaints,life and disease anamnesis, data of examination, data of laboratory and instrumental investigations	Special attention must be paid to differential diagnosis among the intrauterine hypoxia and asphyxia in newborn

		in patient and in similar states. 2.To find differences between complaints, information of life and disease anamnesis, examination data, information about the laboratory and instrumental methods of research and in similar nosology. 3.On the basis of found out differences to exclude similar diseases from the list of credible diagnoses. 4. To conduct differential diagnostics according to the above mentioned algorithm among all of nosologies are having the similar signs, among other nervous system diseases in newborn period. 5.Taking into account the impossibility to exclude the diagnosis of natal injuries from the list of credible diagnoses to draw a conclusion about most probability of such diagnosis.	period, intrauterine infections and neonatal infections, congenital hypothyroidism.
6	To formulate the concluding clinical diagnosis.	1.To formulate the concluding clinical diagnosis. 2. Basing on preliminary diagnosis, additional investigations data, conducted differential diagnosis to substantiate all elements of concluding clinical diagnosis.	Being based on modern classification of natal injuries to formulate a diagnosis, complications of disease and presence of concomitant diseases.
7	To prescribe treatment for patients.	1.To prescribe non medicinal treatment 2.To prescribe the medicinal treatment.	To specify the regimen and detailed diet according to the disease. Taking into account age, severity of patient state, the stage of disease, the presence of complications and concomitant pathology, to prescribe modern medicinal treatment in accordance to the standards of natal injuries therapy.

Materials of control for conclusive classes stage:

The secondary control tests

1. A 1-day-old term newborn experienced two generalized tonic-clonic seizures 5 minutes apart at 12 hours after birth. The child had meconium staining below the vocal cords at delivery and has exhibited increasing respiratory distress, requiring endotracheal intubation and mechanical ventilation.
Of the following, the MOST appropriate treatment for these seizures is
   A. fosphenytoin 5 mg/kg intramuscularly
   B. lorazepam 0.1 mg/kg intramuscularly
   C. midazolam 1 mg/kg endotracheally
   D. phenobarbital 18 mg/kg intravenously
   E. valproic acid 30 mg/kg intravenously

2. A 1-day-old infant who was born by a difficult forceps delivery is alert and active. She does not move her left arm, however, which she keeps internally rotated by her side with the forearm extended and pronated; she also does not move it during a Moro reflex. The rest of her physical examination is normal. This clinical picture most likely indicates
   a. Fracture of the left clavicle
   b. Fracture of the left humerus
   c. Left-sided Erb-Duchenne paralysis
   d. Left-sided Klumpke paralysis
   e. Spinal injury with left hemiparesis

3. In newborn by day of discharching the cephalohematome of appreciable dimensions occurs . What is your tactics:
   A. To puncture in a maternity home
   B. Do not treat
   C. Introduction in a hematoma of sclerosing solutions
   D. Brain CT
   E. Direct after the discharging to neurosurgeon

4. An infant born at 35 weeks' gestation to a mother with no prenatal care from social undeprivated family is noted to be jittery and irritable, and is having difficulty feeding. You note coarse tremors on examination. The nurses report a high-pitched cry and note several episodes of diarrhea and emesis. You suspect the infant is withdrawing from
   a. Alcohol
   b. Marijuana
   c. Heroin
   d. Cocaine
   e. Tobacco

5. In a newborn child in a 2 day of life during the conducting of neurosonography the hemorrhage in brain parenchima was detected. What clinical manifestations are listed below testifies for presence of cramps in this state?

A.Vasomotoric changes
B. All listed manifestatons.
C. Grefe symptom
D. Symptom of the coming sun
E. Sucking movements

6. A child was born with weght of 2650 g, on the fourth day of life his state has significantly worsened, severe oppression of CNS, low blood pressure, weak crying, appeared. What first of all it is necessary to suspect in this case?
A.Intracranial hemorrhage
B.Anomaly of development
C.Development of bacterial infection
D.Meningoencephalitis
E.Sepsis

7. In a child in age of 3 days the disturbances and anxiety has appeared. Labors are prompt. Was born with Apgar score of 6-7 points with weight of 2500 g. What preparations are listed below pathogenically indicated in this case.
A.Trental
B.Ethimisolum
C.Sodium hydroxybutyrate
D.Anaprilinum
E.Cerebrolisinum

8. In a newborn child, that was born with weight of 4100 g in neurosonogrphy the signs of severe internal hydrocephaly were detected. What clinical manifestations are listed below more corresponds to this state?
A. Oppression of CNS
B. Crying
C. Anisocoria
D. Right-hand hemiparesis.
E. All listed above

9. In a child, delivered with weight of 1800 g, in term of 34 w,. from a woman with an extragenital pathology, the hestosis of second pregnancy half-fault, in age of 5 days the icteric of skin appeared, signs of CNS depression, in neurosonography the signs of periventricular hemorrhage detected. What most probably could promote to it development?
A. Hestosis
B. Extragenital pathology of mother
C. Prematurity
D.Bilirubin encepyalopathy.
E.All listed above.

10. In a prematurely born child has delivered with a severe natal trauma of CNS, in age of 25 days take place an anxiety, periodically there are short-term clonic and tonic cramps. What syndrome of natal trauma takes place in this case?

A.Convulsive
B.Hydrocephalic
C.Asthenoneurotic
D.Hypertensive
E.Depression of CNS.

11. A 19-year-old primiparous woman develops toxemia in her last trimester of pregnancy and during the course of her labor is treated with magnesium sulfate. At 38 weeks' gestation, she delivers a 2100-g infant with Apgar scores of 1 at 1 min and at 5 at 5 min. Laboratory studies at 18 h of age reveal a hematocrit of 79%, platelet count of 300,000x 10 9/l, glucose 3,8 mmol/l, magnesium 1.5 mmol/l,(normal- 0,7-1.0), and calcium 1.5 mmol/l. Soon after, this the infant has a generalized convulsion. The most likely cause of the infant's seizure is

a. Polycythemia
b. Hypoglycemia
c. Hypocalcemia
d. Hypermagnesemia
e. Thrombocytopenia

12. In a prematurely born child has delivered with a severe natal trauma of CNS the cramps and tetany have developed in the first day of life .Ca concentration is 6,2 g/l (N - 8,5-10,5). What from following diagnoses are the least probable?

A. Acute hypoxia of fetus.
B. Big amount of intaked phosphorus
C. Diabetes in mother
D. Hypocalcemia
E. Prematurity

13. The most common associated with cephalohematoma complications are

A. Skull fracture and intracranial hemorrhage.
B.Depression of CNS.
C. Periventricular hemorrhage.
D. Hypocalcemia
E. Thrombocytopenia

14. In worn child after the first pregnancy, difficult confinements, there was. cephalohematoma An icterus appeared on 2 day of life, on 3 day-admitted the changing in neurological state: nystagmus, Grefe. Symptom. Urine is yellow, excrements yellow.. Blood type of mother (II)Rh-, child's (II)Rh+. On the third day Hb 200 g/l, RBC.-6,1x10, bilirubin –in the blood-58 mcmol/l due to unbinding fraction, Ht-0,57. How to explain the jaundice in child?

A. Biliary atresia
B. Fetal hepatitis
C. Cranial- natal trauma
D..Htmolytic disease of newborns
E. Physiologic icterus

15. A 1-day-old infant who was born by a difficult forceps delivery is alert and active. She does not move her left arm, however, which she keeps internally rotated by her side with the forearm extended and pronated; she also does not move it during a Moro reflex. The rest of her physical examination is normal. What diagnosis this clinical picture most likely indicates

a. Fracture of the left clavicle
b. Fracture of the left humerus
c. Left-sided Erb-Duchenne paralysis
d. Left-sided Klumpke paralysis
e. Spinal injury with left hemiparesis

16. The infant in the preceding question immediately develops tachypnea with cyanosis. She improves somewhat on oxygen but has predominantly thoracic breathing movements, and the chest x-ray, which appears to have been taken inadvertently at expiration, seems normal. The procedure most likely to provide a specific etiologic diagnosis is

a. Venous blood gas
b. CT scan of the head
c. Ultrasound or fluoroscopy of the chest
d. Bronchoalveolar lavage
e. Blood culture

17. A 19-year-old primiparous woman develops toxemia in her last trimester of pregnancy and during the course of her labor is treated with magnesium sulfate. At 38 weeks' gestation, she delivers a 2100-g infant with Apgar scores of 1 at 1 min and at 5 at 5 min. Laboratory studies at 18 h of age reveal a hematocrit of 79%, platelet count of 100,000/□L, glucose 38 mg/dL, magnesium 2.5 meq/L, and calcium 8.7 mg/dL. Soon after, this the infant has a generalized convulsion. The most likely cause of the infant's seizure is

a. Polycythemia
b. Hypoglycemia
c. Hypocalcemia
d. Hypermagnesemia
e. Thrombocytopenia

18. The signs and symptoms of meningitis in an infant can be different than those in an adult. Which of the signs and symptoms of meningitis listed below is more helpful in an adult patient than in a 4-month-old?

a. Lethargy
b. Jaundice
c. Vomiting
d. Brudzinski's sign
e. Hypothermia

19. A 1-day-old healthy infant with a superficial swelling over the right parietotemporal region that does not cross the suture lines. (SELECT 1 ABNORMALITY)

a. Intraventricular hemorrhage
b. Caput succedaneum
c. Subdural hemorrhage
d. Subarachnoid hemorrhage
e. Cephalohematoma

20. Previous premature infant born at 27 weeks' gestation and now 6 months of age presenting with macrocephaly and hydrocephalus on ultrasonogram. (SELECT 1 ABNORMALITY

a. Intraventricular hemorrhage
b. Caput succedaneum
c. Subdural hemorrhage
d. Subarachnoid hemorrhage
e. Cephalohematoma

Answers to the secondary control tests

1-D, 2-C, 3-E, 4-C, 5-E, 6-C, 7-C, 8-E, 9-A, 10-A, 11-C, 12-D, 13-A, 14-C, 15-C, 16-C, 17-A, 18-D, 19-E, 20-A.

Materials of the medical support for the students' self training: a reference chart for organization of students' independent work with educational literature.

Tasks	Instructions
To study the etiology and pathogenesis of natal injuries in children.Be able to detect syndromes in dependence of natal trauma period.	To enumerate basic etiologic factors, select the key links of natal injuries pathogenesis.
To study clinical manifestations of natal injuries in children.	To establish the symptoms and gather it to clinical syndromes are enable to put the credible diagnosis of natal injuries
To study diagnostic criteria of natal injuries	To make the flow diagram of disease
To study the additional methods of research (laboratory, instrumental)	To work out a plan of patient investigation.
To study the changes in additional investigational methods which are pathognomonic for natal injuries .	To enumerate the basic diagnostic criteria of natal injuries according to the data of additional investigational methods.
To conduct differential diagnostics, s to establish a concluding diagnosis	To substantiate the basic components of diagnosis in accordance with the modern

	classification, and to conduct a differential diagnosis.
To prescribe the individual toiletry to patient with the natal injuries. . To be able to render the first aid in emergency in birth trauma.	To make the prescribing chart specifying the regimen, diet, medicinal treatment, taking into account the age, severity of patient state, stage of disease, presence of complications and concomitant diseases.

THE RECOMMENDED LITERATURE

Basic:

1. Nelson Essentials of Pediatrics, fifth edition, Copyright © 2007 / edited by Richard E. Behrman, Robert M. Kliegman, Ann M. Arvin; senior editor, Waldo E. - Section XII.

2. Rudolph's Pediatrics, 21st Edition.Chapter 2 , Chapter 25.9 .

3. Key Topics in Neonatology. Richard H. Mupanemunda, Michael Watkinson, BIOS Scientific Publishers Limited, 1999, p.21-25.

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Theme 4. RESPIRATORY DISTRESS SYNDROME, PNEUMOPATHIES AND PNEUMONIAS IN NEONATES. Classification of respiratory distress syndrome, pneumopathies and pneumonias in neonates. Etiology, pathogenesis, clinical presentation, diagnostics, differential diagnostics, treatment, prophylaxis of respiratory distress syndrome, pneumopathies and pneumonias in neonates. Prophylaxis. Prognosis.

I**. Actuality of the theme.**

The knowledge of respiratory distress syndrome, pneumopathies and pneumonias manifestations in neonates allows conducting in due time diagnostics, differential diagnostics, medical treatment and prophylaxis. Enormous strides have been made in understanding the pathophysiology of respiratory distress syndrome (RDS) and more particularly the role of surfactant in its cause. Nevertheless, RDS, formerly referred to as hyaline membrane disease, remains a dominant clinical problem encountered among preterm infants. The greatly improved outcome in RDS can be attributed primarily to the introduction of pharmacologic acceleration of pulmonary maturity and the development of surfactant replacement therapy. Because more of the sickest, most immature infants are surviving, the incidence of complications in the survivors of RDS remains significant. These include intracranial hemorrhage, patent ductus arteriosus (PDA), pulmonary hemorrhage, sepsis, and bronchopulmonary dysplasia (BPD), as discussed in Part 4 and elsewhere. It is often impossible to determine whether these disorders are the sequelae of RDS, of its treatment, or of the underlying prematurity. In this section the clinical features and evaluation of infants with RDS are discussed, and therapeutic approaches other than assisted ventilation are outlined

Concrete purposes:

1. To determine the etiologic and pathogenetis factors in RDS, pneumopathies and pneumonias in neonates.
2. To classify and analyse the typical clinical manifestation of RDS, pneumopathies and pneumonias in neonates.
3.To determine the features of RDS, pneumopathies and pneumonias for newborns and put a preliminary clinical diagnosis. To conduct differential diagnostics.
4. To make the plan of examination and analyse the information about laboratory and instrumental data in the classic course of RDS, pneumopathies and pneumonias in neonates.
5. To demonstrate skills of treatment, rehabilitation and prophylaxis in of RDS, pneumopathies and pneumonias in neonates.
6. To diagnose and render an urgent help in RDS, pneumopathies and pneumonias in neonates.

7. To determine the prognosis for life in RDS, pneumopathies and pneumonias in neonates.

8. To demonstrate the skills of medical specialist's moral and deontological principles and principles of professional subordination in pediatrics.

II. Classes (pointing of planned mastering level)

1. A student must have a conception (familiarize): α1

- The place of RDS, pneumopathies and pneumonias in neonates in the structure of diseases in newborn period.
- Statistical information in relation to morbidity, frequency of complications, lethality, the nearest and remote prognosis in patients with RDS, pneumopathies and pneumonias ;
- The history of scientific studying and the contribution of domestic scientists;

2. A student must know (master): α2

- causes of RDS, pneumopathies and pneumonias in newborn period;
- key links of RDS, pneumopathies and pneumonias in newborn period;
- key links of the nervous system, respiratory system and cardivascular system diseases pathogenesis in newborn period ;
- classification of RDS, pneumopathies and pneumonias in neonates ;
- classical clinical manifestation of RDS, pneumopathies and pneumonias in neonates ;
- clinical syndromes in dependence of RDS, pneumopathies and pneumonias in neonates period ;
- classification of respiratory system and cardivascular system development anomalies ;
- laboratory and instrumental diagnosis of RDS, pneumopathies and pneumonias in neonates ;
- complications of RDS, pneumopathies and pneumonias in neonates;
- treatment principles of RDS, pneumopathies and pneumonias in neonates.

3. A student must master: α3

Skills:

- Collection of complaints and anamnesis of disease;
- Examination of patient with natal injuries and revealing the main symptoms and syndromes;.
- To formulate and substantiate the preliminary diagnosis;
- Determination of laboratory and instrumental inspection plan of patient's examination (according to diagnostics' standards);

Abilities:

- To interpret the results of laboratory and instrumental tests.

- To conduct differential diagnosis among RDS, pneumopathies and pneumonias and other nervous system, respiratory system and cardivascular system diseases in newborn period.
- To give recommendations in relation to the patient's regimen and diet with the RDS, pneumopathies and pneumonias, taking into account the stage of the disease, severity of the state and concomitant pathology;
- To complete the treatment plan in RDS, pneumopathies and pneumonias according to standards taking into account the stage of the disease, complications and concomitant pathology.
- To give the first aid in extreme situations in newborn with the RDS, pneumopathies and pneumonias.
- To realize the life prognosis of patients with the RDS, pneumopathies and pneumonias.

III. Aims of personality development (educative aims):

- A student must learn to adhere rules of behaviour and principles of medical etiquette and deontology, to develop bedside manner;
- Be able to set a psychological contact with a patient and his family;
- To master the sense of professional responsibility for a timely and adequate medicare.

IV. Interdisciplinary integration:

Subject	To know	Be able
1. Basic		
Human anatomy	Structure of respiratory system in neonates.	To estimate the state of child with the signs of RDS, pneumopathies and pneumonias
Histology	Normal histology of respiratory system in neonates, normative indexes of laboratory and instrumental investigational methods and their assessment.	To asses the data of laboratory and instrumental investigational methods of patient
Normal physiology	Normal physiology of respiratory system in neonates, normative indices of laboratory and instrumental investigational methods and their assessment.	To asses the data of laboratory and instrumental investigational methods
Physiopathology	Key links of pathogenesis of respiratory system diseases in neonates.	To estimate the function of respiratory system in neonates.

Pathologic anatomy	Morphological features of respiratory system diseases development depending of the stage of the disease .	To analyse and interpret the information about clinical examination and about additional methods of investigation
Pharmacology	Pharmacokinetics and pharmacodynamics, the side effects of preparations are used in the treatment of respiratory system diseases in newborn period	To prescribe age- dependent treatment of patient, taking into account individual features and period of disease, to establish the individual regimen of preparations taking and dosage. To be able to make a prescription.
Propedeutical pediatrics.	Basic stages and methods of patient clinical examination	To collect complaints, anamnesis vitae et morbi, to find out the basic risk factors of respiratory system diseases, conduct patient examination, to reveal the clinical signs of respiratory system diseases, to interpret the data about additional methods of investigation.
Radiology	Normal parameters of ultrasound, X-ray and MRI diagnostics in diseases in newborn period.	To interpret the data of ultrasound, X-ray and MRI diagnostics
2. Interdisciplinary integration		
Birth trauma	Clinical signs of birth trauma	To establish specific clinical signs of birth trauma mani-festations (CNS and spinal) and to conduct differential diagnosis to other nervous system diseases in newborn period.
Intrauterine hypoxia and asphyxia in newborn period	Clinical signs of intrauterine hypoxia and asphyxia in neonates	To establish specific clinical signs of intrauterine hypoxia and asphyxia in neonates and to conduct differential diagnosis with the RDS, pneumopathies and pneumonias.
Intrauterine infections and neonatal infections	Clinical signs of intrauterine infections in neonates and neonatal infections in dependence on time of transplacental transmission.	To determine the clinical signs of intrauterine infections and neonatal infections and conduct differential diagnosis with the RDS, pneumopathies and pneumonias.

V. Contents of theme:

RESPIRATORY DISTRESS SYNDROME, PNEUMOPATHIES AND PNEUMONIAS IN NEONATES

Respiratory distress in the newborn period is a serious emergency. It may be due to:

- depression of the respiratory center in the brain;
- interference with pulmonary ventilation;
- congestive cardiac failure.

Disorders of the respiratory system. The newborn may present with a variety of respiratory disturbances, which may be developmental in origin or may occur at birth or soon after. Specific respiratory disorders of the newborn are reviewed here, after a brief overview of prenatal respiratory system development.

Prenatal development of the respiratory system. Anatomic development begins at 3 weeks' gestation, with the division of the foregut into the esophagus and trachea. Major bronchial branching occurs by 4 weeks' gestation.

The pseudoglandular stage of lung development (5-16 weeks) is characterized by further branching of the conducting airways, the development of tracheal cartilage, and the appearence of bronchial arteries. At 10 weeks, goblet cells appear within the bronchioles. By 15 weeks, capillaries have developed and undifferentiated cubical cells have appeared. By 16 weeks, all of the major branching is complete.

The canalicular stage of lung development (26-40 weeks) is characterized by formation of terminal alveolar sacs, capillaries approximation with the alveolar sacs, and differentiation of types I and II alveolar cells.

The alveolar, or terminal sac, stage (26-40 weeks) is characterized by progressive increase in the number of alveolar sacs, which creates a greater surface area for gas exchange. Surfactant also appears during this stage of development.

Biochemical development. The most important prenatal event is the production of surfactant by type II alveolar cells.

Function and composition of surfactant. The major function of surfactant is to decrease alveolar surface tension and increase lung compliance. Surfactant prevents alveolar collapse at the end of expiration and allows for c jening of the alveoli at a low intrathoracic pressure

The group of phospholipids comprising surfactant also is referred to as 1 cithin. The ratio of lecithin (L) to sphingomyelin (S) in the amniotic fluid is *i* reflection of the amount of intrapulmonary surfactant and lung maturity.

An L/S ratio of 2:1 or greater usually indicates biochemical lung maturity. The presence of phosphatidylglycerol in the amniotic fluid is an additional indicator of biochemical maturity.

The most abundant component of surfactant is phosphatidylcholine. Less abundant but essential for optimal reduction in surface tension is phosphatidylglycerol.

Pathways for surfactant production. There are two major pathways. The methylation pathway is functional by 22-24 weeks' gestation but is easily inhibited by acidosis and hypoxia. The choline incorporation pathway matures at 35 weeks' gestation and is resistant to hypoxia and acidosis. Rate of surfactant production. Factors that accelerate or retard the pro-duction are listed in table.

Developmental disorders. Esophageal atresia with tracheoesophageal fistula. Esophageal atresia is a lack of continuity of the esophagus. Although it may occur alone, it most often is ac-companied by a fistula between the trachea and the distal esophagus (tracheoesophageal fistula). These development disorders are the result of defective differentiation.

Clinical features. These infants have difficulty with copious oral and pharyngeal secretions. If the secretions obstruct the airway or if aspiration occurs, respiratory distress can result.

Diagnosis is suggested by failure to pass a nasogastric tube into the stomach and is confirmed by a chest radiograph that reveals the tube coiled up in the blind pouch of the esophagus.

Therapy. Emergency management involves constant suction of the esophagus, 30-degree elevation of the head to prevent reflux of gastric contents into the lungs, and preparation for definitive therapy due surgical repair.

Choanal atresia is a unilateral or bilateral obstruction of the posterior nasal airway by a membranous or bony septum. This life-threatening anomaly results from failure of the bucconasal mucosa to rupture.

Clinical features. Because most newborns are obligate nose breathers, bilateral atresia usually presents in the delivery room as airway obstruction, apnea, and cyanosis. Unilateral obstruction may be asymptomatic.

Diagnosis is confirmed either by inability to pass junction catheter through the nostrils into the oropharynx or by radiography using radiopaque due to show the area of nasal obstruction.

Therapy. Emergency management consists or establishing an airway either with an oral airway or by endotracheal intubation. Definitive therapy is surgical reconstruction, performed in the neonatal period.

Pulmonary hypoplasia is seen histologically as a decrease in the number of alveoli and capillary beds. The level of bronchial branching that is affected depends on the time during gestation when the insult occurs.

MANAGEMENT OF RDS

The principles include providing warm environment, supplying fluids and calories and providing adequate oxygenation.

Oxygen therapy consists of keeping the spontaneously breathing infant in oxygen hood and providing warm humidified oxygen t maintain arterial Pa 0_2 levels between 50-80 mm Hg. Infant with well established RDS; i.e. RDS scores over 4, and chest X-ray consistent with HMD should be treated with a continues positive airway pressure breathing (CPAP) device.

CPAP can be applied through nares (nasal) or through endotracheal tube. It stabilizes the alveoli and prevents airway collapse, decreases the frequency of apneic spells and improves oxygenation. The amount of pressure applied depends on the severity of disease. Usually start with 3-4 cm H_20 pressure in mild HDM. Higher pressures are used to improved oxygenation and with increasing severity of HDM. We do not use CPAP pressures higher then 8 cm H_20.

HYALINE MEMBRANE DISEASE (HMD) OR RESPIRATORY DISTRESS SYNDROME (RDS)

Epidemiology. Hyaline membrane disease occurs almost exclusively in pre-mature infants, with higher incidence in lower gestational age infants. Presence of maternal diabetes, asphyxia, acidosis and hypothermia are additional risk factor that increase occurrence of HMD.

Etiopathology. Deficiency of pulmonary surfactant is the basic underlying cause. In addition, the lungs of preterm infants have developmental anatomical problems, i.e. smaller alveoli and cylindrical terminal bronchiole which add to alveolar instability.

Pulmonary surfactant is synthesized in type 11 cells lining the alveoli. The major constituent of surfactant is lecithin. Surfactant associated proteins A, B, C are integral to the function of surfactant. Surfactant protein B deficiency has been recently identified as a genetically mediated cause of HMD in a few families. Synthesis of surfactant starts at 20 weeks of fetal life, when about five percent of the phospholipid is produced through methyl transferase pathway. Over 90 percent of surfactant is however produced after 35 weeks of gestation through phosphocholine (cytidyl) transferase pathway.

The alveoli can be compared to air bubbles. As their alveolar radius decreases during expiratory phase, their surface tension increases causing them to collapse. The presence of surfactant lining of the alveoli diminishes the surface tension, thus, pre-venting the alveoli from collapse at the end of expiration. Although the collapsed portions are perfused, no exchange of gases occur leading to hypoxemia. Hypoxemia, in turn, causes severe pulmonary vasoconstriction shunting the blood from right to left. This cycle unless broken, leads to continued hypoxemia and subsequent metabolic and respiratory acidosis.

Ischemia of the alveoli results in transudation of proteins into the alveoli and terminal bronchiole. The material forms a membrane lining the alveoli, which is seen in microscopic examination at autopsy hence the r ,«ne *Hyaline Membrane Disease*.

In healthy term infants, the surfactant pool is quite adequate. Surfactant is rapidly released into the alveoli with first breath. The fornu tion of this air liquid interface in the alveoli with dispersion of surfactant w thin the layer is the first step of maintaining the alveolar stability and establishing normal functional residual volume. In preterm infants, small surfactant pools lead to varying degrees of severity of HMD/RDS.

Hyaline membrane disease (respiratory distress syndrome o: the newborn) is a respiratory disorder that primarily affects preterm infants ho are born before the bio chemical maturation of their lungs.

Pathophysiology. The lungs are poork compliant owing to a deficiency of surfactant resulting in the classic complex of progressive atelectasis intrapulmo-nary shunting, hypoxemia, and cyanosis. The hyaline membrane that forms and lines the alveoli is composed of protein and sloughed enithelium — the result of oxygen exposure alveolar capillary leakage and the forces mechanical ventilation of these infants.

Clinical features. Affected infants characteristically present with tachypnea, grunting, nasal flaring, chest retraction and cyanosis in the first 3 hours of life. There is decreased air entry on auscultation

Clinical course. The natural course is i progressive worsening over the first 48-72 hours of life.

a) After the initial insult to the airway lining the epithelium is repopulated with type II alveolar cells;

b) Subsequently there is increased production and release of surfactant so that there are sufficient quantities in the air spaces by 72 hours of life. This results in improvement in lung compliance and resolution of the respiratory distress.

Transient tachypnea of **the newborn** is thought to result from decreased lymphatic absorption of fetal lung fluid, It most commonly occurs in infants born near term by j cesarean section, without preceding labor. (The

catecholamine surge associ-ated with labor and delivery, which is thought to enhance pulmonary lymphatic drain-age, does not occur in this setting.)

Clinical features. The tachypnea is quiet or mild and usually not associ-ated with retractions. The infant appears comfortable and rarely is cyanotic.

Diagnosis is based on the delivery history and a chest radiograph, which characteristically reveals fluid in the major fissure, prominent vascular markings, in-creased interstitial markings, and hyperinflation. Auscultation may reveal rales.

Therapy is supportive. The tachypnea resolves in a few days. Low-concentrations of supplemental oxygen may be required.

Persistence of the fetal circulation, or persistent pulmonary hypertension of the newborn, usually is a disease of term infants who have experienced acute or chronic in utero hypoxia. It is seen frequently in infants with meconium aspiration syndrome.

Pathophysiology. The primary abnormality is a failure of the pulmonary vascular resistance to fall with postnatal lung expansion and oxygenation.

Normally, at birth, the systemic vascular resistance rises as a result of cessation of blood flow through the placenta, and pulmonary vascular resistance falls with the first breaths. With persistence of the fetal circulation, the pulmonary vascular resistance continues to be high, and may in fact be higher than the systemic resistance. This results in shunting or the deoxygenated blood, which is returning to the right side of the heart, away from the lungs. The right-to-left shunt can occur at both the atrial level (foramen ovale) and through the ductus arteriosus. Because the lungs are bypassed, the blood is not oxygenated and hypoxemia ensues.

Clinical features. These infants have rapidly progressive cyanosis associ-ated with mild to severe respiratory distress. There is a varied response to oxygen administration, depending on the size of the shunt.

Diagnosis. The diagnosis is suggested by u history of perinatal hypoxia and clinical cyanosis at birth combined with a negative cardiovascular examination and negative chest radiograph, although parenchyma! disease may coexist (e.g., group B streptococcal pneumonia, hyaline membrane disease, meconium aspiration syndrome).

Echocardiography should be used to establish the diagnosis, and should demonstrate:

(i) The absence of cyanotic heart disease

(ii) An increased pulmonary vascular resistance

(iii) The presence of right-to-left shunt at the foramen ovale, ductus arteriosus, or both.

Therapy includes supplemental oxygen, mechanical ventilation, hyperventilation, support of systemic blood pressure, and administration of sodium bicarbonate and pulmonary vasodilators.

Prognosis. The overall mortality rate associated with this disease is high. Extracorporeal membrane oxygenation may improve the outcome in certain patients.

Prenatal Diagnosis. Prenatal diagnosis of HDM is important since it may help manage the case properly. Prenatal prediction of lung maturity is made by assay of amniotic fluid for pulmonary phospholipids, lecthin and sphingomyelin(L/S) ratio. In L/S ratio of > 2.0 is considered to reflect mature lungs with no risk of developing HDM.

Ratio between 1.5-1.99 reflects borderline maturity. Those with raiio of 1 - 1.49 develop a mild from of HDM and ratio of < 1.00 develop severe HDM. In infants of diabetic mothers, L/S ratio alone is not a good predictor of pulmonary maturity. The presence of phosphatidyl glycerol (PG) is important to establish pulmonary maturity.

Assessment of fetal pulmonary maturity is important in decision making for elective cesarean section, elective delivery when expected date of delivery is uncertain and preterm labor. It may permit postponement of delivery or transfer mother to higher level of care and also administer prenatal steroids to mother to accelerate lung maturation.

Another simple semiquantitative method to determine pulmonary maturation is the «shake» or «bubble stability" test. The amniotic fluid mixed with alcohol in a test tube is shaken, the production of stable bubbles indicate presence of adequate surfactant and mature lungs.

Postnatal Diagnosis. This is based on clinical findings, chest X-ray and blood gas measurement. Since the lungs do not establish adequate residual lung volume soon after birth, the infant manifests clinical features of HMD from birth onwards.

Some may take a little longer. The major clinical features are (i) increased respiratory rate, (ii) expiratory grunt, (iii) chest wall retraction, (iv) cyanosis and (v) decreesed breath sounds on auscultation. Additionally, infants may exhibit signs of difficulty in breathing such as flaring of alae nasi and other signs of hypoxemia and shock.

Repeated clinical assessment using the RDS score shown in the has been found to be useful in assessing the severity, predicting the need for Q> therapy or ventilator therapy. The scoring system consists of assigning 0,i,2 numbers to the five major clinical signs of respiratory distress. The higher the score, the more severe the disease. Zero score reflects no RDS. Infants whose score remains higher than 4 after two hours require further evaluation by chest X-ray and blood gases. A score of 4-6 is consistent with mild and a score of 7-10 with severe HMD.

All infants presenting with respiratory distress at birth must be admitted to observation/intensive care nursery for observation and management. If untreated, most infants die, within first 3 days of life. Mild cases may recover after 3 days of age. With good supportive management, infants start improving with almost complete recovery within 7-14 days.

The major emphasis should be on prevention.of HMD. Premature delivery should be delayed using tocolytic agents (beta-adrenergic agonist) or $MgS0_4$. Ad-ministration of prenatal glucocorticoid to mother at least 24 hours prior tb delivery in all pregnancies of less than 34 weeks gestation reduces the risk of development of HMD. It is associated with several additional benefits in the preterm infant, i.e. reduction in IVH, PDA NEC and BPD.

EXOGENOUS SURFACTANT THERAPY

Since the underlying problem in HMD is surfactant deficiency, replacement is the mode of treatment. Surfactant replacement requires endotracheal intubation. Indi-cations for surfactant replacement are:

1. Prophylactic treatment of infants who are at risk of developing HMD. Infants < 1000 g are given surfactant within 2 hours of life.

2. Treatment of infants with established diagnosis of RDS.

The dosage is usually 4-5 ml/kg of survanta, a natural surfactant extract from bovine lungs. Exosurf is a synthetic surfactant. Therapy should be initiated at the earliest, i.e. as soon as infant is deemed to require CPAP or mechanical ventilation. Use of surfactant has shown to improve oxygenation, decrease Fi02, mean airway pressure and allow early extubation. A significant improvement in survival rate has been demonstrated in infants treated with surfactant therapy. There is also a steady decrease in the severity of RDS and further complications. Significant de-crease in the incidence of pneumothorax has been demonstrated following surfactant therapy. Bronchopulmonary dysplasia is also noted to decrease.

Antenatal steroid treatment has shown consistent reduction in the it cidence and severity of HMD and overall reduction of mortality and n orbidity even in very, very low birth weight infants.

BRONCHOPULMONARY DYSPLASIA—BPD (CHRONIC LUNG DISEASE FOLLOWING NEONATAL LUNG INJURY)

Diagnostic **criteria.** Bronchopulmonary dysplasia is diagnosed, when the infant has a history of positive pressure ventilation during the first two weeks of life for at least three days and clinical signs of respiratory dysfunction such as tachypnea and, increased respiratory efforts, which persist beyond 4 weeks of age. These patients require supplemental oxygen for more than 4 weeks to maintain their Pa02 at a level above 50 mm Hg. Their chest radiograms show diffuse shadows.

Etiopatnogenesis. Structural and functional immaturity of the lung is impli-cated. Positive pressure ventilation with oxygen, pulmonary edema due to capillary damage or PDA, excessive infusion of fluids and infection of the lung contribute to the development of bronchopulmonary dysplasia. There is an imbalance between the activity of elastase and proteinase inhibitors.

Clinical features and sequelae. Clinical manifestations vary in severity. In stage 1, there is respiratory distress, which continues to worsen for initial several days of life requiring ventilator support. In stage 2 (4-10 days), oxygen requirement in-creases but clinical condition docs not improve. In stage 3 (10-20 days), oxygen dependence persists but it may be possible to wean the child from the ventilator. X-ray chest shows honeycombing or multiple small radiolucent areas. In stage 4 (after 4 weeks), true chronic lung disease manifests. Increased oxygen requirement persists but it slowly decreases over the next few months. Chest shows diffuse rales and rhonchi, hyperinflation and indrawing of lower intercostal spaces. X-ray chest shows radiolucent hyperinflated lungs.

Sequelae. (1) High incidence of fixed and reactive airway obstruction. (2) Cardiac

complications such as hypertension, hypertrophy of ventricles and systemic-pulmonary collateral shunting. (3) Failure to thrive. (4) Neurodevelopmental retardation.

Management

1. Prevention of premature delivery if possible.
2. Alternate day frusemide therapy.
3. Judicious use of beta-adrenergic agonists such as salbutamol administered by nebulizer, is worth trying. Theophylline compounds or even ipratropium bromide may be used
4. Corticosteroid therapy is of unproven value. It should be reserved only for those infants who cannot be easily weaned from ventilator.
5. Patient should be investigated for possible gastroesophageal reflux.

PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

There is inappropriate elevation of the pulmonary vascular resistance resulting in right to left shunt through patent foramen ovale or ductus arteriosus causing systemic hypoxemia, It may be idiopathic or it may follow meconium aspiration, sepsis, pneumonia or asphyxia. Treatment consists in oxygenation and dilatation of pulmonary vasculature by vasodilator drugs (isoproterenol or tolazoline) or by increasing pH through hyperventilation and the use of alkalinizing agents. Persistent pulmonary hypertension remains as a major problem in the preterm infant. These infants have high mortality if they do not respond to conventional ventilatory therapy. Newer mo-dalities of treatment include high-frequency ventilation, nitric oxide inhalation and extracorporeal membrane oxygenation (ECMO), Whereas high frequency ventilation and ECMO have been in use for over a decade. Nitric Oxide treatment is still in investigational phase. NO is a mediator in causing the dilation of pulmonary vessels.

THE INDICATION OF MECHANICAL VENTILATION ARE:

1. Apnea.
2. Failure of CPAP to maintain Pa o_2 > 50-80 mm hg.
3. Increasing Pa co. > 50 mm hg with persistent acidosis.
4. Infants < 1000 g.
5. Clinical deterioration.

Clinical shock.

Infection	pulmonary oedema
Intracraneal hemorrhage	metabolic disturbances (e.g., hypoglycemia, hypocalcemia, hyponatriemia)
Airway obstructions	inappropriate environmental temperature (hot or cold)
Gastroesophageal reflux	
Seizures	

Hypoxia

CAUSES OF APNEA

Infection
Intracraneal hemorrhage
Airway obstructions
Gastroesophageal reflux
Seizures Hypoxia
pulmonary oedema
metabolic disturbances (e.g., hypoglycemia, hypocalcemia, hyponatriemia)
inappropriate environmental temperature (hot or cold)

FACTORS THAT AFFECT FETAL LUNGS SURFACTANT PRODUCTION

Increase production

- Maternal steroid administration in the presence of a female fetus
- Prolonged rupture of the fetal membranes
- Maternal narcotic addition
- Preeclampsia
- Chronic fetal stress
- (i.e., placental insuffiency)
- Thyroid hormone (i.e., a long- acting thyroid, stimulator-associated maternal hypertyroidism or hypotyroidism with" secondary fetal hypertyroidism)

Theophylline

Combined fetal hyper glycemia and hyperinsulinemia as observed in maternal diabetes.

CLINICAL RESPIRATORY DISTRESS SCORING SYSTEM

Clinical sign	**Score**		
	0	1	2
Respiratory rate (per minute)	*<60*	60=80	>80 or apnetic episode
Cyanosis	None	In air	In 40% O_2
Retractions	None	Mild	Moderate to sever
Grunting	None	Audible with Stethoscope	Audible without Stethoscope
Air entry (crying)	Clear	Delayed or decreased	Barley audible

VI. Plan and organizational structure of classes.

№ п/п	Basic stages of classes, their function and maintenance	Educational aims are in the levels of	Methods of control and studies	Educational materials	Distributing of time in minutes

		maste ring			
1 2 3	Preparatory stage Organizational measures Raising of educational aims and motivation Control of basic knowledges and skills level: 1.Etiology of RDS, pneumo-pathies and pneumonias in newborn period. 2 Key links of RDS, pneumopathies and pneumonias pathogenesis. 3. Classification of RDS, pneumopathies and pneumonias. 4. Typical manifestation of RDS, pneumopathies and pneumonias in newborn ,stages of disease, feature of clinic and diagnostics 5. Laboratory and instrumental diagnosis of RDS, pneumopathies and pneumonias. 6.Clinical syndromes of RDS, pneumopathies and pneumonias. 7.Treatment principles of RDS, pneumopathies and pneumonias in newborn period.	 α2	 Individual oral questioning Test control of the second level Individual oral questioning Test control of 2 level Typical situational task of 2 level	I. «Actuality of theme» II. «Educational aims» Tests of the second level The table «classification of RDS, pneumopathies and pneumonias in newborn period» Structurally logical chart of natal injuries Typical situational task of 2 level Tests of 2 level Typical situational tasks of 2 level Kit of medicines.	3 min. 12 min. 20 min
4	Basic stage of professional skills and abilities forming: 1.To conduct the patient management with RDS, pneumopathies and pneumonias, to take complaints and anamnesis. 2.To conduct the pateint examination, to detect main symptoms and syndromes of RDS, pneumopathies and pneumonias in newborn period . 3.To formulate and substan-tiate the preliminary diagnosis 4.To compose the plan of patient laboratory and instrumental investigation.	 α3 α3 α3	 Practical professional training Practical professional training Practical professional training Practical professional training.	 Patient Patient Case history A reference chart for forming of professio-nal abilities. Case	 115 min

	5.To interpret the results of laboratory and instrumental investigation. 6.To conduct differential diagnosis among RDS, pneumopathies and pneumonias in newborn period and other diseases in newborn period. 7.To give the recommenda-tions for regimen and diet of patient. 8.To compose the plan of RDS, pneumopathies and pneumonias patient treatment taking into account the stage of disease and the presence of complications. 9.To be able to render the first aid in extreme situations	α3 α3 α3 α3	The third level test control. The practical professional training in solving of non typical clinical situations. The third level test control. The practical professional training in solving of non typical clinical situations. The third level test control.	history. A reference chart for forming of professional abilities. Case history. A reference chart for forming of professional abilities. Situational typical tasks of 3 level.Third level tests. Prescribing chart Third level non typical situational tasks. Treatment algorithm for the patients with RDS, pneumopathies and pneumonias First aid algorithm in RDS, pneumopathies and pneumonias	
5 6 7	**Concluding stage.** Control and correction of professional abilities and skills. Working out the totals of class. Home work (basic and additional literature on the topic)		Analysis of clinical work. The practical professional training in solving of non typical clinical situations. Estimation of clinical work.	Clinical work. Third level non typical situational tasks. A reference chart for independent work with literature	30 min

Questions for self-control

1. Name the main causes of RDS and features of surfactant?.
2. Point out the classification of RDS and pneumonias in neonates.
3. What the main clinical manifestations of RDS?
4. Silverman's score, ?
5. Define diagnostic and differential diagnostic measures in RDS and pneumonias in neonates.
6. What is the tactics of respiratory therapy in RDS?
7. What are the main consequences of RDS in later periods of childhood and their prophylaxis ?
8. Especialities of antibacterial therapy of pneumonias in neonates in dependence of mature level and causal agent.

The primary control tests

1. For the newborns RDS of any parentage is typically everything except for:

A. Hypothermia
B. Unemotional cry or it absence
C. Hyperreflexia
D. Essential losses of initial body weight
E. Regurgitation

2. For hyaline membranes is characteristically:
A. State is more frequent in newborns with weight of 1000 – 1500 g
B. It is observed in mortinatuses.
C. Insufficient of surfactant synthesis
D. Meets more frequent, if a mother had bleeding for a day to premature births
E. Correct everything except for is observed in mortinatuses

3. Intensive therapy of hyaline membranes includes:
A.CPAP-therapy
B. Additional ventilation of lungs by indications
C. Prescribing of surfactant by indication
D. All except for CPAP therapy
E. All listed above

4. Sourfactant is damaged with:
A. Hyperventilation
B. The washed erythrocytes
C. Artificial ventilation of lights
D. Viruses
E. Correct everything except for the washed erythrocytes

5. Newborn child with a gestational term of 32 weeks and with weight at birth of 1700 g, Apgar score is 5-7-8 points,. in age of 2 hours the dyspnea of breath and expiration grants, appeared. In auscultation are wheezes in lungs. What is the most reliable reason of these symptoms?:
A. Persistent pulmonary hipertension..
B. Transient tachipnoe of newborns.
C. Congenital anomaly of liungs
D. RDS.
E. Syndrome of meconium aspiration.

6.In a premature newborn child with age of 6 hours a respiratory distress-syndrome is clinically diagnosed. What from listed below is the principal reason of this syndrome development?
A Natal trauma
B. Deficit of sourfactant
C. Delay of fetal pulmonary liquid
D. Intranatal infection
E. Syndrome of meconium aspiration.

7. Child of 3 days was born with weight 2200 g. In 3 hours after birth the respiratory disorders as a dyspnea appeared, retractions of a xiphoid process and of intercostal

spaces, pits under a breast, attacks of apnoe. In auscultation the loosened breathing. What more likely is the reason of respiratory disorders?

A. Syndrome of aspiration
B. Intrauterine pneumonia
C..Intracranial trauma
D. Pneumonia.
E. Hyaline membranes

8.Child from 4 pregnancy that proceeded with underlying hestosis of 1 and 2 halves.. A mother has diabetes mellitus and hyperplasia of thyroid gland of 2-3 degree. A child was born in a term 32 weeks of gestation. Apgar score 5-6 points, Silverman score-is 5 points. In a few hours after birth the subsequent worsening of state due to decreasing of respiratory insufficiency admitted. In a next day the Silverman score is 8 - 10 points. What is the diagnosis?:

A Hyaline membranes
B. Postnatal pneumonia
C. Congenital pneumonia
D. Syndrome of meconium aspitration.
E. Neonatal hypotireosis.

9. Woman with the term of pregnancy of 34 weeks, hospitalized in a maternity hospital with the threat of pregnancy breaking caused by hestosis and anemia. What preparation needs to prescribe for pregnant in 3 days prior to delivery with the purpose of SDR prophylaxis?

A. noradrenalin
B. adrenalin
C. tyroxin
D. estrogens
E. dexametasone

10. Intranatal pneumonias develop as a rule:

A. in an antenatal period
B. on a background of urogenital infection of pregnant
C. as a result of viral hematogenous infection of fetus
D. All answers are correct
E. All are correct except for as a result of viral hematogenous infection of fetus.

11. For determination of lungs maturity can be used:

A. Test of Clemens
B. phenolic test
C. foamy test using an aspirate of gastric content
D. lecithin / sfingomielin quotient in investigation of amniotic fluid
E. All answers are correct

12. Hypoxia in hyaline membranes caused by:

A. Shunting of a blood through an oval window and ductus arteriosus from right to left
B. Infringement of bronchuses permeability

C. All answers are correct
D. Correct all except for alveolar hypoventilation
E . Alveolar hypoventilation

13. A mother delivers a neonate with meconium staining and Apgar scores of 3 at 1 and 5 min of life. She had no prenatal care and the delivery was by emergency cesarean section for severe fetal bradycardia. Which of the following sequelae could be expected to develop in this intubated neonate with respiratory distress?

a. Sustained rise in pulmonary arterial pressure
b. Hyperactive bowel sounds
c. Microcephaly with micrognathia
d. Cataracts
e. Thrombocytosis

14. A 3-day-old infant born at 32 weeks' gestation and weighing 1700 g (3 lb, 12 oz) has three episodes of apnea, each lasting 20 to 25 s and occurring after a feeding. During these episodes, the heart rate drops from 140 to 100 beats per min, and the child remains motionless; between episodes, however, the child displays normal activity. Blood sugar is 50 mg/dL and serum calcium is normal. The child's apneic periods most likely are

a. Due to an immature respiratory center
b. A part of periodic breathing
c. Secondary to hypoglycemia
d. Manifestations of seizures
e. Evidence of underlying pulmonary disease

15. An infant of uncertain dates is born via emergent cesarean section. Birth weight was 1075 g. The infant has poor respiratory effort and Immediate intubation and ventilation were successful. She has been extubated for 2 weeks and still requires oxygen to maintain her saturation above 93%. Her chest radiograph now reveals patchy, fluffy infiltrates with areas of lucency. She requires daily diuretic treatment. What is the diagnosis?

A. Bronchopulmonary dysplasia
B. Respiratory distress syndrome (hyaline membrane disease)
C. Pulmonary interstitial emphysema
D. Bronchiolitis
E. Transient tachypnea of the newborn

16. A newborn infant develops respiratory distress immediately after birth. His abdomen is scaphoid. No breath sounds are heard on the left side of his chest, but they are audible on the right. Immediate intubation is successful with little or no improvement in clinical status. The most likely explanation for this infant's condition is

a. Pneumonia
b. Cyanotic heart disease
c. Diaphragmatic hernia
d. Choanal atresia

e. Pneumothorax

17. A term, 4200-g female infant is delivered via cesarean section because of cephalopelvic disproportion. The amniotic fluid was clear, and the infant cried almost immediately after birth. Within the first 15 min of life, however, the infant's respiratory rate increased to 80 breaths per min, and she began to have intermittent grunting respirations. The infant was transferred to the level 2 nursery and was noted to have an oxygen saturation of 94%. The chest radiograph showed fluid in the fissure, overaeration, and prominent pulmonary vascular markings. The most likely diagnosis in this infant is

a. Diaphragmatic hernia
b. Meconium aspiration
c. Pneumonia
d. Idiopathic respiratory distress syndrome
e. Transient tachypnea of the newborn

18. A previously healthy full-term infant has several episodes of duskiness and apnea during the second day of life. Diagnostic considerations should include which of the following?

a. Hemolytic anemia
b. Congenital heart disease
c. Idiopathic apnea
d. Harlequin syndrome
e. Hyperglycemia

19. An infant of uncertain dates is born via emergent cesarean section after the mother was critically injured in a motor vehicle accident. Birth weight was 1075 g. The infant has poor respiratory effort and you begin bag-mask ventilation but find it extremely difficult to cause chest wall movement. A chest radiograph reveals diffuse whiteout of both lungs, with an occasional air bronchogram. What is the diagnosis?

A. Bronchopulmonary dysplasia
B. Respiratory distress syndrome (hyaline membrane disease)
C. Pulmonary interstitial emphysema
D. Bronchiolitis
E. Transient tachypnea of the newborn

20. A term infant delivered via scheduled cesarean section develops, at 15 min of age, tachypnea, grunting, flaring, and retractions. A chest radiograph reveals well-aerated lungs with fluid in the fissure on the right, prominent pulmonary vascular markings, and flat diaphragms. The child is mildly hypoxic on room air with 89% oxygen saturation. Over the next 6 h she improves and no longer requires oxygen. What is the diagnosis?

A. Bronchopulmonary dysplasia
B. Respiratory distress syndrome (hyaline membrane disease)
C. Meconium aspiration
D. Transient tachypnea of the newborn

E. Bacterial pneumonia

Answers to the primary control tests
1-C, 2-E, 3-E, 4-C, 5- D, 6-B, 7-E, 8-A, 9-E, 10-E, 11-E, 12-C, 13-A, 14-A, 15-A, 16-C, 17-E, 18-B, 19-B, 20-D.

Situational tasks
Situational Task 1
1-day-old infant who was born by a difficult forceps delivery is alert and active and immediately develops tachypnea with cyanosis. She improves somewhat on oxygen but has predominantly thoracic breathing movements, and the chest x-ray, which appears to have been taken inadvertently at expiration, seems normal.
1. What procedure is most likely to provide a specific etiologic diagnosis ?
2. What tests are confirmed the suspected diagnosis injury to the phrenic nerve ?
The answers are
1. Ultrasound or fluoroscopy of the chest
2. The paralyzed diaphragm can be noted to remain elevated on a chest x-ray taken during deep inspiration when it will with the opposite normal diaphragm in its lower normal position; on expiration, this asymmetry cannot be seen. On inspiration, not only is breathing impaired since the paralyzed diaphragm does not contract, but the negative pressure generated by the intact diaphragm pulls the mediastinum toward the normal side, impairing ventilation further. The diagnosis can easily be made by fluoroscopy, where these characteristic movements on inspiration and expiration can be seen. Rarely, both diaphragms can be paralyzed, producing much more severe ventilatory impairment. Fortunately, these injuries frequently improve spontaneously.

Situational Task 2
A 3-day-old infant born at 32 weeks' gestation and weighing 1700 g (3 lb, 12 oz) has three episodes of apnea, each lasting 20 to 25 s and occurringafter a feeding. During these episodes, the heart rate drops from 140to 100 beats per min, and the child remains motionless; between episodes, however, the child displays normal activity. Blood sugar is 50 mg/dL and serum calcium is normal.
1. What diagnosis the child's apneic periods are most likely indicates?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.
The answers are
1. The child's apneic periods most likely are due to an immature respiratory center.
2. Apneic episodes are characterized by an absence of respirations for more than 20 s and may be accompanied by bradycardia and cyanosis. A large number of conditions can cause apnea. Periods of apnea are generally thought to be secondary to an incompletely developed respiratory center, particularly when they are seen, as is common, associated with prematurity.
3. Although seizures, hypoglycemia, and pulmonary disease accompanied by hypoxia can lead to apnea, these causes are less likely in the infant described, given that no unusual movements occur during the apneic spells, that the blood sugar level is more than 40 mg/dL, and that the child appears well between episodes. Periodic breathing,

a common pattern of respiration in low-birth-weight babies, is characterized by recurrent breathing pauses of 3 to 10 s.

Situational Task 3

After an uneventful labor and delivery, an infant is born at 32 weeks' gestation weighing 1500 g (3 lb, 5 oz). Respiratory difficulty develops immediately after birth and increases in intensity thereafter. The child's mother (now gravida 3, para 2102) previously lost an infant because of hyaline membrane disease. At 6 h of age, the child's respiratory rate is 60 breaths per min. Examination reveals grunting, intercostal retraction, nasal flaring, and marked cyanosis in room air.

1. What diagnosis is most likely indicates?
2. Why this diagnosis is most likely indicates?
3. What physiologic abnormalities compatible with these data include?

The answers are

1. For the child described in the question, prematurity and the clinical picture presented make the diagnosis of hyaline membrane disease (infant respiratory distress syndrome) likely.
2. In this disease, lung compliance is reduced; lung volume also is reduced, and a significant right-to-left shunt of blood can occur. Some of the shunt can result from a patent ductus arteriosus or foramen ovale, and some can be due to shunting in the lung. Minute ventilation is higher than normal, and affected infants must work harder in order to sustain adequate breathing.
3. Decreased lung compliance, reduced lung volume, right-to-left shunt of blood.

Situational Task 4

A newborn infant develops respiratory distress immediately after birth.
His abdomen is scaphoid. No breath sounds are heard on the left side of his chest, but they are audible on the right and bowel sounds are heard in the chest. Immediate intubation is successful with little or no improvement in clinical status.

1. The is most likely explanation forthis infant's condition?
2. What procedure is most likely to provide a specific etiologic diagnosis ?
3. Conduct differential diagnostics.

The answers are

1. Diaphragmatic hernia occurs with the transmittal of abdominal contents across a congenital or traumatic defect in the diaphragm. In the newborn, this condition results in profound respiratory distress with significant mortality. Prenatal diagnosis is common and, when found, necessitates that the birth take place at a tertiary level center. In the neonate, respiratory failure in the first hours of life, a scaphoid abdomen, and presence of bowel sounds in the chest are common findings. Intensive respiratory support including mechanical ventilation and extracorporeal membrane oxygenation (ECMO) has increased survival. Mortality can be as high as 50% despite aggressive treatment.
2. Emergency chest x-ray.
3. a. Pneumonia b. Cyanotic heart disease c. Choanal atresia d.Pneumothorax

Situational Task 5

A term, 4200-g female infant is delivered via cesarean section because of cephalopelvic disproportion. The amniotic fluid was clear, and the infant cried almost immediately after birth. Within the first 15 min of life, however, the infant's respiratory rate increased to 80 breaths per min, and she began to have intermittent grunting respirations. The infant was transferred to the level 2 nursery and was noted to have an oxygen saturation of 94%. The chest radiograph showed fluid in the fissure, overaeration, and prominent pulmonary vascular markings.

1. What is most likely diagnosis in this infant?
2. Conduct differential diagnostics.
3. Prescribe treatment for patient.

The answers are

1. Transient tachypnea of the newborn

Transient tachypnea of the newborn is usually seen after a normal vaginal or, especially, after a cesarean delivery. These patients have tachypnea, retractions, grunting, and sometimes, cyanosis. The chest examination is usually normal; the chest radiograph demonstrates prominent pulmonary vascular markings with fluid in the fissures and hyperexpansion (flat diaphragms).

2. a. Diaphragmatic hernia b. Meconium aspiration c. Pneumonia
d. Idiopathic respiratory distress syndrome
3. Therapy is supportive, with maintenance of normal oxygen saturation. Resolution usually occurs in the first 3 days of life.

Situational Task 6

A previously healthy full-term infant has several episodes of duskiness and apnea during the second day of life. Diagnostic considerations should include which of the following?

1. What diagnosis is most likely indicates?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.

The answers are

1. Congenital heart disease.
2. Idiopathic apnea is common in premature infants but is not expected in the full-term newborn. When apnea occurs in the term infant, there is almost always an identifiable cause. Sepsis, gastroesophageal reflux, congenital heart disease, seizures, hypoglycemia, and airway obstruction can cause apnea in term newborns.

Harlequin syndrome is a transient change in the skin color of the otherwise asymptomatic newborn (usually preterm) in which the dependent side of the entire body turns red while the upper side remains pale

3. Idiopathic apnea , Harlequin syndrome, sepsis, gastroesophageal reflux, congenital heart disease, seizures, hypoglycemia, and airway obstruction can cause apnea in term newborns.

Situational Task 7

A 1-month-old infant presents to the clinic in the month of December with a several-day history of cough and rhinorrhea, and has now developed difficulty breathing. On examination, the child has marked intercostal and subcostal retractions. There are

both crackles and wheezes diffusely on auscultation, and the infant is mildly hypoxic. The child's radiograph displays a diffuse interstitial infiltrate with some air trapping. The child has been placed on oxygen. A rapid RSV antigen test is positive. What is the next step in initial management?
1. What diagnosis is most likely indicates?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.
4. Prescribe treatment for patient.

The answers are

1. Acute bronchiolitis
2. Acute bronchiolitis is usually a viral illness with a peak incidence at about six months of life. More than half of the cases are caused by respiratory syncytial virus (RSV). Although some children do not respond to any therapy, inhaled epinephrine seems to be more useful than inhaled albuterol. Steroids do not seem to be helpful in children with normal pulmonary function. Bronchiolitis is usually self-limited, but in children with underlying lung disease (such as bronchopulmonary dysplasia), the infection can be severe and sometimes fatal.
3. a. Pneumonia b. Congenital heart disease.
4. Inhaled albuterol, inhaled epinephrine, nebulized steroids, antibacterial therapy, antiviral therapy, respiratory support.

Situational Task 8

An infant born an hour ago to a mother with severe pregnancyinduced hypertension was floppy at birth and required bag-mask ventilation for several minutes. The infant is now in distress and seemingly agitated, with tachypnea, tachycardia, and hypoxia. Perfusion is poor. Diminished breath sounds are noted on the left side of her chest, and her heart sounds are displaced to the right.
1. What is the best initial step in management?
2. What diagnosis is most likely indicates? Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.

The answers are

1. Needle aspiration of the chest.
2. Tension pneumothorax.

A tension pneumothorax occurs when the pressure of free air in the pleural space exceeds that of atmospheric pressure, thereby causing compression of the opposite lung with mediastinal shift. Infants with this condition develop cardiovascular compromise and require emergent needle aspiration of the pneumothorax. When time allows, a chest tube should be placed.

3. a. Diaphragmatic hernia b. Meconium aspiration c. Pneumonia
d. Idiopathic respiratory distress syndrome.

Situational Task 9

A 3-week-old infant has a 1-week history of a mild cough with thick nasal secretions. In the last 12 h she has developed spasmotic coughing fits during which she becomes cyanotic. When not coughing, she appears tired. She has lost weight since the 2-week

visit. The family has not taken her temperature, but she has been feeding less and has not voided in about 16 h. You decide to admit her for observation and rehydration.
1. What diagnosis is most likely indicates? Why this diagnosis is most likely indicates?
2. Conduct differential diagnostics.
3. What is the most appropriate management consideration for this patient?

The answers are

1. Pertussis

Infants under two months of age are not yet immunized against pertussis, and as such are at increased risk of contracting the disease. Pertussis usually has three distinct stages, starting with the *catarrhal* stage, followed by the *paroxysmal* stage (the infant described is in this stage), and concluding with the *convalescent* stage. The paroxysms can be tiring, and many infants experience posttussive emesis. Pertussis is one of the most communicable diseases known and is spread by droplets aerosolized by coughing. Although children are immunized against pertussis, immunity is now thought to wane in the adult years. Hospitalized patients suspected of having pertussis infection should be isolated with droplet precautions.

2. a. Acute bronchiolitis, b. Pneumonia c. Congenital heart disease.

3. a.Chest radiograph, two views; respiratory isolation (droplet precautions), inhaled albuterol, inhaled epinephrine, nebulized steroids, antibacterial therapy.

Situational Task 10

A term infant delivered via scheduled cesarean section develops, at 15 min of age, tachypnea, grunting, flaring, and retractions. A chest radiograph reveals well-aerated lungs with fluid in the fissure on the right, prominent pulmonary vascular markings, and flat diaphragms. The child is mildly hypoxic on room air with 89% oxygen saturation. Over the next 6 h she improves and no longer requires oxygen.
1. What is the diagnosis?
2. Why this diagnosis is most likely indicates?
3. Describe chest radiograph of this infant.
4. Conduct differential diagnostics.

The answers are

1. Transient tachypnea of the newborn.
2. Infants born via cesarean section have a higher risk of transient tachypnea of the newborn, a self-limited condition thought to result at least in part from persistent fetal lung fluid. These infants display evidence of respiratory distress shortly after delivery, occasionally requiring oxygen.
3. The radiograph findings are often described as a “starburst” pattern with diffuse streaky marks that seem to create a star around the mediastinal structures. Over the course of a day or so, the symptoms resolve spontaneously.
4 . Differential diagnosis considerations must include pneumonia.

Situational Task 11

A postterm infant is born at home after a prolonged and difficult labor. The maternal grandmother brings the infant to the hospital at 1 h of life because of fast breathing. Grandmother notes that the child spit up some dark brown particulate fluid shortly

after birth. Physical examination reveals an infant in marked respiratory distress. Other findings include both an umbilical cord and flaking skin with a yellow-green hue. Chest radiograph reveals patchy infiltrates bilaterally.
1. What is the diagnosis?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.

The answers are

1. Meconium aspiration.
2. Infants who are under perinatal stress will occasionally pass meconium in utero. The aspiration of this meconium into the lungs can cause a chemical pneumonitis and subsequent respiratory distress. These infants are also at risk for developing primary pulmonary hypertension (persistent fetal circulation); some become quite ill and require extracorporeal membrane oxygenation (ECMO). Meconium stains skin and umbilical cords.
3. a. Primary pulmonary hypertension b. Respiratory distress syndrome (hyaline membrane disease) c. Bacterial pneumonia

Situational Task 12

An infant of uncertain dates is born via emergent cesarean section after the mother was critically injured in a motor vehicle accident. Birth weight was 1075 g. The infant has poor respiratory effort and you begin bag-mask ventilation but find it extremely difficult to cause chest wall movement. A chest radiograph reveals diffuse whiteout of both lungs, with an occasional air bronchogram.
1. What is the diagnosis?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.

The answers are

1. Respiratory distress syndrome (hyaline membrane disease).
2. Hyaline membrane disease (respiratory distress syndrome, primary surfactant deficiency) is primarily seen in infants of less than 34 weeks' gestation. Pulmonary surfactant starts to be secreted around 28 weeks' gestation; this onset time is remarkably variable, however. Surfactant decreases surface tension in the alveoli and permits inflation of lung tissue at lower pressures. Infants born with immature lung development frequently cannot generate enough negative pressure to inflate lung tissue. Historically these infants required aggressive ventilator support that ultimately resulted in damage to the lung tissue. Since the 1980s, however, exogenous surfactant replacement therapy has been available and is now used routinely in many parts of the world with good results.
3. a. Bacterial pneumonia b. Primary pulmonary hypertension
c. Meconium aspiration d. Transient tachypnea of the newborn

Situational Task 13

An infant of uncertain dates is born via emergent cesarean section after the mother was critically injured in a motor vehicle accident. Birth weight was 1075 g. The infant has poor respiratory effort and you begin bag-mask ventilation but find it extremely difficult to cause chest wall movement. A chest radiograph reveals diffuse

whiteout of both lungs, with an occasional air bronchogram. This infant is now 7 weeks old. She has been extubated for 2 weeks and still requires oxygen to maintain her saturation above 93%. Her chest radiograph now reveals patchy, fluffy infiltrates with areas of lucency. She requires daily diuretic treatment.

1. What is the diagnosis?
2. Why this diagnosis is most likely indicates?
3. Conduct differential diagnostics.

The answers are

1. Bronchopulmonary dysplasia.
2. Bronchopulmonary dysplasia (BPD) is a chronic lung disease diagnosed in premature infants who have persistent oxygen requirements, clinical findings of respiratory difficulties, and abnormal chest radiographs.

These children have airway hyperresponsiveness, and many have pulmonary edema that requires daily diuretic medication. Although the morbidity and mortality rates of children with BPD have improved over the last two decades, these children still have an increased risk of developmental problems and asthma.

3. a. Primary pulmonary hypertension b. Bacterial pneumonia
c. Pulmonary interstitial emphysema d. Pneumothorax

VII. Metohodical materials for the class basic stage supporting.

A professional algorythm of patients management implementation (reference chart) for the practical skills and abilities forming .

№	Task	Sequence of implementation	Remarks and warnings related to self-control
1	To conduct examination of the patient with RDS, pneumopathies and pneumonias.	1.To conduct the complaints and disease anamnesis. 2.To gather thoroughly the patient's life anamnesis. 3.To conduct examination of the patient. 4.To investigate cardiovascular system of the patient (palpation, percussion).	To pay attention to features of disease course, underlying factors, concomitant diseases etc. To establish the risk factors which can cause the development of disease. To assess patient general condition, position in bed, color and humidity of skin and mucose, presence of neck veins and extremities' swelling. To pay a regard to rhythm of pulse, it tension and size on both hands, apex shove, it properties, margines of absolute and relative cardiac dullness, it changes, HR(tachi-or bradicardia, extrasystole), BP.

		5.To conduct of the heart and of the main vessels auscultation. 6.To investigate the pulmonary system (percussion, bronchophony). 7.To conduct lungs auscultation. 8.To investigate the system of digestion.	To pay regard to heart tones weakening or amplifying, appearance of murmurs and additional III, IV tones. To pay attention to features of percussion and auscultation in neonates Pay attention to changes in neonates
2	To formulate the preliminary diagnosis.	1.To formulate the preliminary diagnosis 2.To substantiate all components of preliminary diagnosis based on complaints,anamnesis, and examinations.	To formulate the based on modern classification preliminary diagnosis of RDS, pneumopathies and pneumonias and to substantiate each component of it.
3	To evaluate the parameters of additional laboratory investigations.	1.To evaluate the blood count data. 2. To evaluate the biochemistry data. 3.To evaluate the screening of sera for all components of the TORCH-complex	To pay attention to signs of anemia, leucocytosis, changing of formula, elevation of sedimentation rate. Pay attention to cholesterol, lipids, bilirubin, calcium and glucouse levels, detection of pathogen-specific IgM and IgG.
4	To understand the data of additional and laboratory investigation.	To understand the data of ultrasound, X-ray and MRI diagnostics.	To pay special attention to the normal parameters of ultrasound, X-ray and MRI diagnostics in diseases in newborn period.
5.	To conduct differential diagnosis.	1.Consistently to find the common signs in complaints,life and disease anamnesis, data of examination, data of laboratory and instrumental investiagtions in patient and in similar states. 2.To find differences between complaints, information of life and disease anamnesis,examination data, information about the laboratory and instrumental	Special attention must be paid to differential diagnosis among the natal injuries, intrauterine hypoxia and asphyxia in newborn period, intrauterine infections and neonatal infections, among nervous system, respiratory system and cardivascular system diseases in newborn period.

		methods of research and in similar nosology. 3.On the basis of found out differences to exclude similar diseases from the list of credible diagnoses. 4. To conduct differential diagnostics according to the above mentioned algorithm among all of nosologies are having the similar signs, among nervous system, respiratory system and cardivascular system diseases in newborn period. 5.Taking into account the impossibility to exclude the diagnosis of RDS, pneumopathies and pneumonias from the list of credible diagnoses to draw a conclusion about most probability of such diagnosis.	
6	To formulate the concluding clinical diagnosis.	1.To formulate the concluding clinical diagnosis. 2.Basing on preliminary diagnosis, additional investigations data, conducted differential diagnosis to substantiate all elements of concluding clininical diagnosis.	Being based on modern classification of RDS, pneumopathies and pneumonias to formulate a diagnosis, complications of disease and presence of concomitant diseases.
7	To prescribe treatment for patients.	1.To prescribe non medicinal treatment 2.To prescribe the medicinal treatment.	To specify the regimen and detailed diet according to the disease. Taking into account age, severity of patient state, the stage of disease, the presence of complications and concomitant pathology, to prescribe modern medicinal treatment in accordance to the standards of RDS, pneumopathies and pneumonias therapy.

Materials of control for conclusive classes stage:
The secondary control tests

1. You are evaluating a 3-week-old infant. Her mother reports that the child has been feeding poorly over the preceding week, gained no weight over the past 2 weeks, and perspires with feeding. On physical examination, the pale, thin girl has a respiratory rate of 60 breaths/min, heart rate of 160 beats/min, and blood pressure of 80/50 mm Hg. She has mild retractions with good air entry. Her precordium is active, and there is a gallop rhythm on auscultation. Her liver is enlarged, and her perfusion is adequate. Of the following, the MOST likely cause of her symptoms is

A. congestive heart failure
B. cystic fibrosis
C. glycogen storage disease
D. physiologic anemia
E. vascular ring

2. You are called to the delivery room to evaluate a newborn. The pregnancy was complicated by maternal lupus. The infant is pink, vigorous, and in no distress. He has clear breath sounds and is well perfused. His heart rate is 50 beats/min. You obtain an electrocardiogram. Of the following, the MOST likely diagnosis for this infant is

A. atrial fibrillation
B. first-degree heart block
C. second-degree (Wenckebach) heart block
D. third-degree (complete) heart block
E. Wolff-Parkinson-White syndrome

3. An infant born an hour ago to a mother with severe pregnancy induced hypertension was floppy at birth and required bag-mask ventilation for several minutes. The infant is now in distress and seemingly agitated, with tachypnea, tachycardia, and hypoxia. Perfusion is poor. Diminished breath sounds are noted on the left side of her chest, and her heart sounds are displaced to the right. What is the best initial step in management?

a. Needle aspiration of the chest
b. Extracorporeal membrane oxygenation
c. Nebulized epinephrine
d. Nebulized steroids
e. Systemic steroids

4. A full-term newborn infant is having episodes of cyanosis and apnea, which are worse when he is attempting to feed, but he seems better when he is crying. The most important next step to quickly establish the diagnosis is

a. Echocardiogram
b. Ventilation perfusion scan
c. Passage of catheter into nose
d. Hemoglobin electrophoresis

e. Bronchoscopic evaluation of palate and larynx

5.You are called to a delivery of a term infant, about to be born via cesarean section to a mother with multiple medical problems including a 1-month history of a seizure disorder, for which she takes magnesium sulfas; rheumatic heart disease, for which she must take penicillin daily for life; hypertension, for which she takes propranolol; acid reflux, for which she takes aluminum hydroxide; and a deep venous thrombosis in her left calf diagnosed two days ago, for which she was started on a heparin infusion. The obstetrician is concerned about the possible effects of the mother's multiple medications on the newborn infant.You correctly note that the one medication most likely to cause harm in this newborn infant at delivery is

a. Propranolol
b. Penicillin
c. Aluminum hydroxide
d. Magnesium sulfas
e. Heparin

6. After an uneventful labor and delivery, an infant is born at 32 weeks' gestation weighing 1500 g (3 lb, 5 oz). Respiratory difficulty develops immediately after birth and increases in intensity thereafter. The child's mother (now gravida 3, para 2102) previously lost an infant because of hyaline membrane disease. At 6 h of age, the child's respiratory rate is 60 breaths per min. Examination reveals grunting, intercostal retraction, nasal flaring, and marked cyanosis in room air. Physiologic abnormalities compatible with these data include

A. Decreased lung compliance, reduced lung volume, left-to-right shunt of blood
B. Decreased lung compliance, reduced lung volume, right-to-left shunt of blood
C. Decreased lung compliance, increased lung volume, left-to-right shunt of blood
D. Normal lung compliance, reduced lung volume, left-to-right shunt of blood
E. Normal lung compliance, increased lung volume, right-to-left shunt of blood

7. A term, 4200-g female infant is delivered via cesarean section because of cephalopelvic disproportion. The amniotic fluid was clear, and the infant cried almost immediately after birth. Within the first 15 min of life, however, the infant's respiratory rate increased to 80 breaths per min, and she began to have intermittent grunting respirations. The infant was transferred to the level 2 nursery and was noted to have an oxygen saturation of 94%. The chest radiograph showed fluid in the fissure, overaeration, and prominent pulmonary vascular markings. The most likely diagnosis in this infant is

a. Diaphragmatic hernia
b. Meconium aspiration
c. Pneumonia
d. Idiopathic respiratory distress syndrome
e. Transient tachypnea of the newborn

8. An infant is delivered by emergent cesarean section because of fetal distress from acute placental abruption. The Apgar scores are 1 and 3 at 1 and 5 minutes,

respectively. The cord pH is 6.98, and the base deficit is 20 mEq/L. The infant is resuscitated and admitted to the neonatal intensive care unit for observation of potential injury to the brain and other organs. Of the following, the MOST frequent complication of perinatal asphyxia is

A. hepatic cholestasis
B. myocardial dysfunction
C. necrotizing enterocolitis
D. pulmonary hemorrhage
E. renal failure

9. A 6-hour-old infant delivered at 41 weeks' estimated gestational age has respiratory distress. The clinical history is significant for meconium-stained amniotic fluid. Chest radiography shows bilateral, diffuse, and coarse infiltrates. The infant is receiving mechanical ventilation with a fraction of inspired oxygen of 1.0 and a high mean airway pressure. An arterial blood gas measurement reveals a partial pressure of oxygen of 36 mm Hg. Of the following, the manifestation MOST helpful for the diagnosis of persistent pulmonary hypertension is

A. differential oxygen saturations between right arm and leg
B. elevated partial pressure of carbon dioxide
C. high-velocity murmur of tricuspid regurgitation
D. precordial hyperactivity
E. response to inhaled nitric oxide

10. A 3.7-kg male infant is delivered at 38 weeks' gestation by scheduled repeat cesarean section to a 24-year-old multigravid woman who has intact fetal membranes. The Apgar score is 8 at both 1 and 5 minutes. Physical examination of the infant at 10 minutes after birth reveals mild intercostal retractions and a respiratory rate of 80 breaths/min. He is acyanotic and has a peripheral oxygen saturation of 88% on room air. There is no heart murmur. A chest radiograph reveals expansion of the lungs to nine anterior ribs, perihilar streaking, and a fluid density in the right horizontal fissure. Of the following, the BEST therapy for this infant is

A. intravenous ampicillin and gentamicin
B. intravenous furosemide
C. intravenous prostaglandin E1
D. supplemental oxygen by hood
E. tracheal intubation and surfactant

11. A 3.2-kg boy is delivered at 34 weeks' gestation to a 22-year-old woman who has type 1 diabetes mellitus. The mother's most recent glycosylated hemoglobin measurement was 9%. Of the following, the condition MOST likely to be experienced by the infant that may require admission to the neonatal intensive care unit is

A. anemia
B. hyperbilirubinemia
C. hypercalcemia
D. hyperglycemia
E. surfactant deficiency

12. A 4.0-kg term infant is delivered vaginally 6 hours after rupture of fetal membranes. The amniotic fluid is stained with thick meconium.If the infant is limp, pale, and cyanotic at birth, the BEST sequence of care will be to

A. administer bag/valve/mask positive pressure ventilation immediately after delivery

B. have the delivering physician notify the physician caring for the infant of the history after completing the delivery

C. suction the infant's mouth and hypopharynx after delivery and administer blow-by oxygen

D. suction the infant's mouth and hypopharynx after delivery of the head and assess the need forfurther resuscitation after the 1-minute Apgar score is assigned

E. suction the infant's mouth and hypopharynx after delivery of the head, followed by tracheal suctioning after delivery of the body

13. A term infant is delivered following abruptio placenta. He has flaccid tone, gasping respiration, and cyanosis. He does not respond to positioning, drying, warming, suctioning, tactile stimulation, and free-flowing oxygen. His 1-minute Apgar score is 1 (heart rate of 80 beats/min). Of the following, this infant's MOST urgent need is

A. chest compressions
B. intravenous antibiotics
C. intravenous bicarbonate
D. intravenous fluid bolus
E. positive-pressure ventilation

14.In newborn of 10 days of life there is subfebrile condition, respiratory insufficiency of II stage that increases in dynamics. On X-ray -an interstitial pneumonia. In the routine blood test -an eosinophilia. It is known from anamnesis that before the births in a mother chlamidial colpitis was diagnosed. In the first days of life in newborn the rinitis and blenorrhea admitted. What etiology of pneumonia is most reliable?

A. Chlamidial
B. Staphilococcal
C. Streptococcal
D. Micoplasmal
E. Klebsiellic

15. In a prematured child had been born in a gestational term of 34 weeks, in 4 hours after birth there is tachipnoe, respiration as a swing, retraction of a breast bone, expiratory noises. Breathing frequency is 80 in a minute. In the lungs loosened breathing with inconstant variegrated wheezes auscultated.. On the lungs X-ray the aired bronchogram and nodose reticular netting.. What diagnosis?:

A. Atelectasis of lungs
B. Syndrome of massive meconial aspiration
C. Natal trauma
D. Hyaline membranes

E. Pneumonia of newborns.

16. Newborn child, 42 weeks of gestation, Amniotic fluid with the admixtures of meconium . Start to cry at once, but the attack of the secondary asphyxia appeared in a few minutes, tachipnoe, paradoxical breathing. In lungs auscultation a plenty of variegrated moist rhonchuses. On the X-ray the confluent centers of a pulmonary tissue inspissation, atelectases of lungs. What is the previous diagnosis?

A. Syndrome of air outflow from the lungs
B.Transient tachipnoe of newborns.
C.Hyaline membranes
D.Bronchopulmonary dysplasia.
E. Syndrome of meconium aspiration.

17. A child was born from the second pregnancy proceeded with a nephropathy of II stage, from II protracted urgent labors. Apgar score 5-7 points, Silverman score 4-5 points. From the birth time the breathing of child is unstable, unrhythmical, with insignificant retraction of intercostal spaces, periodically there is a paroxysmal cough. During feeding there was the attack of the secondary asphyxia. From a nose and from the cavity of mouth are allocations. In lungs there are variegrated moist wheezes. In percussion there is a clear pulmonary sound. What from listed below is the most effective measure?

A. Drainage position.
B. Suction of the upper respiratory tract contents
C. Endotracheal introduction of surfactant
D. Oxygen therapy.
E.Corticosteroids

18. In a 10-daily child an acute right-hand pneumonia of staphylococcal etiology is diagnosed. Medical treatment with penicillin is ineffective. What antibacterial preparation you will choose?

A. Vancomicin 20-40 mg/kg/per day
B.Cephalexin 25-100 mg/kg/per day
C.Levomycetinum 50-1000 mg/kg/per day
D.Erythromycin 20-50 mg/kg/per day
E.Ampicillinum 50-200 mg/kg/per day

19. A newborn infant has mild cyanosis, diaphoresis, poor peripheral pulses, hepatomegaly, and cardiomegaly. Respiratory rate is 60 breaths per min, and heart rate is 250 beats per min. The child most likely has congestive heart failure caused by

a. A large atrial septal defect and valvular pulmonic stenosis
b. A ventricular septal defect and transposition of the great vessels
c. Total anomalous pulmonary venous return
d. Hypoplastic left heart syndrome
e. Paroxysmal atrial tachycardia

20. In a mother in delivery the anhydrous period is 28 hours, chorionamnionitis. After 2 day of life child became sickly, muscular oligotrophia, hyporeflexia, respiratory

disorders. A skin is yellow-grey, hemorrhage rashes. Liver +4 cm, spleen +1 cm. From an umbilical wound pus is allocated. On X-ray of thorax there is the center of infiltration. In the blood test the anemia, leucocytosis, deviation formula to the left,acceleration of blood sedimentation rate. What is the most reliable diagnosis?

A. Festering omfalitis
B. Sepsis
C. Fetal hepatitis
D. Pneumonia
E. Biliary atresia

Answers to the secondary control tests

1- A, 2- D, 3- A, 4-C, 5- A, 6-B, 7-C, 8-D, 9-B, 10-D, 11-E, 12-E, 13-E, 14-A, 15-D, 16-E, 17- B, 18-A, 19-E, 20-B.

Materials of the medical support for the students' self training: a reference chart for organization of students' independent work with educational literature.

Tasks	Instructions
To study the etiology and pathogen-nesis of RDS, pneumopathies and pneumonias in children.	To enumerate basic etiologic factors, se-lect the key links of RDS, pneumopa-thies and pneumonias pathogenesis.
To study clinical manifestations RDS, pneumopathies and pneumonias in children.	To establish the symptoms and gather it to clinical syndromes are enable to put the credible diagnosis of natal injuries
To study diagnostic criteria of RDS, pneumopathies and pneumonias	To make the flow diagram of disease
To study the additional methods of research (laboratory, instrumental)	To work out a plan of patient investigation.
To study the changes in additional investigational methods which are pathognomonic for RDS, pneumopathies and pneumonias.	To enumerate the basic diagnostic criteria of RDS, pneumopathies and pneumonias according to the data of additional investigational methods.
To conduct differential diagnostics, s to establish a concluding diagnosis	To substantiate the basic components of diagnosis in accordance with the modern classification, and to conduct a differential diagnosis.
To prescribe the individual holiatry to patient with the RDS, pneumopathies and pneumonias. To be able to render the first aid in emergency in RDS, pneumopathies and pneumonias.	To make the prescribing chart specifying the regimen, diet, medicinal treatment, taking into account the age, severity of patient state, stage of disease, presence of complications and concomitant diseases.

THE RECOMMENDED LITERATURE

Basic:

1. Nelson Essentials of Pediatrics, fifth edition, Copyright © 2007 / edited by Richard E. Behrman, Robert M. Kliegman, Ann M. Arvin; senior editor, Waldo E. - Section XII.
2. Rudolph's Pediatrics, 21st Edition. Chapter 2 .
3. Key Topics in Neonatology. Richard H. Mupanemunda, Michael Watkinson, BIOS Scientific Publishers Limited, 1999, p.38 - 46.

Additional:

1. Martin: Fanaroff and Martin's Neonatal-Perinatal Medicine, 8th ed., Copyright © 2006 Chapters 25, 26, 28 , 42, 43 .
2. Аряєв М.Л. Неонатологія. - Київ: «АДЕФ-Україна.», 2006. - 754 с
3. Шабалов Н.П. Неонатология. Том I - Санкт-Петербург, 2006г.
4. Неонатологія. Навчальний посібник для практичних занять зі студентами медичних факультетів вищих навчальних медичних закладів / Волосовець О.П., Безруков Л.О. та інш. - Чернівці, 2000.

TEME: HEMOLYTIC AND HEMORRHAGIC DISEASES OF NEWBORN. Etiology. Pathogenesis. Classification. Clinical presentation. Diagnostics. Differential diagnostics. Treatment. Prophylaxis. Prognosis.

The amount of studying hours – 4 hours

I. Actuality of the theme.

Jandice is one of symptoms are observed in most of children of newborn period. According to the literature almost in 65% of children jaundice was observed in the first week of life. In 90-95% it is a manifestation of physiological hyperbilirubinemia. The necessity to be able differentiate jaundices in dependence of their etiopathogenesis is causes by possibilities for physical inability or even leads to death, having different levels of hyperbilirubinaemia. More often among jaundices (up to 2,8 % of cases) there is hemolitic disease of newborns with lethality of 0,1 %-1 % till this time, despite the modern treatment methods. Hemolytic diaeses of newborn to be characterized by intencive incrise of indirect bilirubin, what can lead to damage central nervous system, organic damages, lethal outcome ore to durable disability. In case of depression of hemostasis bleeding can to be manifestationed by hypocoagulation (hemorrhagic disease) or hypercoagulation, that is DIC-syndrome. Community of clinical signs of both this per se contrary diseases complicates ascertainment of clinical diagnosis and treatment tactic, which determine result of medication.

II. Classes (pointing of planned mastering level)

1. A student must know (to familiarize): α1

- the place of thyroid diseases in the structure of hemolytic and hemorrhagic diseases in structure of newborn infants diseases;
- statistical information in relation to morbidity, frequencies of complications, lethality, the nearest and remote prognosis in newborns with hemolytic and hemorrhagic diseases;
- history of scientific study and payment of domestic scientists;

2. A student must know: α2

- Anatomic and physiological features of hematopoiesis in fetus and newborn infant, blood system in infants;
- Main etiologic factors of hemolytic and hemorrhagic diseases development:
- Clinical and diagnostic criteria of hemolytic and hemorrhagic diseases in newborns;
- Principles of complex treatment of hemolytic and hemorrhagic diseases in newborns;
- Complications of phototherapy;
- Prophylactic methods of hemolytic and hemorrhagic diseases in newborns and rehabilitation measures after the diseases ending.

3. A student must master: α3
Skills:
- Collection of complaints and anamnesis of disease;
- Examination of newborn infant with hemolytic and hemorrhagic diseases and revealing the main symptoms and syndromes;
- To formulate and substantiate the preliminary diagnosis;
- Determination of laboratory and instrumental inspection plan of patient investigation (to obedience of diagnostics standards);
- Giving the first aid in case of serious course of disease with further evaluation its efficiency.

4. Abilities:
- to evaluate condition of newborn;
- to interpret the result of laboratory and instrumental tests;
- to conduct differential diagnosis among diseases with the same clinic;
- to formulate and substantiate the clinical diagnosis according the classification;
- to determine increase of bilirubin by the hour;
- to be able to order blood for blood transfusion operation;
- to conduct determination of blood group and Rh-factor;
- to conduct diagnostic compatibility blood tests;
- to conduct phototherapy;
- to complete the treatment plan in inflammatory disease according to standards taking into account the stage of disease;
- to render the first aid in extreme situation and exigent state;
- to prescribe recipes according the treatment.

III. Interdisciplinary integration:

Subject	To know	To be able
1. Previous (provided)		
Biology	Basis of genetics, genetic investigation methods in medicine.	To gather material for investigation, to diagnose the main genetic diseases.
Biochemistry	Features of normal and abnormal biochemical indices in newborn and prematures	To evaluate results of biochemical and immunologic indices in children
Normal physiology	Metabolism of bilirubin, blood- forming system, normative laboratory and instrumental test's indices.	To evaluate results of laboratory and instrumental investigations.
Pathologic physiology	Pathogenesis of hyperbilirubinaemia	To evaluate biochemical indices of bilirubin's metabolism.

Obstetrix and gynaecology	Features of pregnancies march in case of blood incompatibility of mother and fetus	To evaluate the march of pregnancy and childbirth.
Pharmacology	Pharmacokinetics, pharmacodynamics and side effects of preparations, which use in treatment of hemolytic and hemorrhagic diseases	Prescribe age dependent and patient individual features treatment, period of disease, to establish the individual regimen of preparations taking and dosage. To prescribe recipes.
Propedeutical pediatrics.	Anatomy and physiological features of newborn's hepatobiliary and blood systems.	To collect complaints, anamnesis vitae et morbi, to findout the basic risk factors, to conduct patients examination, to interpret indexes of laboratory and instrumental investigation.
Faculty pediatrics	Principles of patient's investigation.	To complete case record, to evaluate patients severity
2. Followings		
Hospital pediatrics.	Clinical signs of hemolytic and hemorrhagic diseases, complications in newborn and the tactic of treatment.	To reveal the clinical signs of hemolytic and hemorrhagic complications, to conduct differential diagnosis, to be able to evaluate efficiency of prescribed therapy
3. Interdiscipline integration		
Biliary atresia	Clinical manifestation of hemolytic and hemorrhagic diseases in infants, plan of treatment	-to establish specific clinical signs of biliary atresia and to conduct differential diagnostic with signs of hemolytic syndrome.
Intranatal infections	Clinical manifestation of intranatal infections in newborn	-to establish specific clinical signs of intranatal infections and to conduct differential diagnostic with signs of hemolytic syndrome.
DIC-syndrome	Clinical manifestation of DIC-syndrome in newborn	-to establish specific clinical signs of DIC-syndrome and to conduct differential diagnostic with signs of hemolytic syndrome.
Jaundice of the newborn	Clinical manifestation of jaundice in newborn	To establish specific clinical signs of jaundice of the newborn and to conduct differential diagnosis with hemolytic and hemorrhagic diseases.

IV. Contents of the lessons theme can be represented:

Isoimmunization

The Rh blood group proteins are a highly antigenic group of proteins capable of causing severe isoimmunization with a high risk of fetal hydrops and death. Although several systems of nomenclature exist, the CDE system is most commonly used. These three loci each contain two major alleles (C,c; D,d; E,e) and several minor alleles. Whereas the C and E alleles play relatively minor roles in isoimmunization, the D antigen may produce maternal sensitization with a fetomaternal hemorrhage as small as 0.1 mL. At one time, Rh hemolytic disease was the most common cause of kernicterus. However, maternal prophylaxis with high-titer anti-D immunoglobulin G (RhoGAM) combined with aggressive fetal surveillance and transfusion has greatly reduced the incidence and severity of this disease. Mothers sensitized before the development of immune serum prophylaxis and those without access to preventive treatment continue to deliver affected infants.

Destruction of erythrocytes begins in utero. Elevated COHb levels have been detected in blood obtained by cordocentesis in fetuses of nonsmoking isoimmunized mothers. Although large amounts of bilirubin are also produced in utero, erythroblastotic infants are not icteric at birth because TSB concentrations are kept below 5 mg/dL (86 μmol/L) by transfer of unconjugated bilirubin across the placenta. Jaundice may appear, however, within 30 minutes after delivery. Classically, the serum bilirubin is all indirect reacting, although small amounts of conjugated bilirubin have been noted.

In those neonates who have received intrauterine transfusions, moderate to marked conjugated hyperbilirubinemia has been seen in cord blood or during the first days of life. In these neonates, total cord bilirubin concentrations may be as high as 40 mg/dL (684 μmol/L) with at least 80% direct-reacting bilirubin, whereas conjugated bilirubin is not transported across the placenta. The reason for the retention of a large amount of direct-reacting bilirubin in sera is unknown. It has been speculated that hepatic conjugation may mature more rapidly than usual as a result of chronic exposure to high concentrations of bilirubin in utero, whereas maturation of hepatic excretory function lags behind. In severe erythroblastosis, hepatic excretory function may also be adversely affected by development of hepatic swelling secondary to heart failure, and by congestion caused by severe extramedullary hematopoiesis in liver, anemia, and poor hepatic perfusion.

The Du antigen is a weak D antigen that may not be detected on routine blood typing. It is a weak antigen in the sense that some patients carrying the Du antigen become sensitized to the D antigen when transfused with Rh-positive blood. Mistyping blood from a Du donor as Rh negative has the potential to stimulate the formation of anti-D antibodies when transfused into an Rh-negative patient.

Neonates with group A or B erythrocytes may have increased hyperbilirubinemia, hemolysis, and positive Coombs' tests because of transfer of maternal anti-A or anti-B antibody into the fetal circulation. The disorder may occur in the first-born without prior sensitization of the mother and is generally milder and of shorter duration than Rh erythroblastosis. It, however, may also cause severe hemolysis, jaundice, and kernicterus. The reason for the milder nature of ABO hemolytic anemia may be one or more of the following: (1) the presence, in infants with A or B blood groups, of the antigen in all tissues in the body, effectively diluting and neutralizing transferred maternal antibody, (2) neutralization of maternal antibody by placental A and B antigen prior to its entry into fetal circulation, and (3) the relatively weak nature of A or B antibody, resulting in less intense hemolysis.

More than 100 other erythrocyte antigens are known, but only a few are reported to cause hemolytic anemia and exaggerated unconjugated hyperbilirubinemia in the newborn. Because of the success of Rh immunoglobulin in decreasing the incidence of isoimmunization against the D antigen, the role of the "minor" erythrocyte antigens is receiving more attention. The incidence of isoimmunization against antigens such as Kell, Kidd, and Lutheran now equals or exceeds that of the D antigen.

ISOIMMUNE HEMOLYTIC ANEMIA

Maternal IgG antibodies, usually reacting against fetal ABO- or Rh-incompatible RBCs, can cross the placenta, enter the fetal circulation, and cause hemolysis, anemia, and hyperbilirubinemia. Transfer of antibodies across the placenta depends on the Fc component of the IgG molecule. Because both IgM and IgA antibodies lack this component, only IgG antibodies cause hemolytic disease of the newborn.

Rh Hemolytic Disease

The spectrum of clinical problems caused by Rh hemolytic disease ranges from mild, self-limited hemolytic anemia to hydrops fetalis. A better understanding of the disease, its diagnosis and prognosis, and use of management strategies for affected pregnancies have vastly improved the outcome. Part 2 of this chapter and provide a more comprehensive treatment of the subject.

The Rh blood group consists not only of the Rho or D antigen but also of the related antigen groups Cc and Ee. The three antigens are inherited as a group that never shows genetic crossover. Cells with the D antigen are Rh positive, and those that lack D are Rh negative. The Cc and Ee antigens modify the expression of the D antigen and affect the antigenicity of the Rh-positive red cells. In rare cases anti-c and anti-E isoimmune hemolysis also occurs, as is discussed under Minor Blood Group Hemolytic Disease.

The incidence of Rh disease depends on the prevalence of Rh-negative antigens in the population studied. Even in white populations, only a small percentage of pregnancies are affected because not all women who are Rh negative develop

antibodies, Rh immunization of the mother does not usually occur during the first pregnancy, and some of the second infants will be Rh negative.

Prevalence of Rh-Negative Genotype (CDE/CDE) by Population

POPULATION GROUP	PERCENTAGE AFFECTED
European whites	11–21
U.S. whites	14.4
Indians (India)	8
U.S. African Americans	5.5
Native Americans	0
Chinese	0
Japanese	0

Adapted from Prokop O et al: Human Blood and Serum Groups. Barking, UK, Elsevier, 1969.

The interaction of the anti-D IgG with a D-positive red cell does not usually involve complement, so that hemolysis generally is extravascular. Hyperbilirubinemia and jaundice can occur in the first day of life because the placenta no longer is available to clear bilirubin from hemolysed red cells. The peripheral blood smear might show anemia, reticulocytosis, and macrocytosis. Microspherocytes are seen infrequently. A direct antiglobulin (Coombs) test should demonstrate anti-D IgG.

Intervention with partial or total exchange transfusions may be necessary to reduce the load of antibody and remove the antibody-coated cells. In a series of 101 babies born to Rh-D negative mothers who received one or two doses of anti-D immunoglobulin, no signs of hemolysis were noted in the Rh-D positive or negative infants. Twenty percent of Rh positive babies whose mothers received two doses of anti-D immunoglobulin had a positive direct Coombs test, compared with 2.4% of those whose mothers received only one dose.

ABO Hemolytic Disease

Although the incidence of blood group O mothers delivering babies of blood group A or B is about 15%, ABO hemolytic disease is estimated to occur in only 3% of pregnancies and requires treatment with exchange transfusion in less than 0.1% of pregnancies. In contrast to Rh hemolytic disease, ABO hemolytic disease tends to be less severe, and the severity does not depend on birth order. Maternal anti-A or anti-B IgG antibodies, which might have been raised against A or B substances occurring in food or on bacteria, can cross the placenta and react with the sparsely distributed A or B antigens on the neonatal RBCs.

Hemolysis is primarily extravascular, although intravascular hemolysis that is not induced by complement also occurs. Infants sometimes develop anemia, reticulocytosis, and hyperbilirubinemia within the first 24 hours of life. The hallmark of ABO hemolytic disease is the presence of microspherocytes on the peripheral blood smear. In Rh hemolytic disease, on the other hand, microspherocytes are rarely noted. The direct antiglobulin test should be at least weakly positive for anti-A or anti-B; however, because of the sparse distribution of antigenic sites on a newborn's red cells, ABO hemolytic disease may be present even without a positive result on the direct antiglobulin test. The maternal serum should have high titers of IgG directed against A or B. In the absence of clinical hemolytic disease, laboratory evidence of erythrocyte sensitization should not be considered isoimmune hemolytic disease.

Minor Blood Group Hemolytic Diseases.

The incidence of isoimmune hemolytic disease is related to the antigenicity of the particular blood group antigen. Rare instances of hemolytic disease among the minor group antigens Kell, Duffy, Lewis, Kidd, M, and S have been reported. Most hemolytic diseases not attributed to ABO or Rh incompatibility are due to anti-Kell, anti-E, and anti-c. Although they are rare, severe hemolytic reactions requiring exchange transfusion therapy have occurred. Screening for minor group antibodies is recommended for all women in the 34th week of pregnancy. The diagnosis and treatment of hemolytic disease are identical to those for Rh hemolytic disease.

Natural History of Hemolytic Diseases of the Newborn.

The half-life of IgG molecules is approximately 28 days; therefore, hemolysis should resolve after the first 3 or 4 months. This resolution could occur sooner if the antibodies are cleared by adhering to red cells or by exchange transfusion. Hydrops fetalis is the most severe consequence of hemolysis, but anemia generally is less problematic than hyperbilirubinemia in the acute phase of illness.

Anemia can occur in the first few weeks in both those who received exchange transfusions and those who required only phototherapy for management of hyperbilirubinemia. Many causes for the anemia have been postulated, including ongoing destruction of native cells by anti-blood group IgG, hypersplenism, inadequate replacement by transfused red cells, and shortened survival of transfused red cells.

Thrombocytopenia and bleeding can complicate the hemolytic disease. Usually thrombocytopenia, without other laboratory evidence of disseminated intravascular coagulation (DIC), is noted, but DIC can be triggered by massive hemolysis or shock and acidosis.

Other Immune Hemolytic Anemias

The other immune hemolytic diseases of early childhood are relatively rare. Idiopathic hemolytic anemia occurs, as do anemias associated with infections, drugs,

immunodeficiency syndromes, and collagen-vascular diseases. IgG antibodies, often directed against one of the Rh erythrocyte antigens, are the usual cause. These antibodies are most active at 37°C and often are called warm autoantibodies. The IgG-coated cells, with or without the assistance of complement, are cleared by the spleen.

Congenital infections (syphilis, cytomegalovirus [CMV], rubella, toxoplasmosis, herpes), bacterial infections, and viral infections, such as infection with the human immunodeficiency virus (HIV) and hepatitis, can cause hemolytic anemia and bone marrow suppression with reticulocytopenia. Pharmacologic agents also are associated with autoimmune hemolytic anemias.

IgM autoantibodies can cause disease and usually are referred to as cold agglutinins because they are most active at between 0° and 30°C. These antibodies, with complement, coat RBCs and cause hemolysis. The best-known causes of cold hemagglutinin disease are Mycoplasma pneumoniae and Epstein-Barr virus. IgA-mediated hemolysis is quite rare but is remarkable for its severity.

The natural history of autoimmune hemolytic disease in infancy and childhood generally is that of a rapid onset of anemia with hyperbilirubinemia, splenomegaly, or hepatomegaly. Initially reticulocytopenia may be noted, especially if antibodies are directed against red cell progenitors in the bone marrow, but a brisk reticulocytosis usually follows. Resolution before or within 3 to 6 months is common. A subset of patients under 2 years of age and with a slower onset of disease at presentation develop chronic hemolytic anemia.

Therapy often is limited to treatment of an underlying infection or removal of the offending drug, accompanied by supportive measures to limit hyperbilirubinemia. Occasionally a severe anemia requires treatment with corticosteroids, intravenous γ-globulin, immunosuppressive agents, splenectomy, or plasmapheresis. Difficulties with identifying compatible blood during a hemolytic crisis, especially in IgG-mediated disease, as well as the usually self-limited nature of the disease, restrict blood transfusions to cases in which severe anemia impairs tissue oxygenation.

Anemia with reticulocytosis and spherocytosis may be seen on the peripheral blood smear, but the diagnosis depends on demonstration of antibody-coated cells, with or without complement, in a direct antiglobulin test. The antibody titer correlates with the severity of the disease and sometimes is measured serially to determine the efficacy of therapy or the need for intervention. If fewer than 1000 IgG molecules coat a red cell, the standard direct antiglobulin test could yield a negative result, and a more sensitive radioimmunoassay (super-Coombs) should be used.

HEMORRHAGE

Internal bleeding can occur if the fetus has anatomic abnormalities or defects in the hemostatic system or with a history of interventional obstetric procedures. Often the first signs of internal hemorrhage in the newborn are those of hypovolemic shock

and hypoxemia. Jaundice occurs later when the entrapped RBCs break down. Traumatic deliveries, anatomic abnormalities, and defects in hemostasis of either acquired or congenital origin are the most common causes of bleeding.

A surprisingly large amount of blood can be lost within a cephalohematoma , and even greater bleeding can occur in the subaponeurotic area of the scalp (subgaleal hemorrhage), where bleeding is not limited by periosteal attachments. Traumatic or assisted deliveries and vitamin K deficiency are commonly associated with such bleeding. Robinson's groupdeveloped a formula to estimate the volume of blood loss; it predicts a 38 mL loss for each centimeter of increase in head circumference.

Hemorrhage into the adrenals, kidneys, liver, spleen, or retroperitoneum also can occur after difficult or breech deliveries. Splenic or hepatic rupture can occur after trauma, especially if the organs are enlarged as a result of extramedullary hematopoiesis. Occult or superficial hemangiomas can bleed and sequester large volumes of red cells and platelets (Kasabach-Merritt syndrome).

Intracranial hemorrhage can occur in the fetus, but it most commonly is associated with a premature infant in the early postnatal period; these infants usually experience intraventricular hemorrhages. Full-term infants also might have intracranial bleeding, which usually occurs in the subarachnoid or subdural regions. Although the cause might not be found, full-term infants with intracranial hemorrhage should be evaluated for hemostasis abnormalities, because this type of bleeding is associated with qualitative and quantitative platelet defects and with abnormalities of several of the coagulation proteins.

Anemia Caused by Accelerated Destruction of Red Blood Cells

Accelerated destruction of RBCs is the endpoint of a number of intrinsic, extrinsic, congenital, and acquired red cell abnormalities. In an adult, a hemolytic process occurs when the RBCs are destroyed before the normal life span of 120 days elapses. Because the RBCs of premature infants and newborns have a shorter life span, hemolysis is defined as a process that shortens the survival of the RBCs relative to the life span expected for the infant's gestational and postnatal age. In contrast to anemia caused by blood loss, most infants with hemolysis have some evidence of hyperbilirubinemia. Reticulocytosis should accompany the hemolysis, although in conditions complicated by bone marrow suppression (e.g., congenital infections, chronic illness, or nutritional deficiency), the reticulocyte count may be inappropriately low for the degree of anemia present.

Extrinsic factors that cause hemolytic anemia can be divided into immune and nonimmune etiologies; the most common causes of immune hemolytic disease are discussed first. Various antigens are found on or in the surface of RBCs; immune hemolytic disease results when antibodies directed against a red cell antigen, plus or minus complement, coat the RBCs. The cells then are cleared from the circulation by

the reticuloendothelial (RE) system, as is the case with most IgG-mediated diseases, or they are lysed intravascularly with the help of complement.

Acute Hemolytic Anemia: Causative Mechanisms and Representative Infectious Agents

MECHANISM	INFECTIOUS AGENT
Release of hemolysin	Clostridium perfringens
Direct invasion of red blood cell	Malaria
Alteration of red blood cell surface	
By adherence of organism	Bartonella organisms
By alteration of antigenic phenotype by neuramidase	Influenza virus
By cold agglutinin	Epstein-Barr virus
By absorption of capsular polysaccharide	Haemophilus influenzae
Microangiopathy	Any agent causing disseminated intravascular coagulation or hemolytic-uremic syndrome
Enhanced oxidative damage in patients with enzyme deficiency	Campylobacter jejuni enteritis in neonates with a diminished cytochrome-b5 reductase system

From Ritchey AK et al: Hematologic manifestations of childhood illness. In Hoffman R et al (eds): Hematology: Basic Principles and Practice, 2nd ed. New York, Churchill Livingstone, 1995.

EXCHANGE TRANSFUSION

Exchange transfusion is the standard mode of therapy for immediate treatment of hyperbilirubinemia to prevent kernicterus and for correction of anemia in erythroblastosis fetalis. With this technique, the equivalent of two neonatal blood volumes (160 mL/kg of body weight) is replaced in aliquots not to exceed 10% of the total blood volume. This results in the replacement of approximately 85% of the circulating RBCs. Serum bilirubin concentrations are usually reduced by 50%. Although the procedure is relatively safe when performed by experienced practitioners in term neonates, it nevertheless carries a risk of both mortality (0.1% to 0.5% in term neonates) and morbidity, as well as being time consuming and expensive. The procedure usually takes 1 to 2 hours. Slower exchanges should theoretically increase the quantity of bilirubin removed by permitting equilibration of pigment from tissue, but the differences are too small to justify the increased risk of prolonging the duration of the procedure. The indications for exchange transfusion

need to be individualized, taking into account gestational age and severity of illness. During acute hospitalization, exchange is recommended if TSB rises to the indicated levels despite intensive phototherapy. For readmitted infants, if TSB is above the exchange level, serial TSBs should be performed every 2 to 3 hours, and if TSB remains at or above levels indicated, exchange is recommended after 6 hours of intensive phototherapy. In the past it was regularly recommended that TSB, even in healthy term infants, be kept below 20 mg/dL (342 μmol/L) during the first 28 days of life. In recent years, this has been questioned, and a growing consensus has developed that levels as high as 25 mg/dL (428 μmol/L) are acceptable for otherwise healthy, full-term, asymptomatic infants. When the exchange level is considered, conjugated bilirubin is not subtracted from the total. Despite the inability of direct-reacting bilirubin to enter the CNS, it is possible that direct-reacting bilirubin can partially displace unconjugated bilirubin from albumin-binding sites to increase the risk of kernicterus.

The same criteria are used on the first day of life as on subsequent days, but in the face of rapidly rising TSB concentrations, as may be seen in Rh erythroblastosis or other types of hemolytic disease, the decision to perform the exchange should anticipate the rise (from previous TSB concentrations, hemoglobin concentrations, and reticulocyte count), so that the exchange is under way by the time the critical level is reached.

In the severely affected erythroblastotic neonate, clinical judgment rather than laboratory data should be used to decide whether the neonate requires immediate transfusion after delivery. In this situation, a partial exchange transfusion using packed RBCs, coupled with reduction in blood volume if venous pressure is elevated, and with measures to ensure adequate ventilation and correction of acidosis and shock, will often be life saving. In most exchange transfusions, fresh whole or reconstituted citrate/phosphate/ dextrose-anticoagulated blood should be used. If blood older than 5 days must be used, the pH should be checked and sodium bicarbonate added to correct the pH to 7.1. Full correction to pH 7.4 may result in later excessive rebound alkalosis as the citrate is metabolized. Use of heparinized blood avoids additional osmolar loads and may obviate the need to administer calcium or correct for acidosis but may result in hypoglycemia and markedly increased free fatty acid concentrations.

The administration of salt-poor albumin (1 g/kg) to neonates 1 to 2 hours before exchange transfusion to increase the efficiency of bilirubin removal by shifting more tissue-bound bilirubin into the circulation has been advocated and shown to increase the bilirubin removed by 40%. As the total amount of bilirubin removed during an exchange transfusion is only a small portion of the total body pool of bilirubin, this increase may not significantly alter subsequent bilirubin concentrations or the need

for additional exchange transfusions. In addition, the transient increase in TSB concentration after albumin administration theoretically could increase the risk of kernicterus rather than reduce it if there are local phenomena at the brain level that enhance entry of bilirubin into neurons. Finally, constituents of some albumin solutions may act to displace bilirubin from its binding sites, potentially increasing the percentage of free bilirubin present in the plasma. Thus, pretreatment with albumin before exchange transfusion is not routinely recommended.

The potential complications of exchange transfusion are listed in. Preparations for emergency situations should be made before initiation of the procedure.

The TSB level is one of the major criteria to be evaluated when considering the initiation or escalation of treatment for unconjugated hyperbilirubinemia. Although it is believed that it is the unconjugated fraction that presents the danger of kernicterus, the exact ratio of unconjugated and conjugated bilirubin is difficult to assess because its quantitation exhibits great variability between laboratories. In view of this, the conjugated bilirubin level should not be subtracted from the total bilirubin level unless it constitutes more than 50% of the total. As was stated previously, many variables other than the total bilirubin level influence the susceptibility of a particular patient to the sequelae of unconjugated hyperbilirubinemia; these include genotype, gestational age, chronologic age, and the presence of hemolytic or other disease states. Therefore, it is useful to consider four groups of patients at risk for kernicterus and modify treatment on the basis of the category: the healthy term (greater than 37 weeks' estimated gestational age), the sick term, the healthy premature, and the sick premature neonate.

In 1994, the Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia of the American Academy of Pediatrics published recommendations for the management of unconjugated hyperbilirubinemia in healthy term neonates. It cannot be emphasized too strongly that these guidelines are proposed for healthy near-term and full-term neonates only; extrapolation to the three other groups of newborns (sick term, healthy premature, and sick premature) cannot be made. No recommendations are made for the neonate manifesting jaundice in the first 24 hours of life because these patients are not believed to be healthy.

Neonatologists must remember that as physicians they do not typically encounter "healthy" neonates. Admission to an intensive care unit implies at least a potential for life-threatening disease, and therefore such patients cannot be viewed as healthy until proven to be so. Therefore, it is the opinion of the authors that a more conservative approach should be taken to initiating therapy for hyperbilirubinemia.

Guidelines for the Management of Hyperbilirubinemia Based on the Birthweight and Relative Health of the Newborn

BIRTHWEIGHT	Total Serum Bilirubin Level (mg/dL)			
	Healthy		Sick	
	Phototherapy	Exchange Transfusion	Phototherapy	Exchange Transfusion
<1000 g	5–7	Variable	4–6	Variable
1001–1500 g	7–10	Variable	6–8	Variable
1501–2000 g	10–12	Variable	8–10	Variable
2001–2500 g	12–15	Variable	10–12	Variable

Total serum bilirubin levels rising at a rate greater than 0.5 mg/dL per hour (8,6 μmol/L) indicate a state of active hemolysis; such patients should be considered as falling into the "sick" category. It is exceedingly important in these cases to institute and revise therapies on the basis not only of the current level of bilirubin but also of an estimate of the anticipated peak. Thus, early in the patient's course, phototherapy or exchange transfusion may occur at a relatively lower bilirubin level than for a similar bilirubin level achieved at a later time.

V. Plan and organizational structure of the lesson.

Serial №	**The main periods of lesson, their functions and contents**	**Educational aims in links of learning**	**Methods of control**	**Methodical materials for control, imaging, directory materials**	**Distribution of time in minutes**
1	**Preparatory stage** Organizing measures Setting of educational aims and motivation Control of secondary knowledges and practice level: 1. Etiology of hemolytic and haemorrhagic diseases in newborn infants 2. The main pathogenesis links of hemolytic and haemorrhagic in newborn infants 3. Clinical classification of hemolytic and haemorrhagic diseases in newborn infants	 α2 α2 α2	 Individual verbal questioning Fase-to-fase interlocution Control by the second level tests Solution of typical the second level tasks	 p.I "Actuality of theme" p.II "Educational aims" Tables, pictures, structural schemes Pharmaceutical preparations, slides. Questions for individual inquiry. The second level tests The third level tests The second level tasks	3 minutes 12 minutes 25 minutes

	4. Clinical and diagnostical features of hemolytic and haemorrhagic diseases in newborn infants	α2			
	5.Clinical and diagnostical features of hemolytic and hemorrhagic diseases in preterm and full-term newborn infants 6.Laboratory and instrumental diagnostic of hemolytic and hemorrhagic diseases in newborn 7.Differential diagnostic of hemolytic and hemorrhagic diseases in newborn infants 8.Complications of hemolytic and hemorrhagic diseases in newborn infants 9.Principes of treatment newborn infants with hemolytic and hemorrhagic diseases 10.Prevention of hemolytic and hemorrhagic diseases in newborn infants 11. Deposition of exchange transfusion in hemolytic and hemorrhagic diseases.	α2 α2 α2 α2 α2 α2 α2	Control by third level tests		
2	**The main stage** Formation of professional practices and skills: 1. To conduct clinical examination of newborn infant with hemolytic and hemorrhagic disease, to capture methods of medical histories gathering 2. To conduct clinical examination of infant, to reveal the	α3 α3	Method of forming practices: Practical professional training, solution of typical the third level tasks and tests	Algorithms for creation practical skills. Algorithms for creation professional abilities.	115 minutes

	main symptoms of hemolytic and hemorrhagic diseases 3. To formulate and to prove preliminary diagnosis 4. To compose plan of laboratory and instrumental examination of patient 5. To interpret results of laboratory and instrumental examination 6. To establish differential diagnostic between inflammatory diseases with the same clinical manifestations 7. To give recommendations of regime and nutrition to infant with hemolytic and hemorrhagic disease 8. To compose the plane of treatment the patient 9. To determine the medical tactics in hemolytic and hemorrhagic complications	α3 α3 α3 α3 α3 α3 α3		Patients Medical histories List of medical prescriptions The third level tests The third level tasks Imitational games Equipment: Instructions(on cards), orders of Ukrainian Ministry of Public Health (protocols of review and treatment). Situational atypical the third level tasks. Algorithms of the first aid giving	
3	**Final stage** Control and correction of professional skills and practices Sizing up the lesson		Analysis of clinical work results. Solving atypical the third level tasks and tests.	Results of clinical work. Situational atypical the third level tasks.	25 minutes
4	Home task (basic and additional literature about the topic)		Valuing of clinical work results.	Approximate card for one's own work with literature	

Questions for elementary level of knowledges control

1. To determine conception of jaundices in newborn.

2. To point out at main features of bilirubins metabolism in newborns, risc factors, which can to help in progress of jaundices in newborn.
3. What are etiology and pathogenesis of hemolytic disease of newborn?
4. Classification of hemolytic disease of newborn.
5. What are the clinic manifestations of different types of hemolytic disease of newborn?
6. What are the diagnostic principles of hemolytic disease? Conduct differential diagnostic of jaundices in newborn.
7. What is the first aid in case of hemolytic disease of newborn?
8. To prescribe treatment, prophylactic and rehabilitation measures to patient.
9. Determine conception of hemorrhagic syndrome in newborn.
10. Point at the main features of hemostasis in newborn, which can help to development of hemorrhagic disease in newborn.
11. What are etiology and pathogenesis of hemorrhagic disease of newborn?
12. What is the clinic of hemorrhagic disease?
13. What are the diagnostic principles of hemorrhagic disease ? Conduct differential diagnostic of hemorrhagic syndrome in newborn.
14. What is the first aid in case of hemorrhagic disease of newborn?
15. To prescribe treatment, prophylactic and rehabilitation measures to patient

Examples of tests and tasks:

1.New-born child from a mother with the complicated obstetric anamnesis, from third pregnancy, first delivery. At birth a skin is rose. The Hb of blood is 160 g/l, RBC - 4,6 g/l. Bilirubin of blood from the umbilical vein is 60 mcmol/l. Blood type of mother is (I) Rh (-),of the child is (I) Rh (+). The icterus of skin appeared after 6 hours; bilirubin of blood is 116 mcmol/l, unconjugated. Diagnosis: Icteric - anaemic form of Rh-conflict. Define the tactic of medical treatment.

A. Enterosorbents
B. Light-therapy
C. Exchange blood transfusion
D. Light-therapy + liquid infusion
E. Membranestabilizing preparation.

2. In worn child of one week of age, that was born with the weight 3400g, length 51cm, an icterus has appeared in the first days and increased due to indirect fraction of bilirubin. Hepatic enzymes are normal. Blood type of mother is II Rh -positive, of the child is 0(I) Rh- positive. What pathology is more likely in this case?

A. Biliary atresia
B. Fetal hepatitis
C. Hemolytic disease of newborns
D. Conjugated icterus.
E. Crigler-Najjar syndrome

3. New-born child, gestational age 36 weeks, at birth the weight is 2400g, length 51cm. A child is excited, tremor of extremities, does not suck, dispnoe, gepatosplenomegalia. At the end of the first day the icterus of skin and mucosas has appeared, on the second day the rash on a skin and vesicules in the region of chest. What is your previous diagnosis?

A. Hemolytic disease of newborns
B. Physiological jaundice of newborns
C. Hypoxic- ischemic CNS injury
D. Intrauterine infection
E. Biliary atresia.

4. In a newborn girl that was born in term, second delivery, weight 3500g, Apgar score 8-8 points, the icterus has appeared in first day of life. Indirect bilirubin in a blood is 57 mcmol/l, after 6 hours is 100 mcmol/l. Choose the correct method of medical treatment.

A. Exchange blood transfusion
B. Prescribing of Phenobarbital
C. Light-therapy
D. Liquid infusion
E. Enterosorbent

5. In newborn child with hemolytic disease induced by Rh – conflict the blood type is 0 (I) Rh (+), in mother is (II) Rh(-). What blood must be poured during the operation of exchange blood transfusion?

A. (II) Rh (-)
B. O (I) Rh (+)
C. A (II) Rh(+)
D. A(I) Rh (-)
E. B(III) Rh(-)

6. In newborn child in age of one day there was an icterus. Common bilirubin in blood serum is 144 mcmol/l, indirect bilirubin is 130 mcmol/l. Coumbs test is positive. Child from the first pregnancy. A mother has blood type 0(I) Rh(-). What is more likely causes the jaundice?

A. Biliary atresia
B. The rhesus conflict
C. ABO-incompatibility
D. Physiological jaundice
E. Fetal hepatitis

7. Worn newborn child from the first pregnancy and first delivery. Mother's blood type is (I) Rh (+), child's is (II) Rh (+). An icterus increases progrediently after 2 day of life. Liver +3cm, spleen +1cm. Bilirubin of blood to 3 day of life consists 250 mcmol/l, unconjugated is 240 mcmol/l. Direct test of Coumbs is low positive, Hb 160-160 g/l, RBC. - 4,5x10^12/l, Ht 0,55. What the most reliable diagnosis?

A. ABO-conflict

B. Physiologic jaundice
C. Jaundice of mother milk
D. Conjugated icterus
E. Fetal hepatitis

8. Child in age of 10 days, was born in a term with weight 3000g. Apgar score is 8-9 points. From the first day an icterus of skin admitted, liver +3,5cm., spleen is on the edge of costal arc. Color of urine and feces are not changed. In this time Combs test is positive, hemoglobin 130 g/l, reticulocytes is 4,6%, common bilirubin is 300 mcmol/l, indirect fraction is - 288 mcmol/l, transaminases: ALT - 0,28, AST - 0,26. During medical treatment the state of child became better, intensity of icterus diminished. Up to 9 day of life icterus acquired greenish color, urine became dark, feces white. In ultrasound cholic channels and gall-bladder scanned clear. Establish the diagnosis:

A. Biliary atresia
B. Fetal hepatitis
C. Jaundice of Crigler-Najjar
D. Intrahepatic cholestasis
E. Physiologic jaundice

9. Child was born in term, with gestational age of 40 weeks and weight of 3000g. Apgar score 7-8 points. Mother's blood is AB (IY) Rh (-). Child's is (III) Rh(+). An icterus appeared in the first day. Common bilirubin is 200 mcmol/l, indirect fraction is 190 mcmol/l , direct is 10 mcmol/l, Hb-160 g/l, reticulocytes 4,4%. Liver +4cm, spleen + 1,5cm. Urine is light, feces are painted. Coumbs test is positive. Establish the diagnosis:

A. Physiologic jaundice
B. Hemorrhagic illness of newborns
C. Fetal hepatitis
D. Crigler-Nayyar syndrome
E. Hemolytic disease of newborns

10. Child was born healthy with weight 3500g, length 51cm, Apgar score 8 points. A woman has the first non complicated pregnancy, delivery in term. Mother's blood is (I) Rh (-), father's is (II) Rh (+), child's is (I) Rh (+). What method of prophylaxis of Rh-conflict needs to be appointed for puerpera?

A. It does not need prophylaxis
B. Vitamines
C. Anti-Rh- immunoglobulin
D. Antihistaminic preparations
E. Enterosorbents

11. Child after delivery have following clinical data: icterus, pallor, splenohepatomegalia. Blood type is (III) Rh (+);Hb in blood 150 g/l, RBC is 4,2*10^12/l, reticoulocytes 9 %. Bilirubin of blood is 58 mcmol/l, unconjugated.

Mother's blood is (III) Rh (-), titer of anti- Rh-antibodies during pregnancy are 1:128; 1:256. What test more reliable will help to define the tactic of treatment?

A. Increasing of bilirubin per hour
B. Clinical supervision
C. Routine blood test
D. Proteinogramme
E. Level of hepatospecific enzymes

12. A worn child, Apgar score 6 points. Pale, hamorrhages on a skin, general edema: liver +6cm, spleen +4cm. Mother's blood is (I) Rh (-), child's is (I) Rh (+). The Hb in umbilical cord blood 70 g/l, RBC. 1,5*10^12/l reticulocytes 15%; normoblastes is 70 per 100 leucocytes, in a peripheral blood there is eritroblastes. Bilirubin at birth is 58 mcmol/l, unconjugated. Woman has abortions in her anamnesis. What the most reliable diagnosis?

A. Sepsis of newborns
B.Congenital leucosis
C. Rhesus conflict, edematic form
D. Fetal hepatitis
E. Hereditary hemolytic anemia

13. Worn newborn after the normal pregnancy and physiologic delivery. On a 4 day of life there is severe icterus of skin and mucoses, liver +1 cm, a spleen not palpated. Reflexes and tone of muscles are not broken, child active. Hb 170 g/l, RBC. 5,1*1012, Ht-0,58. Blood type of mother (III) Rh (+), child (III) Rh (+). Bilirubin of blood 430 mcmol/l, unconjugated is 420 mcmol/l. What is the most reliable diagnosis?

A. Hepatitis
B. Conjugated icterus
C. ABO-conflict
D.Physiologic icterus
E. Syndrome of cholestasis

14. Child 2 days. In the end of first day of life an icterus of skin has appeared, a liver was enlarged to 3,5sm. Child is enough active, reflexes and muscular tone are not broken. bilirubin of blood 170 mcmol/l, unconjugated, Hb 150 g/l, RBC -4,7, Ht-0,5. Define the tactic of medical treatment.

A. Hemotransfusion
B. Exchange blood transfusion
C. Extracorporal hemosorbtion
D. Light-therapy
E. Hemotransfusion + membranestabilizing preparations

15. In worn child after the first pregnancy, difficult confinements, there was. Cephalohematoma. An icterus appeared on 2 day of life, on 3 day-admitted the changing in neurological state: nystagmus, Grefe Symptom. Urine is yellow, excrements yellow. Blood type of mother (II)Rh-, child's (II)Rh+. On the third day

Hb 200 g/l, RBC.-6,1x10, bilirubin –in the blood-58 mcmol/l due to unbinding fraction, Ht-0,57. How to explain the jaundice in child?

A. Biliary atresia
B. Fetal hepatitis
C. Cranial- natal trauma
D. Hematolytic disease of newborns
E. Physiologic icterus

16. In newborn, two days of life to the end of the first day an icterus appeared. In clinical examination an- icterus of skin and sclera admitted. A live under edge of costal arc on 4 cm, spleen on 2 cm. Mother's blood type is- (0) the Rh+ child's II Rh(+). In routine blood test the reticulocytosis 15 ‰, RBC 2,8 x 10 12 /l, hemoglobin 120 g/l, bilirubin of umbilical blood is78 mcmol /l, after 8 hour is-190 mcmol /l. Choose the method of medical treatment:

A. Exchange blood transfusion
B. Prescribing of phenobarbital
C. Light -therapy
D. Liquid infusion
E. Intragastral dropping linfusion

17. A new-born child has the diagnosed physiologic icterus. For this state characteristically are:

A. Repeated increasing of icterus intensity after the period of its reduction or disappearance
B. Appearance of icterus during 1 day of life
C. Duration of icterus more than 10 days
D. Level of indirect bilirubin more than 205 mcmol/l
E. Appearance of the yellow skin colouring on a 2-3 day of life

18. In anamnesis of woman the previous child had hemolytic disease of newborn; abortions, medical abortions. Now woman have VII pregnancy with 16 weeks of gestational age, threat of pregnancy, breaking (II) Rh (-), titer of anti-Rh-antibodies 1:512. Specific prophylaxis of Rh-conflict was not conducted. What method of antenatal medical treatment of Rh-conflict most expediently to prescribe?

A. Hepatotropic medicines and vitamins
B. Plasmaferesis
C. Enterosorbents
D. Dimedrol
E. Infusions of glucose

19. Child, 21 day of life, was born on a 38-39 week of gestational age, from 5th pregnancy, 2- delivery, with weight 2480g., length 51cm. On 7th months of pregnancy in a mother the marker of viral hepatitis V revealed. To the end of 1 day of life in child admitted an icterus with gradually increased intensity. To the 7 day of life there is the rise of liver specific enzymes activity was noted, that persists

presently. Cardiac tones are muffled, moderate tachicardia. Hepatoslenomegalia. What are the late complications can be observed in child?

A. Respiratory infections
B. Diabetes mellitus
C. Cirrhosis of liver
D. Leucosis
E. Elastofibrosis

20. Newborn child is in the newborn pathology department with the icteric form of hemolytic disease caused by immune ABO conflict between mother and fetus. With what purpose to this child prescribed the carbolen?

A. Strengthening of hepatocytes transferase activity
B. Breaking of intestinal-hepatic cycle of bilirubin
C. Compacting of hematoencephalic barrier
D. Stabilization of erythrocyte membranes
E. Stimulation of. bile secretion

Tasks

1. A newborn is noted to be quite jaundiced at 3 days of age. Which of the following factors is associated with an increased risk of neurologic damage in a jaundiced newborn?

The answer is neonatal sepsis. Significant unconjugated serum bilirubin levels in full-term newborn infants can lead to diffusion of bilirubin into brain tissue and to neurologic damage. Sulfisoxazole and other drugs compete with bilirubin for binding sites on albumin; therefore, the presence of these drugs can cause dislocation, not increased affinity, of bilirubin to tissues. Metabolic acidosis also reduces binding of bilirubin, and neonatal sepsis interrupts the blood-brain barrier, thus allowing diffusion of bilirubin into the brain. Administration of phenobarbital has been used to induce glucuronyl transferase in newborn infants and can reduce, rather than exacerbate, neonatal jaundice. Other factors that reduce the amount of unconjugated bilirubin bound to albumin (and therefore cause an increase in free unconjugated bilirubin) include hypoalbuminemia and certain compounds (e.g., nonesterified fatty acids, which are elevated during cold stress) that compete with bilirubin for albumin binding sites.

2. A primiparous woman whose blood type is O positive gives birth at term to an infant who has A-positive blood and a hematocrit of 55%. A serum bilirubin level obtained at 36 h of age is 12 mg/dL. Which of the following laboratory findings would be characteristic of ABO hemolytic disease?

The answer is a positive direct Coombs test. If a mother is O positive and her baby is A positive, the baby has a chance of developing hemolytic disease. Hemolytic disease and jaundice caused by a major blood-group incompatibility are usually less severe than with Rh incompatibility. Although the hematocrit of affected infants usually is normal, elevation of the reticulocyte count and the presence of nucleated red blood

cells and microspherocytes in the blood smear provide evidence of hemolysis. In comparison with hemolytic disease caused by Rh incompatibility, where it is usually strongly positive, major blood-group incompatibility is often associated with a direct Coombs test that is frequently weakly positive. Petechiae are usually associated with decreased number of platelets. Crescent-shaped (sickled) red blood cells are found with sickle cell disease.

3. You are speaking to a couple who are expecting their first baby in about 2 weeks. They are concerned about the safety of childhood immunizations and also about "unneeded" medications given to newborns in the hospital. They ask about the purpose of the routine administration of intramuscular vitamin K. You explain to them about hemorrhagic disease of the newborn, stating that the untreated baby can manifest

The answer is a prolonged prothrombin time and a risk of serious hemorrhage in the days following delivery. Prophylactically to newborn infants is associated with a decline in the levels of vitamin K-dependent coagulation factors. In less than 1% of infants (but especially those fed human breast milk), the levels reached are low enough to produce classic hemorrhagic manifestations on the second to seventh day of life. These manifestations include melena, hematuria, and bleeding from the circumcision; intracranial hemorrhage and hypovolemic shock are serious complications. Diagnosis of this condition is indicated by a prolonged prothrombin time, which reflects inadequate concentrations of factors II, VII, IX, and X.

4. You are called to the normal newborn nursery to see a baby who was noted to be mildly jaundiced and has a total serum bilirubin concentration of 12 mg/dL at 48 h of age. The baby is a 3500-g boy who was born at term to a 27-year-old O-positive, Coombs-test-negative primigravida 2 h after membranes ruptured. There were no prenatal complications, and the mother had regular prenatal care. Breast-feeding has been well tolerated, and the baby's vitals have been normal. The most appropriate additional diagnostic studies to evaluate the cause of this infant's jaundice are

The answers is complete blood count, direct serum bilirubin, baby blood type and Coombs, peripheral smear. The development of jaundice in a healthy full-term baby may be considered the result of a normal physiologic process if the time of onset and duration of the jaundice and the pattern of serially determined serum concentrations of bilirubin are in conformity with currently accepted safe criteria. Physiologic jaundice becomes apparent on the second or third day of life, peaks to levels no higher than about 12 mg/dL on the fourth or fifth day, and disappears by the end of the week. The rate of rise is less than 5 mg/dL per 24 h and levels of conjugated bilirubin do not exceed about 1 mg/dL. Concern about neonatal jaundice relates to the risk of the neurotoxic effects of unconjugated bilirubin. The precise level and duration of exposure necessary to produce toxic effects are not known, but bilirubin encephalopathy, or kernicterus, is rare in term infants whose bilirubin level is kept below 18 to 20 mg/dL. Certain risk factors affecting premature or sick newborns increase their susceptibility to kernicterus at much lower levels of bilirubin. The diagnosis of physiologic jaundice is made by excluding other causes of hyperbilirubinemia by means of history, physical examination, and laboratory

determinations. Jaundice appearing in the first 24 h is usually a feature of hemolytic states and is accompanied by an indirect hyperbilirubinemia, reticulocytosis, and evidence of red-cell destruction on smear. In the absence of blood group or Rh incompatibility, congenital hemolytic states (e.g., spherocytic anemia) or G6PD deficiency should be considered. With infection, hemolytic and hepatotoxic factors are reflected in the increased levels of both direct and indirect bilirubin. Studies should include maternal and infant Rh types and blood groups and Coombs tests to detect blood group or Rh incompatibility and sensitization.
Measurements of total and direct bilirubin concentrations help to determine the level of production of bilirubin and the presence of conjugated hyperbilirubinemia. Hematocrit and reticulocyte count provide information as to the degree of hemolysis and anemia, and a complete blood count screens for the possibility of sepsis and the need for cultures. Examination of the blood smear is useful in differentiating common hemolytic disorders. Except for determinations of total and direct bilirubin, tests of liver function are not particularly helpful in establishing the cause of early-onset jaundice. Transient elevations of transaminases (AST and ALT) related to the trauma of delivery and to hypoxia have been noted. Biliary atresia and neonatal hepatitis can be accompanied by elevated levels of transaminase but characteristically present as chronic cholestatic jaundice with mixed hyperbilirubinemia after the first week of life.

5. Since you are a new intern, you ordered all of the diagnostic studies you could think of instead of just the ones your senior resident told you were most appropriate. The nurse calls to inform you that the infant's studies are back. Both the mother and baby have O-positive blood. The baby's direct serum bilirubin is 0.2 mg/dL, with a repeat total serum bilirubin of 11.8 mg/dL. Urine bilrubin is positive. The mother's white count is 13,000/L with a differential of 50% polymorphonuclear cells, 45% lymphocyes, and 5% monocytes. The hemoglobin is 17 g/dL, and the platelet count is 278,000/L. Reticulocyte count is 1.5%. The peripheral smear does not show fragments or abnormal cell shapes. Blood cultures are pending in the laboratory. Liver enzymes and liver ultrasound are normal. G6PD levels and osmotic fragility testing are normal. The most likely diagnosis in this infant is
The answers is physiologic jaundice. The development of jaundice in a healthy full-term baby may be considered the result of a normal physiologic process if the time of onset and duration of the jaundice and the pattern of serially determined serum concentrations of bilirubin are in conformity with currently accepted safe criteria. Physiologic jaundice becomes apparent on the second or third day of life, peaks to levels no higher than about 12 mg/dL on the fourth or fifth day, and disappears by the end of the week. The rate of rise is less than 5 mg/dL per 24 h and levels of conjugated bilirubin do not exceed about 1 mg/dL. Concern about neonatal jaundice relates to the risk of the neurotoxic effects of unconjugated bilirubin. The precise level and duration of exposure necessary to produce toxic effects are not known, but bilirubin encephalopathy, or kernicterus, is rare in term infants whose bilirubin level is kept below 18 to 20 mg/dL. Certain risk factors affecting premature or sick newborns increase their susceptibility to kernicterus at much lower levels of bilirubin.

The diagnosis of physiologic jaundice is made by excluding other causes of hyperbilirubinemia by means of history, physical examination, and laboratory determinations. Jaundice appearing in the first 24 h is usually a feature of hemolytic states and is accompanied by an indirect hyperbilirubinemia, reticulocytosis, and evidence of red-cell destruction on smear. In the absence of blood group or Rh incompatibility, congenital hemolytic states (e.g., spherocytic anemia) or G6PD deficiency should be considered. With infection, hemolytic and hepatotoxic factors are reflected in the increased levels of both direct and indirect bilirubin. Studies should include maternal and infant Rh types and blood groups and Coombs tests to detect blood group or Rh incompatibility and sensitization. Measurements of total and direct bilirubin concentrations help to determine the level of production of bilirubin and the presence of conjugated hyperbilirubinemia. Hematocrit and reticulocyte count provide information as to the degree of hemolysis and anemia, and a complete blood count screens for the possibility of sepsis and the need for cultures. Examination of the blood smear is useful in differentiating common hemolytic disorders. Except for determinations of total and direct bilirubin, tests of liver function are not particularly helpful in establishing the cause of early-onset jaundice. Transient elevations of transaminases (AST and ALT) related to the trauma of delivery and to hypoxia have been noted.
Biliary atresia and neonatal hepatitis can be accompanied by elevated levels of transaminase but characteristically present as chronic cholestatic jaundice with mixed hyperbilirubinemia after the first week of life.

6. A previously healthy full-term infant has several episodes of duskiness and apnea during the second day of life. Diagnostic considerations should include which of the following?
The answer is congenital heart disease. Idiopathic apnea is common in premature infants but is not expected in the full-term newborn. When apnea occurs in the term infant, there is almost always an identifiable cause. Sepsis, gastroesophageal reflux, congenital heart disease, seizures, hypoglycemia, and airway obstruction can cause apnea in term newborns. Harlequin syndrome is a transient change in the skin color of the otherwise asymptomatic newborn (usually preterm) in which the dependent side of the entire body turns red while the upper side remains pale.

7. Parents bring a 5-day-old infant to your office. The mother is O negative and was Coombs positive at delivery. The term child weighed 3055g at birth and had a baseline hemoglobin (16 gm/dL) and a total serum bilirubin (3 mg/dL). He passed a black tarlike stool within the first 24 h of life. He was discharged at 30 h of life with a stable axillary temperature of 36.5C (97.7F). Today the infant’s weight is 3000g, his axillary temperature is 35C (95F), and he is jaundiced to the chest. Parents report frequent yellow, seedy stool. You redraw labs and find his hemoglobin is now 14 gm/dL, and his total serum bilirubin is 13 mg/dL. The change in which of the following parameters is of most concern?
The answer is temperature. There is loss of body weight of 1.5 to 2% per day for the first 5 days of life for a normal newborn infant as excessive fluid is excreted. This would tend to produce an increase in hematocrit, but, to the contrary, the hematocrit

falls as an adaptation to an environment of higher oxygen. Infants usually have several meconium stools during the first day or two of life, changing to soft yellow stools at 1 to 2 days of life. As the hematocrit falls, there is a corresponding increase in serum bilirubin that peaks around 3 to 5 days of life. Temperature should not change; temperature instability in a term infant is frequently a sign of serious infection.

8. A newborn infant becomes markedly jaundiced on the second day of life, and a faint petechial eruption first noted at birth is now a generalized purpuric rash. Hematologic studies for hemolytic diseases are negative. Acute management should include which of the following steps?
The answer is isolation of the infant from pregnant hospital personnel. Although hypothyroid neonates may develop hyperbilirubinemia, the patient described most likely has a congenital or acquired infection requiring immediate diagnosis and treatment. Among the important causes of neonatal sepsis are prenatal infections, including congenital syphilis, toxoplasmosis, cytomegalic inclusion disease, and rubella. Useful diagnostic studies, in addition to cultures for bacteria, include specific serologic tests for pathogens, viral cultures, lumbar puncture, and x-rays of the chest and long bones. Longitudinal striations in the metaphyses are characteristic of congenital rubella, whereas osteochondritis or periostitis usually indicates congenital syphilis. Congenital syphilis, cytomegalovirus, and rubella can be highly contagious. Urine can contain rubella virus for more than 6 months and is, therefore, a special hazard to nonimmune pregnant women.

9. A baby-boy was born at time, it was his mother's 1st pregnancy. The jaundice was revealed on the 2nd day of life, then it progressed. The adynamia, vomiting and hepatomegaly were presented. The indirect bilirubin level was 275 mcmol/L, the direct bilirubin level - 5 mcmol/L, Hb- 150 g/L. Mother's blood group - 0(I), Rh+, child's blood group - A(II), Rh+. Make a diagnosis.
The answer is hemolytic disease of newborn (ABO incompatibility), icteric type. Hemolysis is primarily extravascular, although intravascular hemolysis that is not induced by complement also occurs. Infants sometimes develop anemia, reticulocytosis, and hyperbilirubinemia within the first 24 hours of life. The hallmark of ABO hemolytic disease is the presence of microspherocytes on the peripheral blood smear. In Rh hemolytic disease, on the other hand, microspherocytes are rarely noted. The direct antiglobulin test should be at least weakly positive for anti-A or anti-B; however, because of the sparse distribution of antigenic sites on a newborn’s red cells, ABO hemolytic disease may be present even without a positive result on the direct antiglobulin test. The maternal serum should have high titers of IgG directed against A or B. In the absence of clinical hemolytic disease, laboratory evidence of erythrocyte sensitization should not be considered isoimmune hemolytic disease.

10. Newborn in the age of 3 days, was born from mother that was sick of lupus. Blood count reveals the thrombocytopenia. Objectively: ecchymoses on the trunk and extremities. What is the preliminary diagnosis?

The answer is isoimmune thrompocytopenic purpura. Maternal IgG antibodies, usually reacting against fetal ABO- or Rh-incompatible RBCs, can cross the placenta, enter the fetal circulation, and cause hemolysis, anemia, and hyperbilirubinemia. Transfer of antibodies across the placenta depends on the Fc component of the IgG molecule. Because both IgM and IgA antibodies lack this component, only IgG antibodies cause hemolytic disease of the newborn.

Metohodical materials to support basic stage class.

Professional algorythm of patients management implementation (reference chart) for the practical skills and abilities forming .

№	Task	Sequence of implementation	Remarks and warnings related to self-control
1	To conduct examination of newborn infant with hemorrhagic disease.	1. To conduct the complaints and disease and obstetric anamnesis gathering.	Pay attention to features of disease course, underlying factors, concomitant diseases etc. To establish the availability of risk factors which facilitate disease occurrence.
		2. To conduct examination of the patient.	To assess patient general condition, position in bed, color and humidity of skin and mucouse, presence of hemorrhages and bruises on the skin, and extremities swelling. To pay a regard to presence of haemorrhages, bleeding from mucouses, umbilical wound, nasal bleedings, melena and cephalohematomas, internal hematomas, lung bleedings, so on.
		3. To investigate cardiovascular system of the patient (palpation, percussion).	To pay a regard to rhythm of pulse, it tension and size on both hands, apex shove, it properties, margins of absolute and relative cardiac dullness, it changes, HR (tachi-or bradicardia, extrasystole), BP.
		4. To conduct hart and main vessels	To pay regard to heart tones weakening or

		auscultation. 5. To investigate the pulmonary system 6. To conduct lungs auscultation. 7. To investigate the system of digestion.	amplifying, appearance of murmurs and additional III, IV tones. To pay attention to features of percussion and auscultation. Presence of apneustic breath, character of veesels during the auscultation. Presence of emesis, belches, swellings, fast decline of weight, signs of enterocolitis or peritonitis. Presence of edemas, anuria. Signs of depression or hypoexcitability, crumps.
2	To formulate the initial diagnosis.	1.To formulate the preliminary diagnosis 2.To substantiate all components of preliminary diagnosis based on complaints, anamnesis, and examinations.	To formulate the initial diagnosis of hemolytic or hemorrhagic disease and to substantiate each component of it, based on modern classification
3	To evaluate the parameters of additional laboratory tests.	1.To evaluate the blood count data. 2.To conduct Apt's test in the presence of melena. 3.To evaluate the bleeding time, clotting time, platelete count, clot retraction, platelet aggregation tests (using activetors), thrombin time, prothrombin index, APTT (Activated Partial Thromboplastin Time), ACT, fibrinogen, tests to assessing the fibrinolytic mechanims.	To pay attention to signs of anemia, leucocytosis, changing of formula, elevation of sedimentation rate. To pay attention to bleeding time, clotting time, platelete count, clot retraction, platelet aggregation tests(using activators), thrombin time, prothrombin index, APTT(Activated Partial Thromboplastin Time), ACT, fibrinogen, tests to assessing the fibrinolytic mechanims. To pay attention on US of

		4.To evaluate the results of instrumental patients examination.	internals and brain, ECG, X-ray of chest organs.
4.	To conduct differential diagnosis.	1.Consistently to find out the common signs in complaints, life and disease anamnesis, data of examination, data of laboratory and instru-mental tests in patient and in similar states. 2.To find the differences amog complaints, information of life and disease anamnesis, examination data, information about the laboratory and instrumental methods of examination and in similar nosology. 3.On the basis of find out differences for excluding similar diseases from the list of probable diagnoses. 4. To conduct differential diagnostics according to the above mentioned algorithm among all nosologies are having the similar signs, among other diseases. 5.Taking into account the impossibility to exclude the diagnosis of haemorrhagic disease from the list of probable diagnoses to draw a conclusion about most probability of such diagnosis.	Special attention must be paid to differential diagnosis among the syndrome of "mothers' swallowed blood", intranatal infections, respiratory distress syndrome in premature, thrombopenia, inherited coagulopathy, jaundice, natal trauma.
5.	To formulate the final clinical diagnosis.	3. To formulate the final clinical diagnosis.	Being based on modern classification of

		4. Based on initial diagnosis, additional investigations data, conducted differential diagnosis to substantiate all elements of the final clinical diagnosis.	hemorrhagic diseases to formulate the final clinical diagnosis, complications of disease and presence of concomitant diseases.
6.	To prescribe treatment for patients.	1.To prescribe not medicinal treatment 2.To prescribe the medicinal treatment.	Expressly to specify the regimen and detalized nutrition according to clinic and status of newborn. Taking into account gestational age, severity of patient state, the stage of disease, the presence of complications and concomitant pathology, to prescribe modern medicinal treatment in accordance to the standards of hemorrhagic diseases therapy.

Materials of control for conclusive classes stage:

1. In worn newborn child diagnosed the hemolytic disease by rhesus factor. The amount of bilirubin is critical. Blood type of child (III), mother's is-(II). Exchange blood transfusion is indicated. What selection of donor blood is needed for this purpose?

A. Blood type (III), rhesus factor positive
B. Blood type (II), rhesus ifactor negative
C. Blood type (II), rhesus factor positive
D. Blood type O(I), rhesus factor negative
E. Blood (III) type, rhesus factor negative

2. Child, 25 days of life, was born on a 37 week of gestation with weight 2000g, length 48cm., after the 5 pregnancy is complicated in a 1 and 3 trimester with hestosis, anemias, threating of abortion. Icterus from the moment of birth. Cardiac tones are muffled, moderate tahicardia. respiration puerile, wheezes are not present. A stomach is enlarged, hepatosplenomegalia. Stool white. Urine is dark. What changes of parameters are characteristic for intrauterine hepatitis?

A. High activity of transaminases
B. Low activity of transaminases
C. Decreasing of alfa- fetoprotein comcentration

D. Rising of common bilirubin due to it indirect fraction

E. decreasing of alfa- fetoprotein concentration and low activity of transaminases

3. To what risk group it is possible to attribute newborn child with hemolytic disease?

A. Group I- -a healthy children

B. Group II – children with the risk of chronic pathology manifestation and with the presence of disturbances

C. II-A – newborns without manifestations of diseases, but with a presence of unfavorable factors

D. II-B – children been suffered of any illness intranatally, during the delivery or postnatally

E. groups III-IV, V – children with chronic pathology

4. For the isoimmune conflict prophylaxis it is needed to administrate for mother an anti-D-rhesus immunoglobulin , if following criteria are keeping:

A. In mother the Rh (+), antibodies are not present, in newborn Rh (+)

B. In mother Rh (-), antibodies are not present, in newborn Rh (+)

C. In mother Rh (+), antibodies are not present, in newborn Rh (-)

D. In mother Rh (-), antibodies are present, in new-born Rh (+)

E. In mother the Rh (-), antibodies are not present, in newborn Rh (-)

5. In an expectant mother during delivery admitted the placental detachment. Urgent hemotransfusion to child in birth prescribe, if a critical level of Hb (g/l) is evened:

A. 180

B. 160

C. 140

D. 220

E. 100

6. It is necessary to hold back from conducting of light-therapy in icterus due to holestasis (direct bilirubin higher than 20 %)

A. The statement is incorrect

B. The syndrome of respiratory disorders can arise

C. There is the danger for development of bronze child syndrome

D. Can arise an intracranial hemorrhage

E. Can arise a pneumonia

7. Hyperbilirubinemia with the rise of direct fraction of bilirubin is observed in newborn patients in following cases:

A. Halactosemia

B. Perinatal- TORCH- infections

C. Sepsis

D. Hepatitis

E. All above mensioned states are accompanied with the rise of direct fraction.

8. Diagnostics of hemolytic disease causes by rhesus-conflict in newborn child with clinical manifestation, but without antibodies in a mother you: will prescribe during pregnancy?

A. Direct and indirect Combs tests
B. Direct Combs test
C. Indirect Combs test
D. Level of biliroubinou in an umbilical cord blood
E. Osmotic resistance of erythrocytes

9. Risk factors of holestasis in newborn children?

A. Complete parenteral feeding
B. Hemlytic disease of newborn
C. Antibacterial therapy and infections
D. Hemotransfusion
E. All above mensioned is correct, except for hemotransfusion

10. In a new-born child on a 5 day of life the level of biliroubin in blood is 280 mcmol/l, direct fraction to 90 mcmol/l. These parameters are reflected following states:

A. Hemolisis as a result of glucose-6-phosphat dehidrogenase deficiency
B. CMV -infectiob
C. Viral hepatitis B
D. Syndrome of an intrahepatic cholestasis
E. Everything is correct except for a G-6-PD deficiency

11. Development of hemorrhagic desease in newborns can be connected to the following, except for:

A. Administration to the mother of indirect anticoagulants
B. Administration to the mother of Acidum ascorbinicum
C. Administration to the mother of aspirine
D. Administration to the mother of Phenobarbitalum
E. Administration to the mother of antibiotics

12. Full-term child. Pregnancy was normal. Labors with partial placental detachment. In 12 hours after labors the melena is marked. What diagnostic methode can reveal the reason of bleeding?

A. The Apt test
B. Barium clyster
C. Gastric lavage with solution of natrii chloridi 0,9%
D. Count of thrombocytes
E. Count prothrombin time and partial thromboplastin time

13. Development of hemorrhagic desease of newborns is caused by:

A. Trombocytopathy
B. Deficiency of vitamin K dependent cjagulation factors
C. Deficiency of the eighth factor
D. Deficiency of the ninth factor

E. Thrombocytopenia

14. Positive Apt test is testifying for presence in the liquid investigated:
A. Haemoglobin F (blood of newborn)
B. Indirect bilirubin
C. Direct bilirubin
D. Hemoglobin A (maternal blood)
E. Meconium

15. For conducting of Apt test uses:
A. A discharge from a stump of a umbilical cord
B. A venous blood
C. A capillary blood
D. Bloody vomitive masses or feces
E. A venous blood of mother

16. In anamnesis of woman the previous child had hemolytic disease of newborn; abortions, medical abortions. Now woman have VII pregnancy with 16 weeks of gestational age, threat of of pregnancy breaking (II) Rh (-), titer of anti- Rh-antibodies 1:512. Specific prophylaxis of Rh-conflict was not conducted. What method of antenatal medical treatment of Rh-conflict most expediently to prescribe?
A. Hepatotropic medicines and vitamins
B. Plasmaferesis
C. Enterosorbents
D. Dimedrol
E. Infusions of glucose

17. A baby boy was born in time, it was his mother's 1st pregnancy. The jaundice was revealed on the 2nd day of life, then it progressed. The adynamia, vomiting and hepatomegaly were presented. The indirect bilirubin level was 275 mcmol/L, the direct bilirubin level - 5 mcmol/L, Hb- 150 g/L. Mother's blood group - 0(I), Rh^+, child's blood group - A(II), Rh^+. Make a diagnosis.
A. Hemolytic disease of newborn (ABO incompatibility), icteric type
B. Jaundice due to conjugation disorder
C. Physiological jaundice
D. Hemolytic disease of newborn (Rh - incompatibility)
E. Hepatitis

18. Newborn in the age of 3 days, was born from mother that was sick of lupus. Blood count reveals the thrombocytopenia. Objectively: ecchymomas on the trunk and extremities. What is the preliminary diagnosis?
A.Transimmune thrompocytopenic purpura
B. DIC syndrome
C. Isoimmune Werlhof's disease of newborns
D. Hemorrhagic idisease of newborn
E. Idiopathic Werlhof's disease

19. A baby boy was born in time, it was his mother's 2nd pregnancy. The jaundice was revealed on the 2nd day of life, then it progressed. The adynamia, vomiting and hepatomegaly were presented. The indirect bilirubin level was 305 mcmol/L, the direct bilirubin level - 5 mcmol/L, Hb- 158 g/L. Mother's blood group - 0(I), Rh^+, child's blood group - A(II), Rh^+. Make a diagnosis.

A. Physiological jaundice
B. Jaundice due to conjugation disorder
C. Hemolytic disease of newborn (ABO incompatibility), icteric type
D. Hemolytic disease of newborn (Rh - incompatibility)
E. Hepatitis

20. Child was born in term, with gestational age of 40 weeks and weight of 3000g. Apgar score 7-8 points. Mother's blood is AB (IY) Rh (-). Child's is (III) Rh(+). An icterus appeared in the first day. Common bilirubin is 200 mcmol/l, indirect fraction is 190 mcmol/l, direct is 10 mcmol/l, Hb-160 g/l, reticulocytes 4,4%. Liver +4cm, spleen + 1,5cm. Urine is light, feces are painted. Coumbs test is positive. Establish the diagnosis:

A. Physiologic jaundice
B. Hemorrhagic illness of newborns
C. Fetal hepatitis
D. Crigler-Nayyar syndrome
E. Hemolytic disease of newborns

Materials of the medical support for students' self preparation: a reference chart for organization of students' independent work with educational literature.

Tasks	Instructions
To study the etiology of hemolytic and hemorrhagic diseases in newborn infants.	To enumerate basic etiologic factors of diseases hemolytic and hemorrhagic diseases in newborns.
To study pathogenesis of hemolytic and hemorrhagic diseases in newborns.	To separate out the main pathogenic links of hemolytic and hemorrhagic diseases in newborns.
To study clinical manifestations of hemolytic and hemorrhagic diseases in newborns.	To select clinical symptoms, which can prove the probable diagnosis of hemolytic and hemorrhagic disease in newborn.
To study diagnostic criteria of hemolytic and hemorrhagic diseases in newborns.	To make a structural scheme of disease.
To study additional investigate methods(laboratory and instrumental)	To make a plan of investigation the patient with hemolytic and hemorrhagic disease.

To study pathognomic changes of additional investigative methods	To recapitulate the main diagnostic criteria of hemolytic and hemorrhagic diseases according to the data of additional investigative methods
To conduct differential diagnostics, to establish a concluding diagnosis	To substantiate the basic components of diagnosis in accordance to modern classification, and to conduct a differential diagnosis.
To prescribe individual complex treatment to the newborn patient with hemolytic and hemorrhagic diseases.	To make the prescribing chart specifying the regimen, diet, medicinal treatment, taking into account the age, severity of patient' state, the presence of complications and concomitant diseases.

Basic literature:

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5.Неонатологія: навч.посібник / зп ред. П.С. Мощича, О.Г. Сулими,. – к.: Вища школа, 2004. – С. 130-165.

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2. Неонатология:Руководство / под ред. В.В. Гаврюшова, К.А.Сотниковой'. - Л. Медицина, 19а5. - С. 112-124.

Theme. **INTRAUTERINE INFECTIONS. (TORCH-INFECTIONS). Classification, etiology, pathogenesis. Clinic. Diagnostics. Differential diagnostics, treatment. Prophylaxis, prognosis**.

I. Actuality of the theme.

Intranatal infections are the group of diseases at which an infection originates from a mother in ante- and intranatal period of fetus development. For today it one of important problems of modern perinatology, neonatology and paediatrics in general - through wide distribution, high lethality and unfavourable medical-sotsial consequences. In the structure of perinatal death the rate of intranatal infection makes to 65 %. Polymorphic of clinical signs, absence of patognomonic symptoms makes difficult the timely diagnostics of intrauterine infections.

Inrtanatal infections - one of leading reasons of neonatal and child's morbidity, death rate and disability. intranatal infections predetermine inmaturing of pregnancy, premature births, stillborn, congenital defects of development of central nervous system, cardiovessel system, system of digestion of child. A baby can give birth with the unspecific clinical displays of infection, that in the case of absence of etiologic diagnostics considerably complicates treatment and determines an unfavorable prognosis for a subsequent health and development of child.

Among reasons of perinatal death rate the intranatal infection are 25-30%, from data of A.V.Zinserling even to 68-70%.

II. Classes (with pointing of studies planned mastering level)

A student must know (to familiarize with): α1

- the place of intranatal infections in the structure of perinatal pathologyï.
- statistical information in relation to morbidity, frequency of complications origin, lethality, the nearest and longterm prognosis of patients with intanatal infections;
- history of scientific study and payment of domestic scientists;

A student must know (master): α2

- etiology of intanatal infections;
- key etiologic factors and factors of risk of perinatal infections;

key links of pathogenesis of intranatal infections;

- classification and able to conduct the analysis of clinical picture of perinatal infectious diseases in newborn: intranatal infection, local and generalised infection;
- complication of of intranatal infections;-
- principles of treatment of intranatal infections ;

2. A student must muster: α3

Skills:

- Collection of complaints and anamnesis of disease;

- Examination of patient with thyroid diseases and revealing the main symptoms and syndromes.
- To formulate and substantiate the preliminary diagnosis;
- Determination of laboratory and instrumental plan of patient examination (to obedience of diagnostics standards);

Abilities:

- To determine the features of perinatal infectious diseases of newborn (intruterine infection, local and generalised infection) and put a previous diagnosis;
- o work out a plan of inspection at the perinatal infectious diseases of newborn (intranatal infection, local and generalised infection)
- to interpret the results of laboratory and instrumental researches;
- to conduct differential diagnostics of intranatal infections;
- To give recommendations in relation to the regimen and diet of a patient with intranatal infections, the general state and concomitant pathology;
- To work out a plan of treatment for patient with intranatal infections (in obedience to the standards of treatment) taking into account the stage of disease, presence of complications and concomitant pathology;
- To give urgent help in extreme situations and at the urgent states;
- To carry out the prognosis of life at the perinatal infectious diseases of newborn;

III. Aims of personality development (educative aims):

- A student must demonstrate the domain of medical specialist moral-deontologic principles and principles of professional deference to the rank in neonatology
- A student must learn to adhere to the rules of behaviour and principles of medical etiquette and deontology to develop bedside manner in patients with intrauterine infections;
- to lay hands on ability to set a psychological contact with a patient and his family;
- to master sense of professional responsibility for a timey and adequate medicare

IV. Interdisciplinary integration:

Subject	To know	Be able
1. Previous (providing)		
anatomy	The structure of CNS, cardiovessel system, hepatobiliar system, circulation and innervation.	
Histology	The structure of brain, lungs, alveoles, circulation,	To analyse the normal and pathological changed in cerebral

	hepatobiliar system.	tissue, lungs, vessels of the hepatobiliary system and urinoexcretory tract.
Physiology	Physiology of the basic systems in a norm, normative indexes of laboratory and instrumental methods of research, their value.	To estimate information of laboratory and instrumental methods of inspection of patient
Pathologic physiology	Key links of intrauterine infections pathogenesis	
Pathologic anatomy	Morphological features of intranatal infections development are depending of fetus infecting time	To analyse and interpret the information about clinical examination and about additional methods of investigation
Pharmacology	Pharmacocinetics and pharmacodynamics, the side effects of preparations (antibiotics, chemotherapy drugs, etc.), are using in treatment of patients with intrauterine infections.	Prescribe age dependent and patient individual features treatment, period of disease, to establish the individual regimen of preparations taking and dosage. .To prescribe recipes.
Propedeutic pediatrics	Basic stages and methods of patient clinical examination	To collect complaints, anamnesis vitae et morbi, to find out the basic risk factors of intrauterine infections, to coduct patient examination, to reveal the clinical signs of intrauterine infections, to interpret the data about additional methods of investigation.
Radial diagnostics	Normal ranges of chest X-ray	To interpret the data of chest X-ray.
Ultrasound	Normal ranges of ultrasound investigation in neonates.	To interpret the data of ultrasound in newborns.
2. Followings (provided):		
Hospital pediatrics.	Clinical signs of complica-tions and the features of intrauterine infections course in different age groups and the treatment tactic.	To detect the clinical signs of intranatal infections complications in different age groups, be able to prescribe the treatment.

VI. Plan and organizational structure of classes

№	Basic stages of classes, function and their maintenance	Educational aims are in the levels of mastering	Methods of control and studies	Educational materials	Distri-buting of time in minutes

1 2 3	Preparatory stage Organizational measures Raising of educational aims and motivation Control of basic knowledge and skills level: 1. Etiology of 2. Key links of intranatal infections pathogenesis. 3. Clinical manifestation of intranatal infections depending of agent and the time of invasion. 4. Diagnosis of intrauterine infection. 5. Differential diagnosis of intaranatal infections. 6. Complications of intranatal infections 7. Treatment principles of intrauterine infectoins. 8. Prophylaxis of intranatal infections. 9. Prognosis in intranatal infections.	 α2 α2 α2 α2 α2 α2 α2 α2	 Individual oral questioning Individual oral questioning Test control of second level Typical situational tasks of the second level Typical situational tasks of the second level Typical situational tasks of the second level Test control of the second level Test control of the second level	II «Educational aims» I «Actuality of theme» Second level tests Typical situational tasks of the second level Typical situational tasks of 2 level The second level tests Typical situational tasks of 2 level Kit of medicines. Typical situational tasks of 2 level Typical situational tasks of 2 level	3 min. 12 min. 20 min..
4	Main stage 1.Professional skills and abilities forming 2.To conduct the patient management with intranatal infections, to take com-	 α3 α3 α3	 Practical professional training. Practical professional training. Practical	 Patient. Patient.	 115 min.

	plaints and anamnesis. Conducting of patient examination to reveal the main symptoms and syndromes of intranatal infections. To formulate and substantiate the preliminary diagnosis. To compose the plan of patient laboratory and instrumental investigation. 3.To interpret the results of laboratory and instrumental investigations. 4.To conduct differential diagnosis among clinical conditions accompanied by CNS injuries. .To give the recommendation for regimen and diet of patent with 5.To compose the treatment plan of patient with intranatal infections taking into account the degree and presence of complications. 7. To be able to render the first aid in extreme situations.	α3 α3 α3 α3 α3	professional training Practical professional training Practical professional training The third level test control. ThevTthird level test control. Practical professional training The practical professional training in solving of non typical clinical situations. The third level test control. Practical professional training The third level test control. Practical professional training. The practical professional training is in the solving of non standard clinical situations. The third level test control.	Case history. A reference chart for forming of professional abilities. Case history. A reference chart for forming of professional abilities. Case history. A reference chart for forming of professional skills. Situational typical tasks of the third level. The third level tests. Prescribing chart Non typical situational tasks of third level Treatment algorithm in intranatal infections. Non typical situational tasks.. The first aid algorithms.	
	Concluding stage.				

5 6 7	Control and correction of professional abilities and skills. Working out the totals of class. Home work (basic and additional literature on the topic)		Analysis of clinical work performances Solving of non typical tasks and third level tests. Estimation of clinical work	Clinical work performances Non typical situational tasks of third level A reference chart for independent work with literature	25 min.

Methodical materials to support class basic stage supporting

Professional algorithm of patients management implementation (reference chart) for the practical skills and abilities forming.

№	Task	Sequence of implementation	Remarks and warnings related to self-control
1	To conduct of patient examination with intrauterine infection.	1.To conduct the complaints and disease anamnesis gathering. 2.To conduct the complaints and disease anamnesis gathering. 3. To conduct patient clinical examination 4.Investigate the cardiovessel system of the patient (palpation, percussion).	Pay attention to features of disease course , underlying factors, concomitant diseases etc. To establish the availability of risk factors which facilitate disease occurrence .To assess patient general condition, position in the bed, colour and wetness of skin and mucous, neurologic state.. To pay a regard to rhythm of pulse, it tension and size on both hands, apex shove, it properties, margins of absolute and relative cardiac dullness, it changes, HR(tachi-or bradicardia, extrasystoly),BP.
		5. To conduct of heart and of main vessels auscultation. 6. To investigate the pulmonary system (percussion, bronchophony).	To pay regard to heart tones weakening or amplifying, appearance of murmurs and additional III, IV tones. To pay attention to features of percussion and auscultation in children of

		7. To conduct the lungs auscultation 8. To investigate the system of digestion.	different age. To reveal the changes in auscultation. To pay attention to the signs of intoxication.
2	To formulate the preliminary diagnosis.	1. To formulate the preliminary diagnosis. 2. To substantiate all components of preliminary diagnosis based on complaints, anamnesis, and examinations.	Based on modern classification to formulate the preliminary diagnosis of and to substantiate each component of it.
3	To evaluate the parameters of additional laboratory investigations.	1. To evaluate the blood count data. 2.To interpret the immunoassay data 3. To asses the PCR outcomes.	To ay attention to presence of leucocytosis, shifting of formula, increasing of SR, anaemia. To pay attention to presence in mother's and child blood of elevated Ig G and Ig M against intrauterine infection agents. To pay attention to agents presence in the urine, blood and liquor of the patient.
4	To understand the data of additional and laboratory investigation.	To interpret the data of: 1. Chest X-ray. 2. Neurosonography. 3. Liver ultrasound 4. urinary tract ultrasound 5. Doppler heart ultrasound.	To pay attention to the ultrasound signs of intrauterine infections on NSG, Doppler of heart.
5.	To conduct differential diagnosis.	1.Consistently to find the common signs in complaints, life and disease anamnesis, data of examination, data of laboratory and instrumental investiagtions in patient and in similar states. 2.To find differences between complaints, information of life and disease anamnesis, examination data, information about the laboratory and instrumental methods of research and in similar nosology. 3. On the basis of found out differences to exclude similar	Special attention must be paid to differential diagnosis among the birth trauma, infectious diseases, HIV.

		diseases from the list of probable diagnoses. 4.To conduct differential diagnostics according to the above mentioned algorithm among all of nosologies are having the similar signs included with intranatal infections. 5. Taking into account the impossibility to exclude the diagnosis of intranatal infection from the list of probable diagnoses to draw a conclusion about most probability of such diagnosis.	
6	To formulate the final clinical diagnosis.	5. To formulate the final clinical diagnosis. 6. Based on initial diagnosis, additional investigations data, conducted differential diagnosis to substantiate all elements of concluding clinical diagnosis.	Being based on modern classification of leukemias to formulate a diagnosis, complications of disease and presence of concomitant diseases.
7.	To prescribe treatment for patient.	1.To prescribe not medicinal treatment 2. To prescribe the medicinal treatment.	Expressly to specify the regimen and detailed diet according to a disease. .Taking into account age, severity of patient state, the stage of disease, the presence of complications and concomitant pathology, to prescribe modern medicinal treatment in accordance to the standards of intrauterine infections therapy.

VII. Material for the control and medical providing of the class.

VII.1 Control materials for the preparatory stage of class.

A question for the control of knowledge, skills and abilities level :

1. Etiology and pathogenesis of intrauterine infections.
2. Risk factors of intrauterine infections.
3. Clinical signs of CMV infection.

4. Clinical signs of congenital toxoplasmosis.
.5. Clinical signs of rubella .
6. Clinical signs of HSV infection.
7. Clinical signs of listeriosis..
8. Clinical signs of chlamidial and micoplasma infection.
9. Ethiothropic treatment and principles of prophylaxis of intranatal infection.

THE TESTS:

1. The mother of a 7-day-old infant has developed chickenpox. Which of the following is the most appropriate measure?
a. Isolate the infant from the mother
b. Hospitalize the infant in the isolation ward
c. Administer acyclovir to the infant
d. Administer varicella-zoster immunoglobulin to the infant
e. Advise the mother to continue regular well-baby care for the infant

2. The signs and symptoms of meningitis in an infant can be different than those in an adult. Which of the signs and symptoms of meningitis listed below is more helpful in an adult patient than in a 4-month-old?
a. Lethargy
b. Jaundice
c. Vomiting
d. Brudzinski's sign
e. Hypothermia

3. A 2-year-old boy is being followed for congenital cytomegalovirus (CMV) infection. He is deaf and developmentally delayed. The child's mother informs you that she has just become pregnant and is concerned that the new baby will be infected. Which of the following is true?
a. The mother has antibodies to CMV that are passed to the fetus
b. The mother's infection cannot become reactivated
c. The likelihood that the new baby will become clinically ill is approximately 80%
d. Termination of pregnancy is advised
e. The new infant should be isolated from the older child

4. As you are about to step out of a newly delivered mother's room, she mentions that she wants to breast-feed her healthy infant, but that her obstetrician was concerned about one of the medicines she was taking. Which of the woman's medicines, listed below, is clearly contraindicated in breast-feeding?
a. Ibuprofen as needed for pain or fever
b. Labetolol for her chronic hypertension
c. Lithium for her bipolar disorder
d. Carbamazepine for her seizure disorder
e. Acyclovir for her HSV outbrea

5. A 19-year-old primiparous woman develops toxemia in her last trimester of pregnancy and during the course of her labor is treated with magnesium sulfate. At 38 weeks' gestation, she delivers a 2100-g infant with Apgar scores of 1 at 1 min and at 5 at 5 min. Laboratory studies at 18 h of age reveal a hematocrit of 79%, platelet count of 100,000/μL, glucose 38 mg/dL, magnesium 2.5 meq/L, and calcium 8.7 mg/dL. Soon after, this the infant has a generalized convulsion. The most likely cause of the infant's
seizure is

a. Polycythemia
b. Hypoglycemia
c. Hypocalcemia
d. Hypermagnesemia
e. Thrombocytopen

6. A term infant is born to a known HIV-positive mother. She has been taking antiretroviral medications for the weeks prior to the delivery of her infant. Routine management of the healthy infant should include

a. Admission to the neonatal intensive care unit for close cardiovascular monitoring
b. HIV ELISA on the infant to determine if congenital infection has occurred
c. A course of zidovudine for the infant
d. Chest radiographs to evaluate for congenital *Pneumocystis carinii*
e. Administration of IVIG to the baby to decrease the risk of perinatal HIV infection

7. You are advised by the obstetrician that the mother of a baby he has delivered is a carrier of hepatitis B surface antigen (HBsAg-positive). The most appropriate action in managing this infant would be to

a. Screen the infant for HBsAg
b. Isolate the infant for enteric transmission
c. Screen the mother for hepatitis B "e" antigen (HBeAg)
d. Administer hepatitis B immune globulin and hepatitis B vaccine to the infant
e. Do nothing because transplacentally acquired antibody will prevent infection in the infant

8. The infant presented with hepatosplenomegaly, anemia, persistent rhinitis, and a maculopapular rash. The most likely diagnosis for this child is

a. Toxoplasmosis
b. Glycogen storage disease
c. Congenital hypothyroidism
d. Congenital syphilis
e. Cytomegalovirus disease

9. For the intrauterine infection the followings results of blood cord investigation Are characteristic :

A. the level of imunoglobulinu of M is increased.
B. the level of imunoglobulinu G is reduced;
C. the level of general albumin is reduced;

D. the level of imunoglobulinu M is reduced;
E. all answers are correct;

10. For treatment of CMV encephalitis could be applied:
A. gentamicin;
B. cephodox;
C. Acyclovir;
D. nothing of mentioned above;
E. all marked preparations.

11. 28. In child in 3 week of life a cerebral type of intranatally acquired herpes was established with manifestations of fever, convulsive syndrome., changes in cerebrospinal liquor. The dose of zavirax is:
A. 1 mg/kg per day
B. 5 1 mg/kg per day
C. 10 mg/kg per day
D. 20 mg/kg per day
E. 100 mg/kg per day

12. 27 In child in 3 week of life a cerebral type of intranatally acquired herpes was established with manifestations of fever, convulsive syndrome., changes in cerebrospinal liquor ,
What preparations must be prescribed as a causal treatment?
B. novobiocin
C. flemoxin
D laferon
E. Valtrex

13.26 . Child., was born in37 week of gestation with weight 2800 g. In 3 day of life jaundice appeared. In 4 day the manifestation of conjunctivitis were added. . In NSG the moderate unternal hydropcephaly. - Survey of ophthalmologist:-bilateral cataract. The method of IFA in blood serum a diagnostic titer of low avidity of anti-Rubella Ig G antibodies was registered.
In complex of therapy it is necessary to include:
A. hyperimmune gamma globulin
B. glukcocorticoids
C. antibiotics
D.desagregants
E antioxidants

14. 27 In child in 3 week of life a cerebral type of intranatally acquired herpes was established with manifestations of fever, convulsive syndrome, changes in cerebrospinal liquor ,
Whyat preparations must be prescribed as a causal treatment?
B. novobiocin
C. flemoxin
D laferon

E. valtrex

15.22 Child., 1 day of life, after 3 worn pregnancy. .Weight is 3100 g.,l ength 51 cm. Reflexes of neonates invoked. but quickly exhausted. Skin clear In lungs and heart auscultation without changes.. In 7 month of pregnancy in mother the marker of hepatitis B virus was detected. For prophylaxis of hepatitis to the child need to prescribe a standard immunoglobulin in doses: as follows::

A. 2-3 mg per kg
B. 1 mg per kg
C. 10 mg per kg
D. 10 mg per kg
E. 0,5 mg per kg

16.30. In child., 25 day of life is the congenital herpes infection with dominating CNS injury as a hydrocephalic hypertensive syndrome, intrauterine hypotrophy and the fetal hepatitis, there is an immunodeficiency,

What preparation must be prescribed as immunomodulation?

A. extract of eleuterococcy
B. decaris
C. cimeven
D. .cicloferon
E chloridin

17. A prematurely born child on the tenth day of life presented the interstitsial pneumonia, conjunctivitis. What infection is susoected?:

A. gonococcus;
B. listeriosis
C. CMV infection;
D. syphilis;
E. chlamidial infection.

18. For the congenital toksoplasmosis is characteristically all, except for:

A. icteruses;
B. hepatosplenomegaly;
C. eosinophilia
D. cerebral calcification;
E. pneumonias

19. In prematurely born child from the mother expirienced the mild unconfirmed diseases in 7-8 weeks of gestation the Greg triade observed (microcephaly, CHD, cataract). What agent is most likely the cause of this conditions?

A. CMV;
B. Rubella;
C. Enterovirus;
Д. listeria;
E. micoplasma

20. For the intrauterine CMV infection are characteristic all listed below, except for:

A. jaunduce;
B. hepatoslenomegaly
S. carditis;
D. hematogenous osteomyelitiss;
E. Meningoencephalitis.

Answers: 1 - E, 2 - C, 3 – E, 4 – C, 5 – B, 6 – Д, 7 – C, 8 – Д. 9 – E, 10 – B. 11 – E, 12 – A, 13 – B, 14 – C, 15 – A, 16 – Д, 17 – E, 18 –C, 19 – B, 20 – D.

Situational tasks:

Task 1

Premature child, after II pregnancy, II delivery, at 33-34 weeks of gestation, was born with weigt 2100 g, length -41cm. Apgar score 5-6 points. From the anamnesis reported that first pregnancy ceased with abortion. Current pregnancy with threatened to abortion, toxicosis of first and second half of pregnancy, several times during the pregnancy the body temperature increased. The woman is from rural area, keeps domestic ca and dog. After delivery the common condition is severe. The clinical signs of perinatal CNS injury and hydrocephaly are present. Answer the following questions:

1. To determ the risk factors of this state development.
2 .What is the preliminary diagnosis?
3. What specific clinical signs of intranatal infection in the child?
4. Whether there the specific therapy and what kind of it is indicated in this case?

Task 2

Premature child from the first pregnancy. Was born in the term of 34-35 weeks of gestation with weight of 2400 g, height is 47 cm. After delivery general condition severe: the signs of perinatal – hypoxic ischemic CNS injury, irritability, tremor of extremities, hepathoslenomegaly, at the end of first day of life the hyperbilirubinemia. At third day of life the skin rash appears with separate vesicules clumping on the chest. Mother of the child is ill with genital herpes.

Give the following answers:

1. To enumerate the intranatal infection with signs mentioned above.
2. What laboratory investigation could support the diagnosis?
3. Specify the preliminary diagnosis..
4. What kind of specific therapy must be prescribed?

3

Task 3.

Child’s age is 21 days old. Stay in hospital. From the anamnesis rteported about complicated course of pregnancy during the first trimester. At 24 weeks of gestation the body temperature increased wthout symptoms of viral infection. Women didn’t treated and once been tested for intranatal infection. The increased Ig G to toxoplasmosis detected – 290 IU/ml, Ig M is negative. Delivery at 37 weeks of gestation. Weight 2450 g, height 48 cm. at the end of fiist day of life the jaundice appears. At third day was transferred to neonatology department because of woserning in general condition. The signs of irritation, regurgitation, poor sucking. In examination: pallor of skin, decrased subcutaneuos fat, hydrocephalic head, saggital

suture is open to 0,8 cm., bulging and pulsatile big fontanel, dimensions is 3x3 cm musle tone in adductors. Spleen +1 cm, liver +3 cm.

Questions:

1. What disease is more likely?
2. What additional investigation could confirm the diagnosis?
3. What are the paths of transmission?
4. What specialists must exam the child?
5. What are the treatment principles of the disease?

Task 4

Girl S, 3 days old. From the 5 pregnancy, first delivery. Previous pregnancies ceased by abortions at early stages. Mother had punctulate rash in her face, trunk and extremities is accompanied by body temperature rising during the 2 days at 7-8 week of gestation. There was pain in the nape. In the city where a woman lived there was the epidemy of german measles. Apgar score is 6-7 points. Weght after birth is 2170 g. , height is 43 cm. In examination: Multiply stigmas admitted, severe condition due to RDS, CNS depression. Skin pallor, petechial rash. In the lungs weakened breathing. In heart auscultation the hard murmur is heard. Liver + 3 cm, spleen + 1,5 cm.are dense in palpation. Blood count: Blood count: Hb 125 g/л, erh.: 3,5 x 10 12/l, thromb. 45 x 10 9/l, leucocites 7,1 x 10 9/l, bands- 6 %, s-49 %, eos.- 1 %, lymph. – 32 %, mon. – 12 %, SSR – 4 mm/hour.

Questions:

1. What disease is more likely in this case?
2. What additional investigation must be conducted in this case?
3. What are the signs of classic Gregg tirade?
4. What sighs could be revealed in ophthalmologic examination?.
5. What signs could be revealed in Doppler heart ultrasound?

Task 5

Child D, 15 days old. Was born in term, with weight correspondent to gestation. At 2 day of life the resistant jaundice appears. then, the conjunctivitis with relapsed course occurs. Blood count is unchanged. Mother have chlamidial colpitis.

Questions:

1.In suspicion to chlamidia infection what type of antibodies must be detect to confirm the diagnosis?

2. What investigations must be conducted in this case?
3. What are the main signs of chlamidial infection?
4. What are the main principles of therapy?

Task 6

Boy K., 4 days old.. From the first term pregnancy, the fine rash on the trunk observed, flaccidity, rising in body temperature up to 37,7C. Been not refffered to the physician. The threatening of abortion in 16-18 weeks. Delivery at 38 weeks. Weght 28800 g. height 56 cm. Poorc cried after the slime sucking. On the trunk and extremities the hemorrhagic petechial and fine ecchymomas rash. The respiration is tough in auscultation. The significant systolic murmur on the apex. Liver + 2,5 см., spleen +1,5 см. During the next day the common state worsened because neuralgic signs, regurgitation, clonic and tonic seizures.

Questions:

1. What disease is more likely in this case?
2. In what period of intrauterine developmentabove mentioned signs could occurrs?
3. What is the Gregg tirade?
4. Whether there the BCG vaccination indicated?
5. What specialists must observe the child?

Task 7

Child N., 7 days old, stay in the department of neonatology. From the anamnesis reported that baby from 1 pregnancy complicated by changed urine tests (leucocyturia, mild proteinuria). Delivery is in term. Long period of memebranes rupture to the delivery. Apgar score 5-6 points. Weight 2500 g, height 53 cm. Was no breastfed. At 6 day of life the body temperature rising admitted, became irritated, alertness, monotonic cry, hyperesthesia. Big fontanel 3,5 x 3,5 cm. is bulging. Positive hanging syndrome. The skin is in grey colour. The signs of hepatomegalia.. Positive hanging syndrome. Feces are yellow, with undigested lumps and remnants of mucus.

CSF: protein – 0,660 g/l, :Pandy test: +++, cytosis 600 in 3 mcl, neutrofiles, 30 %, limphocites. – 70%.

In liqour culture test the listerias detected.

: 1.What diseas is more likely in this case?

7. What is the paths of infections?
8. To evaluate the weght to height index. .
9. To evaluate the CSF.
10. What changes is revealed in neurosonography?

Task 8.

Premature child from the 12 pregnancy, 1 delivery, was born with weight 1900 g, height 41 cm. Apgar score is 5-6 points. From the anamnesis is known that previous pregnancies ceased by abortions in early terms. Current pregnancy course with threatening of abortion in I and II trimester and with subfebrile conditions time by time. Women is quite often eat undercooked meat products.

The state of child after birth is severe, the irrutation of CNS admitted with spontaneous Moro and Babinsky reflexes, hydrocephaly, signs of RDS of 3 level. Brain calcifications revealed by neurosonography. Ophtalmologist examination – partial atrophy of ocular nerve disc.

Answer the questions:

1. To determ the leading risk factors of this pathologic state development?.
2. What preliminary diagnosis?
3. What way of feeding for the cild must be choosen?
4. What specific therapy must be prescribed?
5. In what health group this child can be included.?

Task 9

Term child from the first pregnancy was born in term of 38-39 weeks of gestation, weight 2800 g., height 52 cm. After deluivery the state is severe with signs of perinatal hypoxic- ischemic CNS damage, irritability, tremor of extremities,

hepatosplenomegaly, at the end of ifst day – hyperbilirubinemia. At third day of life the rash on skin and palms occurs and separate vesicles to 1 cm in diameter.

Answer the following questions:

1. Specify the preliminary diagnosis
2. What laboratory data are necessary to establish the diagnosis?
3. What specific therapy must be prescribe?
4. When the antituerculous vaccination must be conducted?

Task 10

Child, 17 day of life, stay in the hospital. From the anamnesis is known about mother's toxicosis during the pregnancy, at 16 weesk of gestation the rising of body temperature admitted without signs of infection. She was no treated. Once tested for intranatal infections . The high levels of antibodies against CMV detected - Ig G 20 IU\мml (N - 1 IU/ml), Ig M is negative. The delivery is on 38 week of gestation. Weight is 2950 g., height 51 cm. The jaundice appears at the end of second day at third day transferred to neonatology department because worsening of condition. Child became depressed, regurgitated, the bilirubin elevated to 350 mcm/l, can't keep body temperature. In examination the skin is pale and dry.Thin subcutaneous layer. Hydrocephalic head. Saggital surture open to 1 cm. big fontanel is bulging, pulsatile 2,5x3 cm, small fontanel is 0,5x0,5 cm. Spleen +1 cm, liver + 3 cm. .

Questions:

1. What disease is more likely in this case?
2. What additional investigations need to conduct for confirmation the diagnosis?
3. What pathological conditions must be included in differential diagnosis?
4. What principles of treatment in this case?

Standards of answers:

Task 1:

1. intranatal infections – toxoplasmosis.
2. Presence of live-stock, absence of inspection of woman after 1 th abortion;
3. The syndrom of hemoliqourodynamic impairement of 2 degree, hydrocephaly and brain calcificates, rethinoidochoriothis.
4. Yes, indicated. For the child need to prescribe rovamycin in dose of 150 000 I.U./ kg per day two times a day during the 4-6 days.

Task 2:

1. Listeriosis, syphilis,sepsis, herpes;
2. Blood and urine count, biochemical blood tests, chest and long bones X-ray, TORCH –tests, virusologic and bacteriologic investigation of mother, child and placenta.
3. Intranatal infection- HSV;
4. Zovirax or acyclovir 10-15 mg/kg intravenously during 10-14 days.

Task 3:

1. congenital toxoplasmosis;
2. Mother's and child's TORCH –test.
3. Antenatal hematogenous.

4. Neurologist, ophtalmologist.
5. Ethiotropic therapy, imunomodulation,syndrom therapy.

Task 4

1. congenital rubella;
2. Investigation of mother and child on intrauterine infections, rubella immunoassays to detect specific Ig G and M antibodies against rubella, and low avidity antibodies against rubella. ,
3. Gregg triade includes:
   - Congenital heart diseas;
   - Congenital catharact;
   - Congenital deafness.
4. In ophthalmologic investigation the data about cathract can be find.
5. At Doppler heart ultrasound:
   - VSD
   - ASD;
   - Combined CHD.

task 5

1. specific antichlamidial IgG and Ig M antibodies in mother and child.
   - Blood and urine tests.
   - Biochemical blood tests (transaminases, electrolytes, urea, creatinin, CRP, seromucoids).
   - Conjunctivitis, rhinitis, respiratory diseases(pneumonia).
   - Causative therapy, rovamycin or erhythromycin succinate, immunomodulative therapy, syndrtomal therapy.

task 6.

1. Congenital rubella..
2. embryonic;
3. Gregg tirade includes:
   a. CHD
   b. Congenital cataract.;
   c. Congenital deafness.
4. vaccination is prohibited;
5. neurologist, ophtalmologist. .

task 7

1. listeriosis.;
2. antenatal period, ascendence path
3. weight to height index is decrased that specified to intruterine hypotrophy. Normal range is 60-80.
4. Signs of meningitis.
5. Increased echo density, uneven picture, decraesed pulsation of vessels.

task 8

1. Undercooked meat.
2. Congenital toxoplasmosis.

3. Partial parenteral nutrition часткове парентеральне вигодовування + probe (braest milk or formula), rovamycin 150 000 IU/kg day, 2 times during 4-6 weeks. в
4. II B.

Task 9.

1. syphilitic pemphigus;
2.

- Mother's and child Wasserman test,
- X-ray of long bones.
- Bacteriologic test from the vesicules.
- Penicillin 200 000 IU/kg/day 6 times per day.
- Not earlier than 1 month after recovery of child.
- **Task 10**

1. Congenital CMV.
2. Immunoassay of mothers and child's blood to detect IgG and Ig M, PCR of mother's milk of blood, of child's urine and liquor (by indications)
3. birth trauma- intracranial hemorrhages.
    - To keep optimal temperature.
    - Rational nutrition
    - phototherapy;
    - detoxication.;
    - antiviral therapy;
    - immunoreplacing therapy;
    - syndrome therapy

SHORT EXPOSITION OF EDUCATIONAL MATERIAL (ABSTRACT):

Intrauterine infections

EPIDEMIOLOGY, IMMUNITY, AND PATHOGENESIS

Infections are a frequent and important cause of morbidity and mortality in the neonatal period. As many as 2% of fetuses are infected in utero, and up to 10% of infants are infected during delivery or the 1st mo of life. Inflammatory lesions are found in about 25% of newborn infant autopsies; these lesions are second only to hyaline membrane disease in frequency.

The uniqueness of neonatal infections is a result of a number of factors. (1) There are diverse modes of transmission of infectious agents from mother to fetus or newborn infant. Transplacental hematogenous spread may occur at different times during gestation. Manifestations of congenital infections may be present at birth or may be delayed for months or years. Vertical transmission of infection may take place in utero, just prior to delivery, or during the process of delivery. After birth, the newborn infant may be exposed to infectious diseases in the nursery or in the community. With the increasing complexity of neonatal intensive care, gestationally younger and lower birthweight newborns are surviving and remaining for a longer

time in an environment with a high risk of infection. (2) The newborn infant may be less capable of responding to infection owing to one or more immunologic deficiencies involving the reticuloendothelial system, complement, polymorphonuclear leukocytes, cytokines, antibody, or cell-mediated immunity. (3) Coexisting diseases of the newborn often complicate the diagnosis and management of neonatal infections. Respiratory disorders such as hyaline membrane disease may coexist with bacterial pneumonia. Acidosis impairs functions of polymorphonuclear leukocytes. (4) The manifestations of infectious diseases in the newborn infant are extremely variable. There may be subclinical infection, congenital malformations, focal disease, and poorly localized systemic infection. The timing of exposure in utero, inoculum size, immune status, and the etiologic agent influence the expression of disease in the fetus or newborn infant. A variety of organisms, including bacteria, viruses, fungi, protozoa, and mycoplasma, are etiologic agents (Table 94–{endash}1 Table 94–{endash}1).

The status of the mother's immunity, for example, to rubella, and her exposure to various microorganisms, such as Toxoplasma, determines whether maternal infection occurs during pregnancy. Maternal infection may be clinical, often with nonspecific symptoms and signs, or subclinical, identified retrospectively by serologic methods, as part of the evaluation of suspected neonatal infection. Transplacental transmission of infection to the fetus is variable. The placenta often functions as an effective barrier. Prenatal infections that are known to be transmitted transplacentally include syphilis, Borrelia burgdorferi, rubella, cytomegalovirus (CMV), parvovirus B19, human immunodeficiency virus (HIV), varicella-zoster, Listeria monocytogenes, toxoplasmosis, and tuberculosis. Infection acquired in utero may result in resorption of the embryo, abortion, stillbirth, congenital malformation, intrauterine growth retardation, premature birth, acute disease in the neonatal period, or asymptomatic persistent infection with neurologic sequelae later in life.

Perinatal infections are acquired just before or during delivery with vertical transmission of the microorganism from mother to newborn infant. The organisms may be bacteria that colonize the birth canal, such as group B streptococci, gonococci, L. monocytogenes, Escherichia coli (particularly the K1 capsular strains), Chlamydia, genital Mycoplasma and Ureaplasma. Other microbial species such as enteroviruses and herpes simplex may also be acquired in a similar fashion. Maternal-to-fetal transfusion at delivery is the usual mechanism of transmission of hepatitis B virus and HIV.

The amniotic infection syndrome refers to bacterial invasion of amniotic fluid, usually as a result of prolonged rupture of the chorioamniotic membrane. On occasion, amniotic infection occurs with apparently intact membranes. Amniotic fluid infection may be asymptomatic or may produce maternal fever and local or systemic

signs of chorioamnionitis. Microscopic evidence of inflammation of membranes is uniformly present when the duration of rupture exceeds 24 hr. Difficult or traumatic delivery and premature delivery are also associated with an increased frequency of neonatal infections.

Exposure to and aspiration of bacteria in amniotic fluid lead to congenital pneumonia or systemic bacterial infection with manifestations becoming apparent prior to delivery (fetal distress, tachycardia), at delivery (perinatal asphyxia), or after a latent period of a few hours (respiratory distress, shock). Aspiration of bacteria during the birth process may lead to infection after an interval of 1{endash}–2 days. Although the term early-onset neonatal infection has been used to refer to neonatal infections occurring as late as 1 wk of age, it should be restricted to those infections with a perinatal pathogenesis the usual onset of which occurs within 72 hr (Table 94–{endash}2 Table 94–{endash}2).

The most important neonatal factor predisposing to infection is prematurity or low birthweight; there is a 3- to 10-fold higher incidence of infection and sepsis in these infants than in full-term normal-birthweight infants. Males have an approximately two-fold higher incidence of sepsis than females, suggesting the possibility of a sex-linked factor in host susceptibility. Resuscitation at birth, particularly if it involves endotracheal intubation, insertion of an umbilical vessel catheter, or both, is associated with an increased risk of bacterial infection, possibly due to prematurity or the presence of infection at the time of birth.

Postnatal neonatal infections are acquired after birth during the first 28 days of life. However, similar infections are seen in infants, particularly premature infants, during the first few months of life. The term late-onset neonatal infection is applied to these infections to differentiate them from those with a perinatal pathogenesis. The etiologic agent may be transmitted from a variety of human sources, such as the mother, family contacts, and hospital personnel, or from inanimate sources, such as contaminated equipment.

NOSOCOMIAL NURSERY INFECTION. See also Chapter 249. Neonatal infections acquired in the hospital are nosocomial. Because most early-onset infections are acquired intrapartum, infections that develop later than 48{endash}–72 hr after birth are usually considered nosocomial. However, exceptions include late-onset infections with organisms acquired from the mother's genital tract (e.g., some group B streptococcal infections) and nosocomial infections acquired in the delivery room (e.g., from contaminated equipment), in which signs develop soon after birth. Nosocomial infections may be sporadic or occur as epidemics, and they may occur in the hospital or after discharge.

Nosocomial infections are relatively uncommon in normal, full-term infants; the rate ranges from 0.5{endash}–1.7% of term infants. They usually involve the skin

and are caused by Staphylococcus aureus or Candida (see Chapters 174 and 229). In contrast, the rates of nosocomial infections among low-birthweight infants in neonatal intensive care units are higher than in any other site in the hospital and range from 20{endash}–33%; the incidence increases with the duration of hospitalization and lower gestational ages.

Since any pathogen can colonize infants, personnel, or families in the neonatal intensive care unit (NICU) and can be transmitted by direct contact or indirect contact through contaminated vehicles (intravenous fluids, medications, disinfectants, respiratory equipment, stool, breast milk, blood), the list of organisms causing nosocomial infections is long. The common causes are coagulase-negative staphylococci, gram-negative bacilli (Klebsiella pneumoniae, E. coli, Salmonella, Campylobacter, Enterobacter, Citrobacter, Pseudomonas aeruginosa, Serratia), enterococci, S. aureus, and Candida. Viruses contributing to nosocomial neonatal infections include enteroviruses, CMV, hepatitis A, adenoviruses, influenza, respiratory syncytial virus, rhinovirus, parainfluenza, herpes simplex, and rotavirus. The common infections are those involving the skin, bacteremia associated with catheters, and pneumonia. Exacerbations of respiratory disease in infants with pre-existing pulmonary problems, such as bronchopulmonary dysplasia, are particularly difficult to assess, but pneumonia must be considered. Epidemics of gastroenteritis and necrotizing enterocolitis occur less commonly and may be associated with an identifiable agent or no specific pathogen.

Multiple risk factors influence the probability of nosocomial infection in the NICU. These include low birthweight, length of stay, invasive procedures, indwelling vascular catheters, ventricular shunts, endotracheal tubes, alterations in the skin and mucous membrane barriers, and frequent use of broad-spectrum antibiotics. Colonization of the infant's skin, umbilicus, nasopharynx, and gastrointestinal tract by pathogenic bacteria or fungi is a common prerequisite for subsequent nosocomial infection. Antibiotics interfere with colonization by the normal flora and facilitate colonization by pathogens. Crowding and inadequate infection control techniques (handwashing between patient examinations) may also contribute to the problem.

Surveillance for nosocomial infection is based on the ongoing review of nursery infections and data from the microbiology laboratory; routine surveillance to detect colonization is not indicated. Cultures should indicate the bacterial isolate and the antimicrobial sensitivity pattern. Assessment of other microbial markers (biotype, serotype, plasmid, DNA fingerprint) may be helpful in epidemics. During epidemics, investigation of possible reservoirs of infection, modes of transmission, and risk factors is necessary. Identification of colonized infants and nursery personnel may be helpful.

IMMUNOLOGY AND PATHOGENESIS. There have been many studies that compare immunologic function of newborn infants to that in adults. Diminished concentrations of immunologic factors and decreased function are often demonstrated. Despite these defects in immunity in premature and full-term infants, the rate of invasive infectious diseases is low in the absence of obstetric and neonatal risk factors. It is important to maintain this perspective when evaluating immunologic prophylactic measures such as the use of intravenous immunoglobulin in the newborn. The immunologic system is discussed in Part XIV. This section contrasts the immunologic function of the newborn with that of the older child and adult.

IMMUNOGLOBULINS. There is active transport of immunoglobulin G (IgG) across the placenta with concentrations in the full-term infant comparable to those of the mother. Other classes of Igs are not transferred, although the fetus can synthesize IgA and IgM in response to intrauterine infection. In premature infants, cord IgG levels are directly proportional to gestational age. Studies of type-specific IgG antibodies to group B streptococci (GBS) have shown that the ratio of cord to maternal serum concentrations is 1.0, 0.5, and 0.3 at term, 32 wk, and 28 wk of gestation, respectively. Infants with birthweights less than 1,500 g become significantly hypogammaglobulinemic, with mean plasma IgG concentrations in the range of 200{endash}–300 mg/dL in the 1st wk of life.

The presence of specific IgG antibody in adequate concentrations provides protection to the newborn against those infections in which protection is mediated by antibody (e.g., encapsulated bacteria such as GBS). Specific bactericidal and opsonic antibodies against enteric bacilli are predominantly in the IgM class; the newborn infant lacks protection against Escherichia coli and other Enterobacteriaceae.

COMPLEMENT. Complement mediates bactericidal activity against certain organisms such as E. coli and functions as an opsonin with antibody in optimal phagocytosis of bacteria such as GBS. There is essentially no transfer of complement from the maternal circulation. The fetus synthesizes complement components as early as the first trimester. Full-term newborn infants have slightly diminished classic pathway complement activity and moderately diminished alternative pathway activity. There is considerable variability in both concentration of complement components and activity. The alternative pathway components (B and P) are usually 35–60% of normal. Premature infants have lower levels of complement components and less complement activity than full-term newborns. These deficiencies contribute to diminished complement-derived chemotactic activity and to diminished ability to opsonize certain organisms in the absence of antibody. Many studies have been performed with different strains of microorganisms and different conditions, examining both classic and alternative pathways. In general, opsonization of

Staphylococcus aureus is normal in neonatal sera, but varying degrees of impairment have been noted with GBS and E. coli.

NEUTROPHILS. Chemotaxis of neonatal neutrophils is diminished, and there is decreased adherence, aggregation, and deformability, all of which may delay the response to infection. With adequate opsonization, phagocytosis and killing by neutrophils from healthy newborn infants are comparable to those in adults. However, in infants with respiratory distress, hypoglycemia, hyperbilirubinemia, and sepsis, microbicidal activity is impaired.

The number of circulating neutrophils is elevated after birth in both full-term and premature infants, with a peak at 12 hr, returning to normal by 22 hr. Band neutrophils constitute less than 15% in the normal newborn and may increase in newborns with infection and other stress responses such as asphyxia.

MONOCYTE-MACROPHAGE SYSTEM. The monocyte-macrophage system consists of circulating monocytes and tissue macrophages of the reticuloendothelial system (RES). The number of circulating monocytes in neonatal blood is normal, but the mass or function of the macrophages in the RES apparently is diminished in the newborn and particularly in the premature infant, as estimated by the relative increase in the number of damaged erythrocytes (pocked cells) in the circulation. In both term and premature infants, chemotaxis of monocytes is impaired, which affects the inflammatory response in tissues and delayed hypersensitivity skin tests. Monocytes from neonates ingest and kill microorganisms as well as monocytes from adults.

CYTOKINES. Interferon (INF)-a{alpha} and -b{beta} are normal, but INF-g{gamma} synthesis is diminished. TNF-a{alpha} levels are elevated in infants with neonatal sepsis, but the response may be less consistent than in adults. Interleukin (IL)-2 activity in cord blood from full-term and premature infants was reported to be

The fetus or newborn infant may become infected by the transplacental route, from contamination of amniotic fluid, or by aspiration or ingestion of vaginal secretions. The breakdown of cutaneous or mucous membrane barriers from fetal monitors, vascular catheters, incision of the umbilical cord, surgery, and necrotizing enterocolitis creates additional portals of entry for microorganisms.

CLINICAL ASPECTS

CLINICAL MANIFESTATIONS. Infection in the newborn infant may be limited to a single organ or may involve multiple organs (focal or systemic); it may be mild, moderate, or severe; acute, subacute, or chronic; or it may be asymptomatic. Asymptomatic bacteremia has been demonstrated in infants born to women with risk factors. Infections with different microorganisms may have overlapping patterns; it is usually not possible to make a definitive diagnosis of a specific etiologic agent from the clinical features alone.. Early manifestations of infection may be subtle and

nonspecific such as inability to tolerate feeding, irritability, or lethargy. Signs consistent with infection in the newborn may also be caused by a variety of noninfectious disease processes involving different organs

Only about 50% of infected newborn infants have a temperature greater than 37.8 C (axillary), and fever in newborn infants does not always signify infection. Fever may be caused by increased ambient temperature, dehydration, central nervous system disorders, hyperthyroidism, familial dysautonomia, or ectodermal dysplasia. A single temperature elevation is infrequently associated with infection; fever sustained over 1 hr is more likely to be due to infection. Most febrile infected infants have additional signs compatible with infection, although a focus of infection may not be apparent. In premature infants, hypothermia or temperature instability is more likely to be associated with infection, but some degree of temperature instability is not unusual in low-birthweight infants.

Cutaneous manifestations of infection provide useful clues. Impetigo, cellulitis, mastitis, omphalitis, and subcutaneous abscesses should be recognizable. Ecthyma gangrenosum is indicative of pseudomonal infection. The presence of small salmon-pink papules suggests Listeria monocytogenes infection. A vesicular rash is consistent with herpesvirus infection. The mucocutaneous lesions of Candida albicans are covered later. Petechiae and purpura may have an infectious cause.

Neonatal pneumonia may be difficult to differentiate in premature infants with respiratory distress syndrome or bronchopulmonary dysplasia. Pneumonia should be considered in ventilated infants who have progression of their respiratory failure. Pneumonia is likely in full-term infants with respiratory distress who are not at risk for hyaline membrane disease.

DIAGNOSIS. The maternal history may provide important information about maternal infection, exposure to infection in a sexual partner, maternal immunity (natural or acquired), maternal colonization, and obstetric risk factors (prematurity, prolonged ruptured membranes, maternal chorioamnionitis; Table 95–{endash}2 Table 95–{endash}2). Serologic screening tests may have been performed for Treponema pallidum, rubella, and hepatitis B virus. Maternal cultures may have been taken for Neisseria gonorrhoeae, GBS, herpes simplex, or Chlamydia.

The acronym TORCH refers to toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex. It was modified to STORCH to include syphilis. Although the term may be helpful in remembering some of the etiologic agents of neonatal infections, the TORCH battery of serologic tests has a poor diagnostic yield, and the appropriate diagnostic studies should be selected for each etiologic agent under consideration.

Intrauterine infections due to toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and syphilis present a diagnostic dilemma because (1) their clinical features

overlap and may initially be indistinguishable; (2) disease may be inapparent; (3) maternal infection is often asymptomatic; (4) special laboratory studies may be needed; and (5) specific treatment for toxoplasmosis, syphilis, and herpes simplex is predicated on an accurate diagnosis and may reduce significant long-term morbidity. Common shared features that should suggest the diagnosis of an intrauterine infection include prematurity, intrauterine growth retardation, and hematologic involvement (anemia, neutropenia, thrombocytopenia, petechiae, purpura), ocular signs (chorioretinitis, cataracts, keratoconjunctivitis, glaucoma, microphthalmia), central nervous system symptoms (microcephaly, hydrocephaly, intracranial calcifications), and other organ system involvement (pneumonia, myocarditis, nephritis, hepatitis with hepatosplenomegaly, jaundice), or nonimmune hydrops.

The maternal history and physical examination of the newborn add additional diagnostic information; however, neonatal IgG titers are often difficult to interpret because IgG is acquired from the mother by transplacental passage and neonatal IgM titers to specific pathogens are technically difficult to perform and are not universally available. IgM titers to specific pathogens have high specificity but only moderate sensitivity; they should not be employed to exclude infection. Paired maternal and fetal-neonatal IgG titers with higher newborn IgG levels or rising IgG titers during infancy may be used to diagnose some congenital infections. Total cord blood IgM, IgA (both are not actively transported across the placenta to the fetus), or the presence of IgM-rheumatoid factor in neonatal serum may be used as a screening tool to identify infants at risk for any intrauterine infection. Total IgM has a high rate of both false-positive and false-negative results.

Identification of a bacterial or fungal infection may be made by isolating the etiologic agent from a body fluid that is normally sterile (blood, cerebrospinal fluid [CSF], urine, joint fluid), by demonstrating endotoxin or bacterial antigen in a body fluid (CSF, urine, or serum), or by demonstrating bacterial infection at autopsy. It is preferable to obtain two specimens for blood culture by venipuncture from different sites to avoid confusion caused by skin contamination. Samples should be obtained from an umbilical catheter only at the time of initial insertion. A peripheral venous sample should also be obtained when samples for cultures are drawn from central venous catheters. Blood cultures performed by radiometric methods may demonstrate growth within 24{endash}–72 hr. Although blood cultures are usually the basis for a diagnosis of bacterial infection, the bacteremic phase of the illness may be missed by poor timing or blood sample size (sample size may be as little as 0.2 mL, but more than 0.5{endash}–1 mL is optimal). Focal infections that produce systemic manifestations such as meningitis, arthritis, and urinary tract infections may be diagnosed by positive culture results from specific sites in the absence of positive

blood cultures. Bacterial pneumonia has been reported at autopsy in infants with negative blood cultures before antimicrobial therapy.

Interpretation of tests for bacterial antigen may also be difficult. Latex particle agglutination and counterimmunoelectrophoresis are used for identification of GBS and E. coli K1 capsular polysaccharides in biologic fluids. The commercially available antigen detection kits are not as sensitive as blood cultures, and false-positive results may occur, particularly errors from contamination of urine collected in bags. Because urine is an excellent fluid for use in antigen detection, this test should be confirmed with specimens collected by suprapubic aspiration or catheterization.

When the clinical presentation suggests infection and the focus is unclear, additional studies should be performed. This includes, in addition to blood cultures, a lumbar puncture, urine examination and culture, gastric aspirate for Gram stain and culture, and a chest roentgenogram. Urine should be collected by catheterization or suprapubic aspiration; urine culture can be omitted in early-onset infections because urinary tract infection is rare at this time. Demonstration of bacteria and inflammatory cells in Gram-stained gastric aspirates on the 1st day of life may reflect maternal amnionitis, which is a risk factor for early-onset infection. Examination of the buffy coat with Gram or methylene blue stain may demonstrate intracellular pathogens, whereas similar stains of endotracheal secretions in infants with early-onset pneumonia may demonstrate the gram-positive cocci of GBS.

The total white blood cell count and differential and the ratio of immature to total neutrophils provide immediately predictive information when compared to age standards. Neutropenia is more common than neutrophilia in severe neonatal sepsis, but neutropenia also occurs in association with maternal hypertension, neonatal sensitization, NEC, periventricular hemorrhage, seizures, surgery, and possibly hemolysis. An immature neutrophil-total ratio of 0.16 or greater suggests bacterial infection.

Diagnostic evaluations may be indicated for asymptomatic infants because of maternal risk factors. The probability of neonatal infection and subsequent neonatal sepsis correlates with the degree of prematurity and bacterial contamination of amniotic fluid. In an asymptomatic term infant whose mother has chorioamnionitis, two blood cultures and a gastric aspirate should be examined to confirm the maternal diagnosis and identify presumptively the organisms by Gram stain. Presumptive treatment should be initiated. A lumbar puncture is not indicated because infants with meningitis are symptomatic. If the blood culture is positive or if the infant becomes symptomatic, lumbar puncture should be performed. Prolonged rupture of membranes for longer than 18 hr suggests the need for blood cultures in premature

infants but not necessarily in asymptomatic term infants without signs of fetal distress.

TREATMENT. Once infection has been suspected and appropriate cultures have been obtained, intravenous or intramuscular antibiotic therapy should be instituted immediately. Initial treatment of suspected neonatal infection is determined by the pattern of disease and the organisms that are common for the age of the infant and the flora of the nursery (see Table 94–{endash}2 Table 94–{endash}2). Initial empiric treatment of early-onset and late-onset community-acquired infections should consist of ampicillin and an aminoglycoside (usually gentamicin). Nosocomial infections acquired in the neonatal intensive care unit (NICU) are more likely to be caused by staphylococci, a variety of Enterobacteriaceae, Pseudomonas, or Candida. Thus, an antistaphylococcal drug, nafcillin for S. aureus or vancomycin for coagulase-negative staphylococci should be substituted for ampicillin. A history of recent antimicrobial therapy or the presence of antibiotic-resistant infections in the NICU suggests the need for a different aminoglycoside agent (amikacin) and vancomycin is used for methicillin-resistant staphylococci. Doses of the commonly used antibiotics are provided in Table 95–{endash}3 Table 95–{endash}3. When the history or the presence of necrotic skin lesions suggests Pseudomonas infection, initial therapy should be ticarcillin or carbenicillin and gentamicin.

Once the pathogen has been identified and the antibiotic sensitivities determined, the most appropriate drug(s) should be selected. For most of the gram-negative enteric bacteria, ampicillin and an aminoglycoside, or a third-generation cephalosporin (cefotaxime or ceftazidime) should be used. Enterococci should be treated with both a penicillin (ampicillin or piperacillin) and an aminoglycoside, since synergism has been demonstrated with this combination of antibiotics in many strains. Ampicillin alone is adequate for L. monocytogenes, and penicillin will suffice for GBS. Clindamycin or metronidazole is appropriate for anaerobic infections.

Third-generation cephalosporins such as cefotaxime are valuable additions for treating documented neonatal sepsis and meningitis because (1) the minimal inhibitory concentrations needed for treatment of gram-negative enteric bacilli are much lower than those for the aminoglycosides; (2) there is excellent penetration into CSF in the presence of inflamed meninges; and (3) much higher doses can be given. The end result is much higher bactericidal titers in serum and CSF than are achievable with ampicillin-aminoglycoside combinations. However, cephalosporins should not be used alone as empiric therapy or indiscriminantly because they have only modest activity against S. aureus and L. monocytogenes and enterococci are uniformly resistant. Moreover, rapid emergence of resistant organisms is possible with frequent usage in the NICU.

Therapy for most infections should be continued for a total of 7–10 days or for at least 5–7 days after a clinical response has occurred. The course of treatment for meningitis caused by GBS is usually for 14 days and for a minimum of 14 days after sterilization of the CSF in gram-negative meningitis. A blood culture result taken 24–48 hr after initiation of therapy should be negative. If the culture results are positive, the possibility of an infected indwelling catheter, endocarditis, an infected thrombus, an occult abscess, subtherapeutic antibiotic levels, or resistant organisms should be considered. A change in antibiotics and longer duration of therapy may be indicated.

Management of newborn infants whose mothers received antibiotics during labor should be individualized. If in utero infection is likely, then treatment of the infant should be continued until there is evidence that there was no infection (the infant remains asymptomatic for 24{endash}–72 hr) or there is clinical and laboratory evidence of recovery. Antigen detection tests may be helpful in symptomatic infants but are not indicated in asymptomatic infants. The size of the bacterial inoculum needed to produce a positive test in urine should lead to signs of infection.

PREVENTION. Aggressive management of suspected maternal chorioamnionitis with antibiotics before delivery, rapid delivery of the newborn infant, and selective intrapartum chemoprophylaxis appears to have decreased the morbidity and mortality rates of neonatal bacterial infections.

Prevention of neonatal nosocomial infection is complex and includes a 2-min scrub before entering the nursery, 15-sec washing between patients, scrub suits for nurses and residents, adequate nursing staff, avoidance of overcrowding, and specific isolation precautions. Control of outbreaks depends on the pathogen and epidemiology. Commonly used measures include investigation of the extent of colonization in infants and caretakers, a search for a common source or reservoir, cohorting of infants and caretakers, changes in handwashing solutions and protocols, and antimicrobial prophylaxis. Cord care, equipment sterilization, and handwashing are essential, whereas gowns have not consistently been demonstrated to be effective.

Clinical Syndromes

INTRAUTERINE INFECTION AND PRENATAL DIAGNOSIS

Investigations of fetal infection have made enormous advances in the last decade. In particular, the ability to delineate a diagnosis during early gestation is now possible in many situations. Nevertheless, some physicians still elect to use only serologic studies of the mother or, in other cases, await delivery to test the cord blood. This approach is problematic for several reasons. First, the fetus may die in utero, and the correct diagnosis may never be made. Second, the fetal response to viral infection may wane by late gestation so that the infectious agent cannot be identified. Third, the correct prenatal diagnosis may alter the management of both the mother in late gestation and the newborn postpartum. For example, treatment of an

infectious agent may be initiated at an earlier period. Alternatively, an accurate diagnosis of fetal infection as the cause of intrauterine growth retardation prevents a preterm delivery based on concerns about uteroplacental insufficiency. Finally, the diagnosis of fetal infection alerts both obstetric and pediatric staffs to follow universal precautions to avoid spread of infection.

The emphasis of this chapter is on the prenatal investigation of fetal infection. The current protocols for fetal diagnosis include both noninvasive and invasive procedures . The invasive techniques include amniocentesis, cordocentesis (percutaneous umbilical blood sampling) and chorionic villus sampling. A common noninvasive technique is ultrasound. In many cases, a fetal abnormality detected by ultrasound is the reason for referral of a pregnant woman to a fetal diagnostic center. In the following discussion, an outline is presented for evaluation of suspected fetal infection. Congenital toxoplasmosis is reviewed as an example. Chapter 97 contains the sections on congenital and perinatal viral infections.

TECHNIQUES FOR PRENATAL DIAGNOSIS. Amniocentesis is monitored by constant ultrasound visualization. The amniotic fluid is aspirated after the percutaneous insertion of a narrow-gauge abdominal needle. As much as 36 mL of amniotic fluid can be safely removed after 15 wk of gestation. When amniocentesis is performed before 15 wk, approximately 1 mL of fluid per week of gestation may be removed. Even the lower quantities of fluid are adequate for diagnosis of infectious agents. The complications are minimal, and the risk of fetal loss is less than 1%.

Fetal blood sampling by percutaneous puncture of the umbilical cord, cordocentesis, was developed as a technique for prenatal diagnosis of infection (see Chapter 81). Cordocentesis is usually performed after 15 wk using high-resolution ultrasound. The umbilical vein is punctured, and fetal blood (1{endash}–8 mL) is obtained for diagnostic studies. Complications include transient bleeding from the puncture site in the vein or the uterine wall and transient fetal bradycardia. The rate of fetal loss is slightly higher than for amniocentesis but is generally below 2%.

Chorionic villus sampling allows prenatal diagnosis as early as 7 wk of gestation (see Chapter 81). However, because of associated risks of fetal death, subsequent fetal limb anomalies, and cavernous hemangiomas, there is little indication to recommend the procedure for prenatal diagnosis of a suspected infection.

DIRECT EVIDENCE OF INFECTION

MATERNAL SEROLOGY. When a pregnant woman has a febrile illness and concern is raised about fetal infection, maternal serologic testing is the traditional method to evaluate the mother. The acronym TORCH was established to remind the physician of toxoplasmosis, rubella, cytomegalovirus (CMV), and herpes (HSV). Subsequently, S was added because of the resurgence of syphilis as an agent of fetal

infection (STORCH). The acronym now also encompasses the known pathogens such as parvovirus and varicella-zoster virus (VZV).

Routine screening of maternal sera for all components of the STORCH profile is now discouraged because of the low yield of useful information. Rather, the physician is encouraged to obtain a thorough history about potential maternal exposures to specific infectious agents and to test the mother for the pathogen in question. In most cases of suspected fetal infection, concern is not raised until the pregnant woman has been ill for several weeks or is only raised in retrospect at parturition. At this time, the maternal immune response to the suspected pathogen may no longer reflect an acute infection, i.e., the specific immunoglobulin (Ig)M response is no longer detectable and the IgG response has already reached a plateau. Also, many of the pathogen-specific IgM serologic assays require considerable skill to perform and tend to be less reliable than the more common IgG assays. For this reason, the results of the IgM assays can be either falsely negative or falsely positive.

FETAL SEROLOGY. If there is a high likelihood of maternal infection with a known teratogenic agent, fetal ultrasound examination is strongly recommended. If the examination demonstrates either delayed growth for gestational age or a physical abnormality, examination of a fetal blood sample may be warranted. Cordocentesis can provide a sufficient sample for both total and pathogen-specific IgM assays. The total IgM value is important because the normal fetal IgM level is less than 5 mg/dL. Any elevation in total IgM may indicate an underlying fetal infection that has stimulated the fetal immune system. For example, a fetus infected by gestational chickenpox at 20 wk had a highly elevated total IgM level of 30 mg/dL at 32 wk. The fetus was delivered at 34 wk and, by 2 wk postpartum, had a low total IgM level. Likewise, fetuses infected in utero with toxoplasmosis may no longer have elevated levels of total IgM at birth. It is also important to remember that cord serum samples with low levels of total IgM (<20 mg/dL) may be unacceptable for detection of pathogen-specific IgM. For these reasons, these IgM tests are only useful when the results are strongly positive. A negative pathogen-specific IgM finding does not necessarily rule out that pathogen as a cause of fetopathy.

CULTURE. If the serologic studies on the mother point to a specific pathogen, it is sometimes possible to culture the organism from amniotic fluid. For example, CMV is a frequent concern, and the maternal serologic test often fails to show a positive IgM response even when there is a very high IgG titer. Under these circumstances, amniocentesis can be performed and the fluid sent for viral culture. The presence of CMV in the amniotic fluid indicates that the fetus is infected and at high risk but does not always mean that the fetus will have severe sequelae. Toxoplasma also can be grown from amniotic fluid samples. In contrast, HSV and VZV are rarely isolated from amniotic fluid samples. Both CMV and Toxoplasma

also can be isolated from cordocentesis sampling. Chorionic villus sampling to obtain tissue for virus culture is usually contraindicated because of its associated high risks.

ELECTRON MICROSCOPY. The use of electron microscopy to diagnose a prenatal infection is not always necessary, but it may be extremely helpful when parvovirus is the most likely diagnosis. Parvovirus does not grow in the cell cultures commonly available in the virology laboratory. Furthermore, an IgM response is not always detectable in women with primary infections. When a fetus is infected with parvovirus, large quantities of viral particles are usually present in fetal serum, effusions, or amniotic fluid. The likelihood of viral visualization can be increased by first aggregating the viral particles with parvovirus-specific antiserum before placing the sample on a grid for examination by electron microscopy.

POLYMERASE CHAIN REACTION. Polymerase chain reaction (PCR) has achieved rapid acceptance as a method to produce large quantities of viral DNA from a small initial sample. PCR can be combined with reverse transcriptase methods to produce DNA from an RNA viral genome. However, for each pathogen-specific PCR assay result, a different pair of oligonucleotide primers is required. Thus, the physician must first have some idea of the suspected agent when PCR is applied toward the detection of a teratogen. Otherwise, the virology laboratory must perform a large series of PCR amplifications on the fetal sample. PCR is particularly helpful to diagnose human immunodeficiency virus (HIV) infection in blood samples taken from the newborn infant. Furthermore, the same sensitive PCR technique could be applied toward the diagnosis of HIV infection in cordocentesis samples.

DIAGNOSIS. Once the possibility of fetal infection has been raised, several steps may make it possible to diagnose the pathogen. Maternal serologic tests alone rarely provide the answer, except when the obstetrician has tested the woman before pregnancy for antibodies to pathogens such as Toxoplasma . This practice should be encouraged because a woman known to be immune to an agent cannot have a primary infection with that pathogen during gestation. Conversely, a woman known to be seronegative for toxoplasmosis could be at high risk if a repeat serologic test during a subsequent pregnancy yielded a positive result. If maternal serologic data are inconclusive, the pregnant woman can undergo amniocentesis and possibly cordocentesis. Samples obtained by one or both of these methods are often sufficient to make a correct diagnosis of fetal infection. Therefore, the parents can be counseled about the potential sequelae of the fetal infection long before delivery, and important decisions should be made about potential therapeutic interventions during the remainder of gestation. Finally, it is important to consider conditions that can mimic a fetal infection . .

PRENATAL DIAGNOSIS AND TREATMENT OF CONGENITAL TOXOPLASMOSIS. This parasitic disease can cause a fetopathy if a woman is

infected for the first time while pregnant. Pregnant women can ingest Toxoplasma cysts by eating raw or undercooked meat, or they can come into accidental contact with oocysts in contaminated cat feces. From the bloodstream, the tachyzoite forms of the parasite cross the placenta to reach the fetal circulation, where tissue cysts form within the fetal tissues, leading to dysmorphogenesis. Fetopathy includes hepatosplenomegaly, chorioretinitis, hydrocephaly, microcephaly, meningoencephalitis, and cerebral calcifications. The risk of transmission of the parasite to the fetus increases with advancing gestational age; however, dysmorphogenesis is most severe when the primary maternal infection occurs during the first trimester.

In France, a national program screening pregnant women for antibody to Toxoplasma demonstrated that those who were seropositive before pregnancy were at no risk. Those lacking antibody during early gestation were at high risk. If subsequent testing of this high-risk group during the same pregnancy demonstrated Toxoplasma-specific antibody, the woman may have had an acute infection with this agent. Because not all fetuses contract the infection after maternal toxoplasmosis, infected fetuses were identified by culture of either amniotic fluid or fetal blood obtained by cordocentesis and amniocentesis. Fetal serum IgM antibody to Toxoplasma was not very sensitive, probably because most fetuses do not produce IgM until after 20 wk of gestation. Treatment of women having acute toxoplasmosis during pregnancy with a regimen that included spiramycin, followed by pyrimethamine, sulfadiazine, and folinic acid (leucovorin) reduced the likelihood of fetal infection. Spiramycin was given to prevent intrauterine transmission of toxoplasmosis. If prenatal testing indicated that the fetus was infected, the regimen sometimes excluded spiramycin but included pyrimethamine, sulfadiazine, and folinic acid. Treatment of both mother and fetus reduced the sequelae to the fetus. . Treatment protocols for pregnant women with acute toxoplasmosis are still under active investigation.

VIRAL INFECTIONS OF THE FETUS AND NEWBORN

This chapter includes a discussion of the common viral agents that cause disease in both the fetus and newborn. For a virus to infect a fetus, the replication process in the woman must include a viremic phase during which the placenta is an inadvertent target. In many cases, the viral agents not only grow within the fetal tissues, but they also behave as teratogens, e.g., rubella. Because of recent technologic advances, most of these infections can be diagnosed at the intrauterine stage (see Chapter 96). See Chapter 100 for discussion of neonatal hepatitis.

Cytomegalovirus

Because the infection is commonly transmitted among toddlers and adults within a child care setting, cytomegalovirus (CMV) is sometimes called the child care virus (see Chapter 250). Today CMV is the most common cause of congenital infection because rubella vaccination has almost eliminated congenital rubella syndrome.

EPIDEMIOLOGY. CMV is a frequent infection thoroughout the world. Depending on the geographic location, the CMV seroprevalence among adults ranges from 40% to greater than 70%. Risk to the fetus is greatest when the pregnant woman experiences a primary CMV infection; about 40% of such cases have a fetal infection. In contrast, only 1% of fetuses are infected when pregnant women have a recurrence of a previous CMV infection.

In the United States, about 1% of all newborns are congenitally infected with CMV, from 30,000 to 40,000 infants annually. About 5–10% of the cases are symptomatic at birth; 90–95% are asymptomatic. The more symptomatic the case, the more likely it is that the mother had a primary CMV infection. Of great interest, the risk of a congenital CMV infection may increase considerably if the pregnant woman has an underlying human immunodeficiency virus (HIV) infection in addition to a previous CMV infection.

CLINICAL MANIFESTATIONS. The condition of symptomatic congenital CMV infection was originally called cytomegalic inclusion disease. The disease involves most organs; signs include intrauterine growth retardation, hepatosplenomegaly and jaundice, thrombocytopenia and purpura, and interstitial pneumonitis. The central nervous system (CNS) is frequently involved, as evidenced by microcephaly and ventriculomegaly. Intracranial calcifications may be present in a periventricular distribution. Other neurologic problems include chorioretinitis and sensorineural deafness. These newborns are usually easy to identify; when purple skin lesions caused by dermal erythropoiesis are prominent, they have been compared with a blueberry muffin in appearance. In some instances, the stigmata of congenital toxoplasmosis can closely resemble those of congenital CMV infection .

The main concern with asymptomatically infected newborns is the subsequent development of sensorineural hearing loss in as many as 20% of these infants. Other auditory processing disorders that may develop include abnormal speech perception and slowed auditory processing times. Some infants having asymptomatic congenital CMV infection may have computed tomographic abnormalities in the brain, such as periventricular radiolucencies or punctate calcifications.

DIAGNOSIS. CMV infection of the fetus can be diagnosed by culture of the amniotic fluid obtained during amniocentesis. Although isolation of CMV by this means documents fetal infection, it does not indicate whether the newborn will have a symptomatic or an asymptomatic infection. It is not known whether every intrauterine CMV infection will have CMV in the amniotic fluid because of lack of

knowledge about the interval between the maternal infection and the fetal infection, i.e., how long after the presumed maternal infection amniocentesis findings become positive.

Postpartum, CMV can be easily isolated from the urine or saliva of congenitally infected infants. For more rapid diagnosis, cell culture has been combined with a CMV-specific antibody for detection of virus-specific antigens before the appearance of cytopathic effect. In general, CMV-specific immunoglobulin (Ig)G antibody tests are reliable; the CMV-specific IgM assays are less sensitive; and a negative IgM assay result for CMV antibody does not eliminate the possibility of an acute infection. CMV DNA can be detected by polymerase chain reaction (PCR) technology, but this test usually is not required because the virus is readily isolated in cell culture.

TREATMENT. CMV is relatively insensitive to acyclovir. Ganciclovir is currently undergoing evaluation in infants with congenital CMV infection; the intravenous dosage is 6 mg/kg every 12 hrs for 6 wk. Early results indicate that ganciclovir treatment will reduce the excretion of virus and moderate the postpartum disease. However, viral excretion often resumes once treatment is stopped. As yet, there is no information about whether one course of ganciclovir will alter the long-term progression of congenital CMV disease. A frequent side effect of ganciclovir therapy is bone marrow suppression, and, therefore, it should only be used for newborns as part of an approved investigational protocol.

PREVENTION. Pregnant women who are CMV seropositive are at low risk of delivering a symptomatic newborn. If possible, pregnant women should have a CMV serologic test, especially if they care for young children who are potential CMV excretors. Those who are CMV seronegative should be counseled regarding hygienic measures, e.g., good handwashing and avoidance of contact with oral secretions. There is no efficacious CMV vaccine.

PROGNOSIS. The mortality rate in symptomatic CMV congenital infection is around 12%, and most of the surviving infants have permanent sequelae, which include visual deficits, hearing loss, seizure disorders, and motor and intellectual retardation. Virtually all infants with asymptomatic CMV congenital infection survive, although, in up to 20%, hearing deficits and learning problems eventually develop.

Herpes simplex virus (HSV) type 1 causes fever blisters or cold sores; HSV type 2 is the major cause of genital herpes. HSV type 1 can also cause a genital infection after orogenital sexual contact. Both primary and reactivated HSV infections during pregnancy are associated with fetal infection, but more commonly, neonatal disease is acquired from the maternal genitourinary tract during parturition.

EPIDEMIOLOGY. The number of adults in the United States with genital herpes infection ranges from 16–25%. However, there is enormous geographic

variation, e.g., in some urban areas, more than 50% of the sexually active adults may be HSV-2 seropositive. The likelihood of transmission of herpes from the pregnant woman to her fetus or newborn depends on whether the woman has a primary HSV genital infection during the pregnancy or whether she has a recurrence. If she has a primary infection, the risk of neonatal HSV infection is 44%; for a recurrence, the risk is only 3%. HSV-2 is the agent responsible for more than 75% of all neonatal infections, although genital lesions are present at parturition in less than 10% of cases, and a history of gestational genital HSV infection is obtained from only a minority of mothers who deliver infected infants.

Postnatally, HSV infection can be acquired by close contact between a newborn and an adult with active herpes labialis (HSV-1). Under these circumstances, transmission can occur if an infant is kissed on the mouth or eye by a caregiver who has active recurrent oral herpes, even if the person is asymptomatic.

CLINICAL MANIFESTATIONS OF THE FETOPATHY. Intrauterine HSV infection is uncommon but may result in prematurity and death. In a large collaborative study of HSV-infected neonates, only 5% appeared to have contracted the infection in utero. The principal sites of involvement are the skin, eyes, and the CNS. Skin involvement is very common and includes vesicular rashes; scarring over the scalp, trunk, or extremities; and vesicles around the scars, presumably a sign of viral reactivation. CNS abnormalities are similarly frequent and include microcephaly, often associated with atrophy of the brain or cystic encephalomalacia (Fig. 97–{endash}1 Fig. 97–{endash}1), involvement of the spinal cord, chorioretinitis, and microphthalmia. In addition, hepatitis and calcifications in the lungs and adrenal glands have been reported.

PATHOGENESIS OF THE FETOPATHY. The fetal disease probably is acquired by a transient maternal viremia, which seeds the placenta. The virus causes a disseminated infection of the fetus, but the neurotropism is particularly evident by the damage to the developing brain and eye. The infection is persistent, and the virus frequently re-emerges postpartum, often at sites of prior injury. The ability to isolate HSV-2 from a newborn within the first few days of life is a major diagnostic criterion of intrauterine herpes infection. There are many similarities between this infection and congenital varicella syndrome (see Chapter 97.3).

CLINICAL MANIFESTATIONS OF PERINATAL DISEASE. About 90% of the cases of neonatal herpes are contracted by contamination with infectious secretions in the genital tract at parturition. Because the virus must replicate in the newly infected host, the infant usually does not become symptomatic until late in the 1st wk or early in the 2nd wk of life. Disease is predominantly due to HSV-2, although HSV-1 is cultured in 10{endash}–20% of the cases. The patterns of disease are based on their presentation. The disseminated pattern is similar to that seen in

intrauterine disease, with multiorgan involvement, including the brain. Unless the infant has vesicular lesions, the early manifestations are similar to bacterial sepsis. In a few cases, disseminated herpes disease presents with an interstitial radiologic pattern of pneumonia. Cutaneous HSV disease may involve the skin, mouth, or eyes. Like the disseminated disease, it usually appears around days 9{endash}–11 of life. The vesicles may be observed on the presenting part, whether the vertex or the buttocks (breech). If present, eye findings may include keratoconjunctivitis. Unless promptly recognized and treated, cutaneous disease can progress to disseminated disease. The encephalitic form of neonatal herpes tends to occur in the late 2nd wk and 3rd wk of life. The manifestations may include lethargy, irritability, and seizures, often in the absence of cutaneous lesions.

In addition to intrapartum acquisition, neonatal herpes can be spread in the first few days postpartum. In this instance, the virus is usually HSV-1. The source is a caregiver or relative with oral herpes, who transmits the infection by direct contact with the baby, e.g., kissing the baby on the face or toes. The consequences are the same as described for intrapartum infection.

DIAGNOSIS. Prenatal diagnosis has not been pursued; HSV DNA might be present in cord blood samples, but correct timing of testing in relation to maternal symptoms is unknown. Postpartum, HSV can be easily isolated in cell culture by inoculation of vesicle fluid, nasopharyngeal or conjunctival swabs, urine, stool, tracheal secretions (pneumonia), duodenal aspirates (hepatitis), and occasionally cerebrospinal fluid (encephalitis). For rapid viral diagnosis, cells scraped from the base of a vesicle onto a glass slide can be probed with HSV-specific fluorescein-conjugated monoclonal antibody, which attaches to the viral antigens. Monoclonal antibodies also can differentiate HSV-1 and HSV-2 antigens. The Tzanck cytologic test is nonspecific and should be discontinued.

TREATMENT. Acyclovir is highly efficacious in treating this infection. It is selectively activated by HSV thymidine kinase to a phosphorylated derivative that subsequently acts as an inhibitor of viral DNA synthesis. In an infected neonate without evidence of CNS disease, acyclovir is administered in an intravenous dose of 10 mg/kg every 8 hr, usually for 14 days. A longer course (21 days or more) should be given for encephalitis. Some experts routinely treat all forms of neonatal herpes for at least 21 days; others now use a higher dose of 15 mg/kg every 8 hr, especially when there is CNS disease. After a successful treatment course with acyclovir, in some infants, recurrent cutaneous vesicles develop; these herpetic lesions usually are not due to acyclovir resistance but possibly to reduced HSV-specific immunity after acyclovir therapy. Because an occasional infant with isolated recurrent cutaneous disease may subsequently demonstrate late signs of encephalitis, some authorities recommend suppressive oral acyclovir therapy for these patients during the first

4{endash}–6 mo after birth. A suggested dosage of acyclovir syrup is 5 mg/kg every 8 hr.

The main complication of intravenous acyclovir therapy is renal dysfunction as a result of crystal formation in the tubules; therefore, serum creatinine levels should be obtained every 3 days during treatment. The dosage should be reduced if the creatinine level begins to rise above twice the initial value. The administration of two renal toxic drugs at the same time, e.g., acyclovir and gentamicin, should be done with care.

PREVENTION. Cesarean section is routinely recommended in the pregnant woman with a documented primary genital herpes infection during late gestation, if continued virus shedding is documented. Cesarean section remains a common practice when herpes is cultured from the urogenital tract of a near-term pregnant woman with a history of genital herpes predating the current gestation. However, recent studies, which indicate a 3% risk of infection to infants born to mothers with recurrent herpes, suggest that other approaches be considered. In women who are asymptomatic at the onset of labor, experts suggest vaginal delivery, with the option of obtaining viral cultures of the birth canal. If the delivery culture is positive, cultures from the skin, eyes, pharynx, and rectum of the newborn are recommended. Parents are given thorough instructions about symptoms of neonatal herpes. If any signs of illness appear, the infant is returned for a repeat examination and possible treatment for herpes. Likewise, if the initial cultures on either mother or infant are positive, the infant (even if completely well) is returned for a second examination and repeat cultures. If the maternal cultures are positive, positive newborn cultures at birth may only indicate maternal contamination and not true neonatal infection. Therefore, a second set of newborn cultures will clarify the issue. Intrapartum herpes infection usually becomes symptomatic around the beginning of the 2nd wk of life; preferably, acyclovir treatment should begin at or just before this period. If there are concerns about neonatal infection at any stage of this process, the infant can be admitted for intravenous treatment while awaiting subsequent culture results.

Alternatively, some infectious disease specialists advocate suppressive oral acyclovir therapy (400 mg twice daily) for every pregnant woman with known recurrent genital herpes, to reduce the need for cesarean section. Prospective studies to evaluate the safety and efficacy of acyclovir therapy in late pregnancy are underway. Initial reports from the Acyclovir in Pregnancy Registry (Burroughs Wellcome Company) have found no increased risk for birth defects among 601 infants born to women exposed to acyclovir during pregnancy. Even if a pregnant woman is given suppressive acyclovir therapy, viral cultures should be taken from mother and baby postpartum.

PROGNOSIS. Despite the advent of effective acyclovir therapy, disseminated neonatal HSV infections and localized encephalitis have considerable morbidity and mortality rates. The outcome is improved by early identification and prompt initiation of treatment before the onset of disseminated disease, shock, or coma. The prognosis for neonatal encephalitis caused by HSV-1 appears to be better than that for HSV-2 infection.

Varicella-zoster virus (VZV) is one of the seven human herpesviruses. Primary infection leads to chickenpox, after which the virus remains latent in the dorsal root ganglion. On reactivation, the virus causes the disease shingles (herpes zoster). Gestational chickenpox can cause a distinct intrauterine syndrome and a serious neonatal disease.

EPIDEMIOLOGY OF FETAL INFECTION. About 3 million cases of chickenpox occur annually in the United States. Although most children contract this infection, the minority who do not incur the disease will remain susceptible as adults. When pregnant women contract chickenpox, they may also infect the fetus during the viremic phase. The precise risk to the fetus has been difficult to establish, but it appears to be about 25%. However, not every infected fetus has congenital varicella syndrome. Based on one German study of pregnant women with chickenpox, only about 3 of every 100 infants born to women with gestational chickenpox had stigmata of congenital infection. The risk extends throughout the first half of gestation.

CLINICAL MANIFESTATIONS OF THE FETOPATHY. The stigmata of congenital varicella syndrome are listed in Table 97–{endash}1 Table 97–{endash}1. The sequelae involve mainly the skin, extremities, eyes, and brain. The characteristic cutaneous lesion has been called a cicatrix, a zigzag scarring, often in a dermatomal distribution. The other hallmark of this syndrome is one or more shortened and malformed extremities (Fig. 97–{endash}2 Fig. 97–{endash}2). Frequently, the atrophic extremity is covered with a cicatrix. The remainder of the torso may be entirely normal in appearance. Alternatively, there may be neither skin nor limb abnormalities, but the infant may show cataracts or even extensive aplasia of the entire brain. Occasionally, calcifications are evident within a microcephalic head (Fig. 97–{endash}3 Fig. 97–{endash}3).

PATHOGENESIS OF THE FETOPATHY. Most of the stigmata can be attributed to virus-induced injury to the nervous system. The limb and eye manifestations appear to be caused by denervation secondary to VZV invasion of fetal nerves, such as the cervical or lumbosacral cord or the optic stalk. However, there is no obvious explanation why certain regions of the body are preferentially infected during fetal VZV infection; the virus may select tissues that are in a rapid developmental stage, e.g., the limb buds. Histologic examination of the brain of an infected fetus demonstrated necrotizing cerebral lesions involving the leptomeninges,

the cortex, and the adjacent white matter. Pathologic changes are also observed in the spinal cord, and they include shrunken and gliotic posterior horns and lateral columns. The characteristic cicatricial scarring may represent the cutaneous residua of VZV infection of the sensory nerves.

The period of greatest risk to the fetus correlates with the gestational period when there is major development and innervation of the limb buds, and maturation of the eyes. Fetuses infected at 6{endash}–12 wk of gestation appear to have maximal interruption with limb development; fetuses infected at 16{endash}–20 wk may have eye and brain involvement. In addition, viral damage to the sympathetic fibers in the cervical and lumbosacral cord may lead to divergent effects such as Horner syndrome and dysfunction of the urethral or anal sphincters.

DIAGNOSIS. The diagnosis of VZV fetopathy is based mainly on the history of gestational chickenpox combined with the stigmata seen in the fetus. Virus cannot be cultured from the affected newborn, but viral DNA can be detected in tissue samples by a hybridization technique. Some infants have VZV-specific IgM antibody detectable in the cord blood sample, although the IgM titer drops quickly postpartum. The diagnosis can be made antenatally by obtaining a fetal blood sample for VZV-specific IgM titer. However, VZV has not been cultured from the amniotic fluid.

TREATMENT AND PREVENTION OF FETAL DISEASE. The damage caused by fetal VZV infection does not progress postpartum, an indication that there is no persistent viral replication. Thus, antiviral treatment of infants with congenital VZV syndrome is not indicated. Since the varicella vaccine is now available for general use, VZV fetopathy will be preventable by immunization of VZV-susceptible young women. Vaccination of the same group of women is also indicated because morbidity and mortality rates of gestational chickenpox are considerable.

NEONATAL CHICKENPOX. There is confusion about the terminology of fetal infection when it occurs in the 9th mo of gestation. Although the initial infection is intrauterine, the baby often develops clinical chickenpox postpartum, i.e., after a 10{endash}–14-day incubation period. For example, if neonatal chickenpox is first seen on day 5 of life, the infection was contracted about 5 days before delivery. The risk to the newborn under these circumstances reflects the likelihood that the fetus obtained maternal anti-VZV antibody. If there was at least a 1-wk interval between maternal chickenpox and parturition, it is likely that the newborn infant received transplacental antibody to VZV. If the interval was less than 1 wk, the newborn may have no protective VZV antibody. Under the latter circumstances, neonatal chickenpox can be exceptionally severe. Neonatal chickenpox can also follow a postpartum exposure. Chickenpox is a more serious illness throughout the entire 1st yr of life than in later childhood, with more hepatic and CNS involvement. The

mortality rate is around 1:13,000; that for older children is less than 1:40,000. The mortality rate is also strikingly increased in pregnant women with chickenpox.

TREATMENT AND PREVENTION IN THE NEONATAL INFANT. The recommendations for varicella-zoster immune globulin (VZIG) reflect the increased risks to the exposed infant. A full-term infant born to a mother who has chickenpox less than 1 wk before parturition should receive one vial of VZIG by intramuscular injection. Every premature infant born to a mother with active chickenpox (even if present longer than 1 wk) should receive VZIG. Because of the higher mortality rate of chickenpox throughout the 1st yr of life, oral acyclovir suspension can be administered as soon as an infant develops chickenpox. The dosage is 80 mg/kg/24 hr, administered as 20 mg/kg every 6 hr. If an infant with chickenpox has signs of pneumonia, hepatitis, or encephalitis, immediate hospitalization and treatment with intravenous acyclovir should be considered.

PROGNOSIS. Many infants with congenital varicella syndrome have severe neurologic deficiencies. However, another group (presumably those infected later in gestation) may have only isolated stigmata, such as cataracts, which can be treated surgically. The latter infants develop normally throughout childhood. Infants with neonatal chickenpox have an excellent prognosis as long as they receive treatment with acyclovir as soon as the diagnosis is made.

EPIDEMIOLOGY. Parvovirus infection causes fifth disease, also known as erythema infectiosum. Most children contract the infection by their teenage years, but those who escape infection as children are susceptible as adults. Transmission is presumably by the respiratory route, probably by droplet aerosol. Gestational fifth disease is associated with spontaneous abortions and stillbirths. However, the incidence of maternal parvovirus infection is low. Unless a stillborn fetus has signs of nonimmune hydrops, the diagnosis of parvovirus is unlikely.

CLINICAL MANIFESTATIONS OF FETAL INFECTION. Primary HPV infection in pregnant women is similar to that in children, i.e., the woman may have a subclinical disease or she may complain of sore throat and arthralgia; a skin rash reminiscent of rubella may be seen. During the viremia, maternal HPV infection may be transmitted to the fetus. There are several consequences of fetal infection. The fetus may be infected but have no untoward residua. Alternatively, spontaneous abortion may occur in the first half of pregnancy, or, in the second half, a stillbirth with hydrops fetalis may occur. Live births may also exhibit hydrops, a condition characterized by generalized edema of fetal tissue as a result of fluid extravasation from the intravascular compartment as the result of cardiovascular failure induced by severe fetal anemia. .

PATHOGENESIS. Transplacental transmission of parvovirus has been proved by detection of viral DNA and viral particles in fetal tissues. Although the virus is

found in all tissues, there is a strong predilection for erythroid precursor cells. Parvoviral cytopathic effects are seen in erythroblasts of the bone marrow and sites of extramedullary hematopoiesis in the liver and spleen. Presumably, fetal infection can occur as early as 6 wk of gestation, when erythroblasts are first found in the fetal liver; after the 4th gestational mo, hematopoiesis switches from the liver to the bone marrow.

DIAGNOSIS. Acute parvovirus infection sometimes can be diagnosed in a pregnant woman by detection of virus-specific IgM antibody. Because the disease often occurs in a community-wide outbreak, the diagnosis can be assumed in those with compatible signs and symptoms. Prenatal diagnosis can be accomplished by either detection of viral DNA in fetal blood or visualization of viral particles by immune electron microscopy.

TREATMENT AND PREVENTION. Because HPV usually is spread rapidly through a community, there are few means for prevention. There is neither a vaccine nor a specific antiviral medication to treat HPV infection. Infected fetuses with hydrops can be managed by percutaneous umbilical blood transfusions.

PROGNOSIS. The prognosis of congenital parvovirus infection is difficult to establish because the number of asymptomatic intrauterine infections has not been determined. Once severe hydrops is diagnosed in a fetus, the mother should be referred to a fetal therapy center for further evaluation because of the very high risk for serious complications.

Rubella is an enveloped RNA virus that causes the disease sometimes called "3-day measles" or "German measles." The disease has almost been eliminated by the production of a live attenuated rubella vaccine. It is the only virus for which a vaccine was made mainly to eliminate the consequences of fetal infection.

EPIDEMIOLOGY OF THE FETOPATHY. Before rubella vaccination, pandemics of rubella occurred every 10–20 yr. In 1964–1965, an epidemic in the United States caused more than 12 million cases of rubella and an additional 20,000 infants with congenital rubella syndrome. After the initiation of a national rubella immunization program in 1969, the number of rubella cases declined by more than 99%. In the early 1990s, there was a modest increase in rubella cases, including congenital rubella syndrome, because of a failure to immunize all children in the United States.

Rubella virus is distinguished by its propensity to infect a fetus. During the first trimester of gestation, a primary maternal rubella infection has an 80% likelihood of transmission to the fetus, and most infected fetuses have rubella fetopathy. Transmission from mother to fetus also occurs in the early second trimester (50%) and persists throughout gestation.

CLINICAL MANIFESTATIONS IN THE FETUS. Rubella involves virtually all organ systems. The most common manifestation is intrauterine growth retardation. Another common finding is cataracts, bilateral or unilateral. Cataracts are frequently associated with microphthalmia. Myocarditis and structural cardiac defects, e.g., patent ductus arteriosus or pulmonary artery stenosis, are common. Blueberry muffin skin lesions, similar to those in CMV infection, may occur. Hearing loss from sensorineural deafness is another common defect. The infants may have active meningoencephalitis at birth; later sequelae include motor and mental retardation. Persistent infection leads to pneumonia, hepatitis, bone lucencies, thrombocytopenic purpura, and anemia in the infant with congenital rubella syndrome.

DIAGNOSIS. Most diagnoses can be made solely on a clinical basis. The diagnosis can be confirmed by finding virus-specific IgM antibody in the neonatal serum or by culturing rubella virus from the infants' urine or tissues. Virus can be shed in the urine for 1 yr or longer. Prenatal diagnosis of fetal rubella infection can be made either by virus isolation from amniotic fluid or by identification of rubella-specific IgM in cord blood.

TREATMENT AND PREVENTION. Congenital rubella syndrome is most easily prevented by universal immunization of all young children with rubella vaccine. When acute rubella infection is documented in a pregnant woman during the first half of gestation, there is a high likelihood of fetal infection with multiple fetal stigmata. Therefore, prenatal diagnosis is recommended so that termination of pregnancy can be considered. There is no effective antiviral medication for treatment of congenital rubella syndrome.

PROGNOSIS. Infants with the complete spectrum of the congenital rubella syndrome have a grim prognosis, especially when the disease continues to progress throughout infancy. The prognosis is obviously better for infants with only a few stigmata of the syndrome, presumably those who were initially infected later in gestation.

Over the past decade, there has been an extraordinary increase in our knowledge of HIV infection and pediatric acquired immunodeficiency syndrome (AIDS). This chapter focuses on intrauterine HIV infection and its consequences.

EPIDEMIOLOGY OF FETAL HIV INFECTION. Pediatric AIDS is nearly always acquired from an infected mother, either by intrauterine or intrapartum transmission. The mother becomes infected by being a member of one of the following risk groups: intravenous drug users who share needles with HIV-infected individuals; prostitutes who contract the disease from one of their partners; or less commonly, recipients of contaminated blood transfusions before 1985; and women married to men who were HIV seropositive, including male hemophiliac patients treated with factor VIII that contained HIV.

The geographic distribution of perinatal AIDS in the United States is heavily concentrated in the coastal metropolitan areas, such as New York/New Jersey, Miami, and Los Angeles, regions that include most women with AIDS. Epidemiologic studies suggest that about 7,000 HIV-seropositive women in the United States will become pregnant annually. The transmission rate to the fetus or newborn depends on maternal factors, such as the severity of her disease and the degree of viremia. For some pregnant women with AIDS, the rate of fetal and perinatal infection may approach 70%. However, a vertical fetal transmission rate for known HIV-seropositive women is around 25%. In the exceptional circumstance in which a woman contracts her primary HIV infection during early gestation, the risk for fetal transmission appears to be higher than 25%.

There are many examples of HIV infection in the second trimester documented by tissue isolation of the virus. There are fewer examples of vertical transplacental transmission during the first trimester, but HIV antigens and nucleic acids have been found in tissues removed from three 8-week-old fetuses. Three mechanisms have been proposed for intrauterine HIV transmission. First, virus in the maternal system is released from decidual cells and subsequently phagocytosed by syncytiotrophoblasts. Second, trophoblasts that are invading decidual tissue come into contact with HIV-infected maternal CD4 lymphocytes. Third, infected maternal macrophages invade the villous stroma. Phagocytosis may be a more important mechanism of intrauterine transmission than the specific CD4-receptor{endash}–mediated events because nucleated cells that express the CD4 cell surface molecule have not been observed until 12{endash}–14 wk of gestation.

DIAGNOSIS. Both viral culture and HIV-specific PCR assay can be successful in the prenatal diagnosis of HIV infection from fetal blood samples. Amniocentesis and cordocentesis have been carried out successfully in HIV-seropositive pregnant women, but the relative role and timing of these invasive procedures is problematic because the chronology of most intrauterine HIV transmission is uncertain. There is also concern about potential fetal transmission as a result of the procedure itself, especially cordocentesis.

TREATMENT AND PREVENTION. Zidovudine treatment during pregnancy was effective in reducing the risk of fetal infection from HIV-infected women in the 14–34th wk of pregnancy who were not already receiving zidovudine because they had CD4 lymphocyte counts greater than 200 cells/mm3 without clinical AIDS. The women received oral zidovudine therapy (100 mg five times daily) throughout the remainder of gestation. During labor, the drug was administered intravenously; a loading dose of 2 mg/kg given over 1 hr was followed by continuous infusion of 1 mg/kg/hr until delivery. The newborns received 6 wk of antiviral therapy (zidovudine

syrup at 2 mg/kg every 6 hr), beginning 8{endash}–12 hr postpartum. This resulted in a 67.5% relative risk reduction.

PROGNOSIS. In 1993, the median age to AIDS diagnosis of all HIV-infected infants was 12 mo, although many children first became symptomatic much later in childhood.

Computed tomogram of newborn with congenital herpes infection. The head tomogram shows diffuse encephalomalacia, poorly developed gyri, and deep thalamic and periventricular calcifications (arrows). The fact that calcifications were demonstrable in the brain of a 4-day-old infant confirmed that the central nervous system infection occurred in utero.

Newborn with congenital varicella syndrome. The infant had severe malformations of both lower extremities and cicatricial scarring over his left abdomen. Also see Magnetic resonance image of newborn with encephalitis secondary to congenital varicella syndrome. The intrauterine infection occurred about 3 mo antepartum, at which time there was extensive necrosis of the cerebral hemispheres. The image of the newborn head was taken with the patient supine; therefore, there is a fluid/fluid interface in the dependent occiput (A). The hydrocephalus (C) and calcifications in the basal ganglia (D) are visible; a cranial artifact (B) is seen secondary to a scalp vein needle.

Tests:

1. . Child T., 1 day of life, was born on a 39-40 week of gestation with weight 2450 g., length 48 cm. Regurgitation, active movements are lowered. Reflexes of neonate period depressed. Skin is pale. Tones of heart are muffled, a rhythm is stable. In lungs there is puerile breathing, wheezes are not present. Abdomen is soft. A liver comes forward on 1 cm. from the edge of costal arc. Spleen is not palpated. .In a mother the Wassermann test is sharply positive. What preparation it is necessary to use for the prophylaxis of syphilis in a child?

A. Rovamycin
B. Erythromycin
C. Penicillin
D Ampiox
E. Cephsolum

2. Child C., 2 day of life, was born on a 39-40 week of gestation with weight 2450 g., length 48 cm. Regurgitation, active movements are lowered. Reflexes of neonate period depressed. Skin is icteric. Turgor of skin is reduced. Cardiac tones some muffled, a rhythm is well-kept. In lungs the respiration is carried out in regular intervals, wheezes are not present. Abdomen is soft, accessible to palpation. Stool and urination are normal. In a mother on the last month of pregnancy syphilis is diagnosed.

What dosage of penicillin must be indicated to child?

A. 200000 U / kg / per day
B. 10000 U / kg / per day
C 30000 - 400000 U / kg / per day
D. 250000 U / kg / per day
E. 50000 - 100000 U / kg / per day

3. Child S., 3 day of life, was born on a 34-35 week, of gestation with weight 1850 g., length 43 cm., in the asphyxia of a 2 degree. Form of skull is hydrocephalic, small and lateral fontanels are opened, large fontanel 3,5x3 cm. Skin " marble". Cardiac tones are muffled, a rhythm is stable. In lungs the respiration is carried out in regular intervals
, wheezes are not present. Abdomen is soft. The phenomena of hepatoslenomegaly.
What test is more informative for the diagnosis of intrauterine infection?
A. reaction of complement fastening
B. radiological research
S. immunoenzyme assay
D. research of spinal liquid
E. RBTL

4. Child F., 20 days of life, on the basis of clinical and paraclinical data a congenital toxoplasmosis diagnosed, Disease manifested with innate hydropcephaly, hepatitis, iridocyclitis. Specific Ig antibodies are detected in a diagnostic titer, Ig M antibodies are not detected. In a 5 day of life to the child the tansfusion of packed red cells conducted.
Indicate the way of child was infected with:
A Hemotransfusion
B. mother's milk
C.. intranatally
D . transplacental
E. medical personnel

5. . Child F., 24 day of life, on the basis of clinical and paraclinical data a congenital toxoplasmosis diagnosed. Disease manifested with innate hydropcephaly innate oligotrophy of a 2 degree, hepatitis, partial atrophy of visual nerve of OD. In blood serum the specific anti TOXO Ig G and Ig M antibodies are detected in a diagnostic titer.
What preparation must be prescribe as causal medical treatment?
A. Reaferon
B. Rovamycin
C Diclofenac
D Cimeven
E. Erythromycin

6. Child F., 3 week of life, was born worn with weight deficit of 2 degree. In a 7 day of life the rise of transaminases level are marked. The manifestations of anemia added to the 10th day of life. On neurosonography- expansion of lateral and 3

ventricles to 8-9 mm. Congenital toxoplasmosis established after IFA Tindurin must be prescribed in follow doses :

A. 1 mg / kg / per day
B. 5 mg / kg / per day
C. 10 mg / kg / per day
D. 15 mg / kg / per day
E. 50 mg / kg / per day

7. Child D., 21 day of life, was born from 3 pregnancy proceeded physiologically Was born in the asphyxia of a 2-degree. In a 3 day of life there were a manifestations of conjunctivitis with relapsed course In scrape from buccal and conjunctival epithelium with immunoenzyme assay the Chlamydia trachomatis detected,.

Indicate preparation of causal medical treatment:

A Reaferon
B. Laferon
C. . Rovamitsin
D. Thimalin
E. Tindurin

8. Child D., 5 day of life, was born worn with weight 1950 g., length 48 cm., in the asphyxia of a 2 degree. In a 2 day of life the state of child became worse, regurgitation, areflexia appeared. To the end of 3 day an icterus appeared, in a 4 day — conjunctivitis. Specific immunological tests for verification of intrauterine infection was not conducted.

What changes in the clinical blood tests are most characteristic for majority of intrauterine infection?

A. polycythemia
B. agranoulocytosis
C. trombocytosis
D. trombocytopenia
E. eosinopenia

9. Child D., 21 day of life, was born from 3 pregnancy proceeded physiologically Was born in the asphyxia of a 2-degree. In a 3 day of life there were a manifestations of conjunctivitis with relapsed course In scrape from buccal and conjunctival epithelium with immunoenzyme assay the Chlamydia trachomatis detected,. What is the duration of erhythromycin adminisration?

A.during 10 days
B. during 7 days
C. during 1 month
D. during 3 months
E. during 21 day

10. Child D., 21 day of life, was born from 3 pregnancy proceeded physiologically

Was born in the asphyxia of a 2-degree. In a 3 day of life there were a manifestations of conjunctivitis with relapsed course In scrape from buccal and conjunctival epithelium with immunoenzyme assay the Chlamydia trachomatis detected,.

The dose of erihythromicin is:

A. 1 mg/kg/per day
B. 50 mg/kg/per day
C. 10 mg/kg/per day
D. 5 mg/kg/per day
E. 200 mg/kg/per day.

11. Child., 19 day of life, was born worn from IX pregnancy, II delivery were proceed with anemia of the II degree and underlying hestosis. Weight in a birth is 2750 g, length 51 cm. An icterus appeared on 3 day of life and proceeded to 15 day. The manifestation of relapsed conjunctivitis is after 4 day of life.

In suspicion for chlamidial infection to establish a diagnosis it is enough to detect::

A.. The specific antichlamidial Ig M antibodies in a child
B.High titer of the specific antichkamidial Ig G antibodies in a mother and father.
C. High titer of the specific antichlamidial Ig G antibodies in a mother
D. High titer of the specific antchlamidial Ig M antibodies in a mother
E. The specific antichlamidial Ig G and Ig M antibodies in a child

12. To 3 weeks of life in a child the pneumonia with chlamidial conjunctivitis has appear. Disease began from rise in temperature to 37,5C, paroxysmal cough. Then, an expiratory dyspnea appeared. What are the X-ray especialities for chlamidial pneumonia?

A. Air bronchogram
B. Homogeneous inspissations of sites in a pulmonary tissue
C. Interstitial bronchopneumonia
D. Decrease of the sizes of pulmonary fields
E. The centers of a destruction

13. Child, 10 day of life, was born after 37 week of gestation, after V pregnancy proceeded with underlying hestosis and anemia. The result of previous pregnancies is: I –abortion, II and III –medical abortions. The fourth child has died to the fifth day of life. This child was born in asphyxia of 3 degree with weight2210 g, length 44 cm. In 3 day of life the exchange blood transfusion conducted caused by hemolytic disease. In immunoenzyme assay in diagnostically significant titer the anti CMV – antibodies were detected. In what way child was infected?

A. intranatally,
B. antenatally,
C. hemotransfusion of packed red cells
D. within the mother’s milkчерез материнське молоко,
E. medical personnel / healthy virus carriers

14. Child, 10 day of life, was born after 37 week of gestation, after V pregnancy,II delivery пологи II, was born in asphyxia of 3 degree with weight2210 g, length 44 cm An icterus appeared in a 3 day of life, to 4 days the manifestations of hemorrhage disease as melena and bleeding from the points of injections were added. By a method of IFA in a diagnostic titer registered specific anti - CMV Ig G-antibodies..

What preparation must be prescribed as a causal medial treatment?

A. reaferon.
B. rovamycin
C. aciclovir
D. intraglobin
E. thienam

15. Child, 10 day of life, was born worn with weght 2350 g., length 50 cm., after 9 pregnancy, 2 delivery. An icterus appeared to the end of 2 day of life and proceeded to 14 day. From a 10 day the- rising of transaminases level admitted. In NSG the- width of 3 ventricle is 9-10 mm. By a method of IFA in a diagnostic range registered Ig G of low avidity against CMV. .

What is the dose of aciclovir in medical treatment of generalized CMV? :

A. 1-2 mg / kg / per day
B. 50 mg / kg / per day
C. 0,5 mg / kg / per day
D. 30 mg / kg / per day
E. 10 mg / kg / per day

16. In child of 21 day of life established generalized CMV infection with dominating injuries of CNS as a syndrome of liquor hypertension, symptomatic trombocytopenia and the fetal hepatitis.What is the group of preparations used for basic therapy?

A. vitamins
B. anabolic steroids
C. antibacterial preparations
D. antiiviral preparations
E. glucocorticoids and cytostatic

17. . In child of 3 weeks of life established generalized CMV infection with dominating injuries of CNS as a syndrome of liquor hypertension, fetal hepatitis, oligotrophy of 2 degree. Registered the state of immunodeficiency What preparation must be prescribed to child as a immunomodulation?.

A. Zovirax
B. Cimeven
C. Valtrex
D. Thimalin
E. Foscarnet

18. Child, 4 day of life. Was born with weight 2900 g, length 50cm.Gestational age is 40 weeks. For the third day of life there was an unitary vomiting with admixtures of

blood. in a hemogram a prothrombin time is 18 sec., prothrombin ratio – 60 %, the beginning of coagulation is 2 min., calcium-clotting time of plasma is 120 sec. fibrinogenum 4g/l, trombocytes $160x10^{9.}$/ This condition is typically for:

, A. Disseminated intravascular coagulation in the phase of hypercoagulation
B. Hemorrhagic disease
C. Physiological
D. Disseminated intravascular coagulation in the phase of hypocoagulation. .
E.Intrauterine infection.

19. Child,10 day of life, was born worn after 2 delivery, with weight 2600 g, length 51 cm, after 5 pregnancy., proceeded with anemia In 7 month of pregnancy in mother the marker of hepatitis B virus was detected. Up to the end of the first day of life in child the fever was marked To the 21 day of life jaundice has appear. From the 7 day of life decreasing of ALT admitted. Skin is icteric. Cardiac tones are muffled, moderate tachicardia. In lungs puerile respiration. Wheezes are not present.. Stomach is soft. Hepatoslenomagaly. Stool is acholic..Urine is dark..
What testifies for intrauterine infection?

A appearing of Ig M and decreasing of Ig G concentrations
B. decreasing of Ig M concentration
C. decreasing of Ig G concentration
D. increasing of Ig M concentrations
E. .appear of Ig A and increasing of Ig M concentration.

20. Child 21 day of life, was born after 38-39 week of gestation, after2 delivery, with weight 2480 g, length 51 cm.. In 7 month of pregnancy in mother the marker of hepatitis B virus was detected. Up to the end of the first day of life in child the jaundice was marked with gradually increasing intensity. After 7 day the increasing of hepatospecific enzymes admitted which is kept till now.. Cardiac tones are muffled, moderate tachicardia. Hepatoslenomagaly
What are the late complications can be observed in this child?

A. Cirrhosis of a liver
B. Diabetes mellitus
C. Leucosis
D. Frequent respiratory infection
E. Elastofibrosis.

Answers:

1- E, 2 - A, 3 - D, 4 - Д, 5 - A, 6 - C, 7 - E, 8 -B, 9 - A, 10 -C, 11 - C, 12 – B, 13 – E, 14 – E, 15 –A, 16 – A, 17 – D, 18 – D, 19 – D, 20 – E.

VII. Materials of the medical support for the students independent prepapation: a reference chart for organization of students independent work with educational literature.

Tasks	Instructions
To study the etilogy and pathogenesis of intranatal infections	To enumerate basic etiologic factors of intranatal infections
To study the pathogenesis of intranatal infections dependent of the agent.	To select the key links of pathogenesis in intrauterine infections.
To study clinical signs of CMV, toxoplasmosis, HSV, herpes, rubella, clamidial, micoplasmial infectons, congenital syphilis.	To detect the symptoms, to group it in syndromes that allows to establish probable diagnosis of intrauterine infection.
To study diagnostic criteria of intrauterine infections.	To compose the structural scheme of disease.
To study the additional methods of research (laboratory, instrumental)	To work out a plan of patient investigation.
To study the changes in additional investigational methods are pathognomonic for lintranatal infections.	To enumerate the basic diagnostic criteria of intrauterine infections. according to the data of additional investigational methods.
To conduct differential diagnostics, to establish a concluding diagnosis	To substantiate the basic components of diagnosis in accordance to modern classification, and to conduct a differential diagnosis.
To prescribe individual complex treatment for patients with intrauterine infections.	To make the prescribing chart specifying the regimen, diet, medicinal treatment, taking into account the age, severity of patient state, stage of disease, presence of complications and concomitant diseases.

Literature:

Main literature:

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3.Майданник В.Г. Педиатрия. Учебник (2-е издание, испр. и доп.) - Харьков: Фолио, 2002. - 1125 с.

4.Шабалов Н.П. Детские болезни. Учебник. -Питер-Ком, С-Пб., 2002. - 1080 с.

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2..Майданник В.Г., Майданник И.В. Справочник современных лекарственных средств. - М.: АСТ; Харьков: Фолио, 2005. - 1024 с.

3. Накази МОЗ України «Про удосконалення амбулаторно-поліклінічної допомоги дітям в Україні», «Про удосконалення організації медичної допомоги дітям підліткового віку», та по протоколах за спеціальностями «педіатрія» та ін. МОЗ України. - Київ, 2005. - 414 с

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5.Ситуаційні завдання з педіатрії /За ред. чл.-кор. АМН України, проф. В.Г. Майданника. - К., 2006. - 204 с.

TEME: BACTERIAL INFECTIONS IN NEWBORN INFANTS.

Classification of bacterial infections in newborn Etiology, pathogenesis, clinical presentation, diagnostics, differential diagnostics, treatment, prophylaxis of inflammatory disease of skin and subcutaneous connective tissue, inflammatory disease of umbilical cord, umbilical wound and omphalic vessels in newborn infants. Neonatal sepsis: classification, etiology, pathogenesis, clinical presentation, diagnostics, differential diagnostics, treatment, prophylaxis, prognosis.

The amount of studying hours – 4 academic hours

I. Actuality of the theme.

Neonatal sepsis, sepsis neonatorum, and neonatal septicemia are terms that have been used to describe the systemic response to infection in the newborn infant. There is little agreement on the proper use of the term, i.e., whether it should be restricted to bacterial infections, positive blood cultures, or severity of illness. Currently, there is considerable discussion of the appropriate definition of sepsis in the critical care literature. The incidence of neonatal sepsis varies according to definition from 1{endash}–4/1,000 live births in developed countries with considerable fluctuation over time and geographic location. Hospital-to-hospital variability in incidence may be related to rates of prematurity, prenatal care, conduct of labor, and environmental conditions in nurseries. Attack rates of neonatal sepsis increase significantly in low-birthweight infants and in the presence of maternal (obstetric) risk factors or signs of chorioamnionitis such as prolonged rupture of membranes (>18 hr), maternal intrapartum fever (>37.5є{degree} C), maternal leukocytosis (>18,000), uterine tenderness, and fetal tachycardia (>180 beats/min).

Host risk factors include male sex, developmental or congenital immune defects, galactosemia (Escherichia coli), administration of intramuscular iron (E. coli), congenital anomalies (urinary tract, asplenia, myelomeningocele, sinus tracts), omphalitis, and twinning (especially the second twin of an infected twin). Prematurity is a risk factor for both early-onset and late-onset sepsis. That is why the early diagnosis is very important.

II. Classes (pointing of planned mastering level)

1. A student must know (to familiarize): α1

- the place of bacterial infections in the structure of diseases of neonatal period;
- statistical information in relation to morbidity, frequencies of complications, lethality, the nearest and remote prognosis;

2. A student must know: α2

- risc factors of begigning and pathogenesis of septic diseases in newborn

infants;

- clinical classification of inflammatory diseases of newborn infant;
- classic clinical manifestation of septic diseases of newborn infant;
- lincs of perinatal sepsis;
- features of septical course in full-term and premature infant;
- classic clinical manifestation of septical shock;
- laboratory and instrumental diagnosis of inflammatory diseases in newborn infants;
- treatment principles of inflammatory diseases in newborn infants;
- main measures of inflammatory diseases prophylaxis in newborn;
- organisation of dispensary observation at newborn infants, who was ill with sepsis.

3. A student must master: α3

Skills:

- Examination of newborn infant with septic diseases and revealing the main symptoms and syndromes.
- To evaluate charater of rush on newborns skin and mucous cover;
- To form the scheme of diagnostical search;
- To formulate and substantiate the initial diagnosis;
- Determination of laboratory and instrumental plan of a patient's examination (according to diagnostics standards);
- To give the first aid in DIC-syndrome.

4. Abilities:

-evaluating condition of newborn's health;

-collection of complaints and anamnesis of disease;

-interpreting results of laboratory and instrumental tests;

-to complete treatment plan in inflammatory disease according to standards taking into account the stage of disease;

-to render the first aid in extreme situations and exigent states;

-to prescribe recipes according the treatment.

III. Interdisciplinary integartion:

Subject	To know	To be able
1. Previous (providing)		
Histology	Histological features of newborns skin	
Biochemistry	Normal and abnormal biochemical indexes in children	To evaluate results of biochemical indices in children
Microbiology and	Characteristic of the main causal organism in septic	To evaluate results of microbiological and serological

epidemiology	infection	tests
Pathologic physiology	Key links of pathogenesis of inflammatory, its features in newborn infants, pathogenesis of DIC-syndrome	

Pharmacology	Pharmacokinetics and pharmacodynamics, the side effects of preparations	To prescribe age-dependent treatment of patient, tacing into account individual features and period of disease, to establish the individual regimen of taking the preparations and their dosage. To precribe recipes.
Propedeutical pediatrics.	Complaints, basicstages and methods of patient's clinical examination.	To collect complaints, anamnesis vitae et morbi, to findout the basicrisk factors of septic diseases, to conduct patient's examination.
Faculty pediatrics	Principles of dispensary observation at infants with inflammatory diseases of skin	To complete plan of rehabilitational treatment and dispensary observation at infants
2. Followings		
Hospital pediatrics.	Clinical signs of septic complications in newborn and treatment tactics.	To reveal the clinical signs of septic complications, to conduct differential diagnosis, to be able to evaluate efficiency of prescribed therapy
3. Interdiscipline integration		
Intranatal infections	Clinical manifestation of septic diseases in infants, plan of treatment	-to establish specific clinical signs of intranatal infections and to conduct differential diagnostic with signs of septic diseases
Coagulopathy	Clinical manifestation of coagulopathy in infants	To establish specific clinical signs of coagulopathy and to conduct differential diagnosis with septic diseases
Jaundice of the newborn	Clinical manifestation of jaundice of the newborn	To establish specific clinical signs of jaundice of the newborn and to conduct differential diagnosis with septic diseases
Birth injury	Clinical manifestation of birth injury	To establish specific clinical signs of birth injury and to conduct differential diagnosis with septic diseases

IV. Contents of the lessons theme can be represented:

Neonatal sepsis, sepsis neonatorum, and neonatal septicemia are terms that have been used to describe the systemic response to infection in the newborn infant. There is little agreement on the proper use of the term, i.e., whether it should be restricted to bacterial infections, positive blood cultures, or severity of illness. Currently, there is considerable discussion of the appropriate definition of sepsis in the critical care literature. This is a result of an explosion of information on the pathogenesis of sepsis and the availability of new potentially therapeutic agents, e.g., monoclonal antibodies to endotoxin and tumor necrosis factor (TNF), which can alter the lethal outcome of sepsis in animal experiments. To evaluate and utilize these new therapeutic modalities appropriately, "sepsis" requires a more rigorous definition. In adults, the term systemic inflammatory response syndrome (SIRS) is used to describe a clinical syndrome characterized by two or more of the following: (1) fever or hypothermia, (2) tachycardia, (3) tachypnea, and (4) abnormal white blood cells (WBC) or increase in immature forms. SIRS may be a result of trauma, hemorrhagic shock, other causes of ischemia, pancreatitis, or immunologic injury. When it is a result of infection, it is termed sepsis. These criteria have not been established in infants and children and are unlikely to be applicable to the newborn infant. Nevertheless, the concept of sepsis as a syndrome caused by metabolic and hemodynamic consequences of infection is logical and important. In the future, the definition of sepsis in the newborn infant and child will become more precise. At this time, criteria for neonatal sepsis should include documentation of infection in a newborn infant with a serious systemic illness in which noninfectious explanations for the abnormal pathophysiologic state are excluded or unlikely. Serious systemic illness in the newborn infant may be caused by perinatal asphyxia, respiratory tract, cardiac, metabolic, neurologic, or hematologic diseases. Sepsis occurs in a small proportion of all neonatal infections. Bacteria and Candida are the usual etiologic agents, but viruses and, rarely, protozoa may also cause sepsis. Blood cultures may be negative, increasing the difficulty in establishing infection etiologically. Finally, infection with or without sepsis may be present concurrently with a noninfectious illness in the newborn infant, child, or adult.

EPIDEMIOLOGY. The incidence of neonatal sepsis varies according to definition from 1{endash}–4/1,000 live births in developed countries with considerable fluctuation over time and geographic location. Hospital-to-hospital variability in incidence may be related to rates of prematurity, prenatal care, conduct of labor, and environmental conditions in nurseries. Attack rates of neonatal sepsis increase significantly in low-birthweight infants and in the presence of maternal (obstetric) risk factors or signs of chorioamnionitis such as prolonged rupture of membranes (>18 hr), maternal intrapartum fever (>37.5є{degree} C), maternal leukocytosis (>18,000), uterine tenderness, and fetal tachycardia (>180 beats/min).

Host risk factors include male sex, developmental or congenital immune defects, galactosemia (Escherichia coli), administration of intramuscular iron (E. coli), congenital anomalies (urinary tract, asplenia, myelomeningocele, sinus tracts), omphalitis, and twinning (especially the second twin of an infected twin). Prematurity is a risk factor for both early-onset and late-onset sepsis.

ETIOLOGY. Bacteria, viruses, fungi, and rarely protozoa may produce neonatal sepsis. The most common causes of early-onset sepsis are group B streptococci (GBS) and enteric bacteria acquired from the maternal genital tract. Late-onset sepsis may be due to GBS, herpes simplex virus (HSV), enteroviruses, and E. coli K1. In very low-birthweight infants, Candida and coagulase-negative staphylococci (CONS) are the most common pathogens in late-onset sepsis.

PATHOGENESIS. Rarely, inhalation of infected amniotic fluid may produce pneumonia and sepsis in utero, manifested by fetal distress or neonatal asphyxia. Exposure to pathogens at delivery and in the nursery or community is the mechanism of infection after birth.

The physiologic manifestations of the inflammatory response are mediated by a variety of proinflammatory cytokines, principally TNF, interleukin-1 (IL-1), and IL-6, and by-products of activation of the complement and coagulation systems. Studies in the newborn infant are limited, but it appears that some cytokine production may be diminished, which is consistent with an impaired inflammatory response. However, elevated levels of IL-6, TNF, and platelet-activating factor have been reported in newborn infants with neonatal sepsis and necrotizing enterocolitis (NEC). IL-6 appears to be the cytokine most often elevated in neonatal sepsis.

CLINICAL MANIFESTATIONS. Infection is considered in the differential diagnosis of many physical signs in the newborn infant. All of these may have noninfectious explanations. When there is multisystem involvement or when the cardiorespiratory signs are consistent with severe illness, sepsis should be considered. The initial presentation may be limited to only one system, such as apnea, tachypnea with retractions, or tachycardia, but a full clinical and laboratory evaluation will usually reveal other abnormalities. Infants with suspected sepsis should be evaluated for multiorgan system disease. Metabolic acidosis is common. Hypoxemia and carbon dioxide retention may be associated with adult and congenital respiratory distress syndrome (RDS) or pneumonia.

Many newborn infants with infections do not have serious systemic physiologic abnormalities. Many infants with pneumonia and infants with stage II NEC do not have sepsis. In contrast, stage III NEC is usually accompanied by the systemic manifestations of sepsis, and urinary tract infections (UTIs) secondary to obstructive uropathy may have hematologic and hepatic abnormalities consistent with sepsis. Each infant should be re-evaluated over time to determine whether physiologic

changes secondary to infection have reached a moderate to severe level of severity that is consistent with sepsis.

Late manifestations of sepsis include signs of cerebral edema and/or thromboses, respiratory failure as a result of acquired respiratory distress syndrome (ARDS), pulmonary hypertension, cardiac failure, renal failure, hepatocellular disease with hyperbilirubinemia and elevated enzymes, prolonged prothrombin time (PT) and partial thromboplastin time (PTT), septic shock, adrenal hemorrhage with adrenal insufficiency, bone marrow failure (thrombocytopenia, neutropenia, anemia), and disseminated intravascular coagulation (DIC).

DIAGNOSIS. Documentation of infection is the first diagnostic criterion that must be met. It is important to note that infants with bacterial sepsis may have negative blood cultures so that other approaches to identification of infection should be taken. Tests to demonstrate an inflammatory response include erythrocyte sedimentation rate, C-reactive protein, haptoglobin, fibrinogen, nitroblue tetrazolium dye, and leukocyte alkaline phosphatase. In general, these tests have limited sensitivity and are not helpful. Only the total WBC count with differential and the ratio of immature to total neutrophils provide immediately predictive information compared with age standards. Neutropenia is more common than neutrophilia in severe neonatal sepsis, but it also occurs in association with maternal hypertension, neonatal sensitization, periventricular hemorrhage, seizures, surgery, and possibly hemolysis. An immature neutrophil-total neutrophil ratio of 0.16 or greater suggests bacterial infection.

Criteria for the magnitude of physiologic change in newborn infants with sepsis are not currently defined but should be consistent with the systemic effect of endogenous mediators on one or more organ systems. For example, the effect of sepsis from pneumonia on respiratory function should exceed the local damage in the lung. Thus, a workup for sepsis should include the laboratory studies.

TREATMENT. Treatment of neonatal sepsis may be divided into antimicrobial therapy for the suspected or known pathogen and supportive care. Fluids, electrolytes, and glucose should be monitored carefully with correction of hypovolemia, hyponatremia, hypocalcemia, and hypoglycemia and limitation of fluids if there is inappropriate antidiuretic hormone secretion. Shock, hypoxia, and metabolic acidosis should be identified and managed with inotropic agents, fluid resuscitation, and mechanical ventilation. Adequate oxygenation of tissues should be maintained because ventilatory support is frequently necessary for respiratory failure caused by congenital pneumonia, persistent fetal circulation, or adult RDS (shock lung). Refractory hypoxia and shock may require extracorporeal membrane oxygenation, which has reduced mortality rates in full-term infants with septic shock and persistent fetal circulation. Hyperbilirubinemia should be monitored and treated

with exchange transfusion because the risk of kernicterus increases in the presence of sepsis and meningitis. Parenteral nutrition should be considered for infants who cannot sustain enteral feedings.

DIC may complicate neonatal septicemia. Platelet counts, hemoglobin, PT, PTT, and fibrin split products should be monitored. DIC may be treated by management of the primary sepsis, but if bleeding occurs, DIC may be treated with fresh frozen plasma, platelet transfusions, or whole blood.

Because neutrophil storage pool depletion has been associated with a poor prognosis, a number of clinical trials of polymorphonuclear replacement therapy have been conducted, with variable results. Sepsis that is unresponsive to antibiotics with persistent neutropenia may be an indication for granulocyte transfusion. The use of granulocyte-macrophage colony{endash}–stimulating factor (GM-CSF) is under investigation. Treatment with intravenous immunoglobulins (IVIG) containing specific antibodies is currently under clinical investigation. Currently, granulocyte transfusion, granulocyte colony{endash}–stimulating factor (G-CSF), and IVIG are experimental therapies of undetermined value.

It is important to remember that nonbacterial infectious agents can produce the syndrome of neonatal sepsis. Herpes simplex infection requires specific treatment, as does systemic candidal infection. Such agents should be considered in all patients who have negative cultures but whose condition continues to deteriorate despite supportive care and the use of broad-spectrum antibiotics.

Meningitis in the newborn infant may be caused by bacteria, viruses, fungi, or protozoa. The incidence is 0.2{endash}–0.4/1,000 live births and is higher in preterm infants. Meningitis may be associated with sepsis or present as a focal infection. Currently, meningitis occurs in less than 20% of newborn infants with early-onset invasive bacterial infections.

ETIOLOGY. The most common bacterial causes of neonatal meningitis are GBS, E. coli K1, and Listeria. Other streptococci, nontypeable Haemophilus influenzae, both coagulase-positive and coagulase-negative staphylococci, Klebsiella, Enterobacter, Pseudomonas, Treponema pallidum, and Mycobacterium tuberculosis may also produce meningitis. Citrobacter diversus is an important cause of brain abscess. Additional pathogens include Mycoplasma hominis, Ureaplasma urealyticum, Candida albicans and other fungi, Toxoplasma gondii, and viruses (enteroviruses, HSV type 2 more often than type 1, rubella, cytomegalovirus [CMV], human immunodeficiency virus [HIV]).

PATHOLOGY AND PATHOGENESIS. Most cases of meningitis result from hematogenous dissemination. Less often, it results from contiguous spread as a result of contamination of neural tube defects, congenital sinus tracts, or penetrating wounds from fetal scalp sampling or internal fetal electrocardiographic monitors.

Cerebritis and septic infarcts are common in bacterial meningitis. Abscess formation, ventriculitis, hydrocephalus, and subdural effusions occur more often in newborn infants than in older children.

CLINICAL MANIFESTATIONS. The initial signs and symptoms may be indistinguishable from those of other infectious and noninfectious diseases of the newborn infant. Neurologic signs may or may not be present. Neurologic manifestations include lethargy (50{endash}–90%); bulging or full fontanel (20{endash}–30%); focal, generalized, or subtle seizures (30{endash}–50%); nuchal rigidity (10{endash}–20%); and, rarely at initial presentation, signs of increased intracranial pressure.

DIAGNOSIS. The diagnosis is confirmed by examination of the cerebrospinal fluid (CSF) and identification of a bacterium, virus, or fungus by culture or antigen detection. Blood culture and complete blood count are part of the initial evaluation because 70{endash}–85% of neonates with meningitis have a positive blood culture. The incidence of positive blood cultures is highest with early-onset sepsis and meningitis.

Lumbar puncture may be deferred in a severely ill infant if the lumbar puncture would further compromise respiratory status. In these situations, blood culture and antigen detection assays should be performed and treatment initiated for presumed meningitis until a lumbar puncture can be safely performed.

Normal, uninfected neonates frequently have elevated CSF protein levels (term 90 mg/dL [range 20{endash}–170], preterm 115 mg/dL [range 65{endash}–150]), reduced glucose (term 52 mg/dL [range 34{endash}–119], preterm 50 mg/dL [range 24{endash}–63]), reduced CSF-to-blood glucose ratios (51% term, 75% preterm), and elevated CSF leukocyte counts (term 7/m{mu}L [range 0{endash}–32], preterm 8/m{mu}L [range 0{endash}–29]) with 57{endash}–61% neutrophils. In addition, preterm infants may develop elevated CSF protein levels and leukocytes and hypoglycorrhachia following intraventricular hemorrhage. Many nonpyogenic congenital infections also can produce asymptomatic alterations of CSF protein and leukocytes (toxoplasmosis, CMV, syphilis, HIV).

The Gram stain of CSF is positive in as many as 85% of patients with GBS meningitis and 61% of those with gram-negative meningitis. The leukocyte count is often elevated with a predominance of neutrophils (>70{endash}–90%); the number is often greater than 1,000 in patients with gram-negative meningitis but may be less than 100 in those with GBS disease. Microorganisms are recovered from most patients who have not been pretreated with antibiotics. Bacteria have also been isolated from CSF that did not have an abnormal number of cells (<25) or an abnormal protein level (<200 mg/dL). This is more typical of GBS meningitis but emphasizes the importance of performing a culture and Gram stain on all CSF

specimens. Culture-negative meningitis should suggest antibiotic pretreatment, infection with M. hominis, U. urealyticum, or Bacteroides fragilis, a brain abscess, enterovirus infection, or HSV.

Head ultrasonography or computed tomographic (CT) scan with contrast enhancement may be helpful in diagnosing ventriculitis and brain abscess. Neonatal HSV meningitis may be confirmed by isolation of the virus from the CSF or other site (skin, eye, mouth) or by HSV antigen or DNA detection.

TREATMENT. Presumptive antimicrobial therapy of bacterial meningitis should include ampicillin and cefotaxime or ampicillin and gentamicin unless staphylococci are likely, which would be an indication for vancomycin. Susceptibility testing of gram-negative enteric organisms is important because resistance to cephalosporins and aminoglycosides occurs. Most aminoglycosides administered by parenteral routes do not achieve sufficiently high antibiotic levels in the lumbar CSF or ventricles to inhibit growth of gram-negative bacilli. Although intraventricular administration of aminoglycosides has been proposed as therapy for gram-negative meningitis and ventriculitis, many authorities recommend a combination of ampicillin and a third-generation cephalosporin for the treatment of neonatal gram-negative meningitis. Cephalosporins should not be used as empiric monotherapy because Listeria monocytogenes is resistant to all cephalosporins.

Meningitis from GBS usually responds within 24{endash}–48 hr and should be treated for 14{endash}–21 days. Gram-negative bacilli may continue to grow from repeated CSF samples for 72{endash}–96 hr after therapy despite the use of appropriate antibiotics. Treatment of gram-negative meningitis should be continued for 21 days or for at least 14 days after sterilization of the CSF, whichever is longer. Meningitis from Pseudomonas aeruginosa infection should be treated with ceftazidime. Metronidazole is the treatment of choice for infection caused by B. fragilis. Prolonged antibiotic administration, with or without needle drainage for treatment and diagnosis, is indicated for neonatal cerebral abscesses. CT scans are indicated for patients with suspected ventriculitis, hydrocephalus, or cerebral abscess (initial and follow-up assessments) and for those with an unexpectedly complicated course (prolonged coma, focal neurologic deficits, persistent or recurrent fever). Neonatal herpes meningoencephalitis should be treated with acyclovir. Although there are no definitive studies, some clinicians use IVIG to treat enteroviral meningoencephalitis.

Supportive care includes management of sepsis, if present; anticonvulsants for seizures; and management of cerebral edema, inappropriate antidiuretic hormone secretion, and hydrocephalus. Although monitoring of gentamicin and vancomycin drug levels is currently recommended, modification of these guidelines is likely.

Bell WE, McGuinness GA: Suppurative central nervous system infections in the neonate. Semin GBS is a major cause of severe systemic and focal infections in the newborn. Since its emergence as a dominant pathogen in the 1970s, extensive research has provided information on epidemiology, immunity, and prevention, resulting in a decline in incidence and mortality rates.

ETIOLOGY. Streptococcus agalactiae is the species of streptococci belonging to Lancefield group B. It is a facultative, encapsulated gram-positive diplococcus that produces a narrow zone of b{beta}-hemolysis on blood agar. Occasional strains are nonhemolytic. Most strains are resistant to bacitracin and show a positive CAMP test. Strains of GBS are classified serologically by capsular polysaccharide and protein antigens and include types Ia, Ib, Ia/c, II, III, and IV. There is also a provisional type V. Early-onset disease may be due to any serotype, whereas late-onset disease is due to type III in 90% of cases. Types IV and V and nontypeable strains are less often associated with neonatal disease. GBS produce extracellular substances, which include hemolysin, CAMP factor, hippuricase, nucleases, protease, neuraminidase, and lipoteichoic acid. The latter two factors may be associated with increased virulence of pathogenic GBS.

EPIDEMIOLOGY. The organism is a common inhabitant of the maternal genitourinary and gastrointestinal tracts and colonizes approximately 20% (range 4{endash}–40%) of pregnant women. The highest recovery rates for GBS are reported from studies that used selective media, multiple sample sites, and sequential samples over time. Pregnant women are usually asymptomatic but may have UTIs, chorioamnionitis, or endometritis. Infants born of women who are heavily colonized are more likely to become colonized. Overall, colonization at birth is noted in 40{endash}–70% of infants born to colonized mothers. Approximately 6% of infants born to culture-negative mothers become colonized with GBS from other sources. Colonization rates are influenced by maternal factors, including lower socioeconomic status, teenage status, and sexual activity; choice of media (selective more than nonselective, broth more than agar); and the number and location of body sites sampled in the mother (cervix, vaginal, urine, rectum), newborn infant (external auditory canal > nares, umbilicus, anorectum), or 48-hr-old neonate (throat, anorectum, umbilicus). Maternal colonization may be chronic, transient, or intermittent. Women colonized in the second trimester may have negative findings at term (30%), and women with negative results in the second trimester may become colonized at term (8%). Concordance of prenatal and delivery cultures is related to the interval between prenatal culture and delivery. Nearly 50% of sexual partners of genitally colonized women have positive cultures for GBS, which is evidence for sexual transmission.

GBS is acquired by newborn infants after vertical transmission, e.g., ascending infection through ruptured amniotic membranes or contamination after passage through the colonized birth canal. Infection also occurs in the absence of ruptured membranes. Identical serotypes are found in mother and newborn. The rate of vertical transmission is approximately 50% and varies with the inoculum size. However, lightly colonized women may deliver infected infants. There is a direct correlation between duration of membrane rupture and incidence of early-onset GBS infection. Neonates may also acquire GBS after horizontal transmission in the nursery or from adults other than their mothers. Infant-to-infant and adult-to-infant spread has produced colonization, late-onset GBS disease, and, rarely, epidemics of GBS in nurseries.

Early-onset GBS disease occurs within the first 5 days of life. The incidence is 0.7{endash}–3.7/1,000 live births or 0.5{endash}–2% of newborn infants born to colonized mothers. With increased use of maternal chemoprophylaxis, these rates are diminishing. Many infants (50%) with early-onset GBS are symptomatic at birth, indicating an intrauterine infection. The highest attack rate of early-onset GBS disease occurs among very low-birthweight infants; the incidence is more than 8/1,000 in infants weighing less than 1,500 g and less than 1/1,000 in infants weighing more than 2,500 g. Nonetheless, full-term infants account for approximately 50% of cases. The rate of neonatal infection is also influenced by prolonged rupture of the amniotic membranes, prolonged labor, and most importantly by maternal endometritis-chorioamnionitis (fever, tender uterus, leukocytosis). Late-onset GBS disease occurs after the 1st wk of life and is due to serotypes acquired from maternal and nonmaternal sites (nursery personnel, community), is not associated with obstetric risk factors, has an incidence of 0.5{endash}–1.8/1,000 live births, and may be seen as late as the 7th mo of life.

The rate of early- and late-onset GBS disease is also related to the degree of colonization at birth. Heavily colonized infants are 12 times as likely to have early-onset disease as lightly colonized infants. Case fatality rates for early- and late-onset disease have fallen below 20%.

PATHOLOGY. Intrauterine death may occur at any time during gestation. In intrauterine and early-onset infections, pulmonary inflammation is characterized by interstitial and/or alveolar neutrophil exudates, vascular congestion, edema, and varying degrees of pulmonary hemorrhage. Premature and full-term infants who die of early-onset sepsis frequently have hyaline membranes. This may be a result of surfactant deficiency in premature infants and ARDS in full-term, and perhaps premature, infants.

The inflammatory response in early-onset disease is variable, in part because of the duration of illness and the ability of the infant to mount an inflammatory

response. In early-onset meningitis, most infants have little evidence of inflammation. Bacteria are prominent, and there is thrombosis, hemorrhage, and perivascular inflammation. Periventricular leukomalacia may be found in infants who survive GBS septic shock.

Although late-onset sepsis may be rapid, with pathologic features similar to early-onset disease, the inflammatory response is usually similar to that in older infants who die of pyogenic infections. There is a substantial inflammatory response, and abscess formation is common.

PATHOGENESIS. Early-onset GBS disease is associated with immature host defense mechanisms among low-birthweight infants and exposure to heavily colonized maternal genitourinary tract sites (ascending vertical transmission through ruptured amniotic membranes). GBS may cause local inflammation of intact membranes, causing subsequent weakness and rupture of amniotic fluid membranes, thus initiating premature labor. The attack rate is 0.7/1,000 with membrane rupture occurring at less than 19 hr and 18.3/1,000 with rupture occurring at 30 hr or more. Fetal infection may also develop through intact membranes. Amniotic fluid contains low levels of type-specific GBS antibodies, complement, phagocytic cells, and other nonspecific defense components and is a good culture medium for GBS. Rarely, fetal aspiration of infected amniotic fluid may initiate fetal and subsequent neonatal pneumonia, bacteremia, and septic shock.

Opsonophagocytic defects present in neonatal phagocytes are further compromised in the infant with GBS infection, owing to a deficiency of maternally derived type-specific antibody. Serum levels of greater than 1 to 2 m{mu}g/mL of IgG antibody to type-specific capsular polysaccharides of GBS are associated with effective opsonophagocytosis and killing of GBS and protection in animal models of infection. Only 10{endash}–20% of adult women have antibody levels of this magnitude. In premature infants, transplacental passage of antibody is impaired. At 28 and 32 wk of gestation, levels of anticapsular GBS antibodies are 33% and 50% of maternal levels, respectively. Although newborns with early-onset GBS infection are deficient in type-specific antibody, other colonized infants with similar levels remain well. Thus, other factors mediating virulence and host defense mechanisms affect pathogenesis.

Early-onset GBS disease is usually characterized by pneumonia with bacteremia and complicated by pulmonary hypertension. The latter may be attenuated by inhibition of thromboxane synthesis, suggesting a role for the activity of the pulmonary cyclo-oxygenase pathway in the pathogenesis of GBS-associated pulmonary hypertension. The development of pulmonary hypertension in full-term babies is apparently related to the ARDS.

The pathophysiology of late-onset GBS may be related to an initial colonization, alterations of the mucosal barrier by a prior viral respiratory tract infection, elaboration of large amounts of GBS type III capsular polysaccharide, and possibly reduced amounts of maternal antibody. The pathophysiology of late-onset GBS osteomyelitis is atypical and may be due to an early-onset asymptomatic bacteremia, inoculation into a traumatized bone, and subsequent late onset of a single site of osteomyelitis. These infants may have few systemic symptoms. The presence of type-specific IgG antibody to GBS type III suggests that the infant produced antibodies and restricted the infection to a metaphyseal location. Acquisition of type-specific IgM antibodies may explain the age-specific incidence of GBS disease.

CLINICAL MANIFESTATIONS The spectrum of early-onset infections ranges from asymptomatic bacteremia to septic shock. Early-onset disease may present at birth, and most infants become ill within 6 hr of age. In utero infection may result in fetal asphyxia, coma, or shock. Respiratory symptoms are prominent and include cyanosis; apnea; tachypnea; grunting; flaring; retractions; and roentgenographic findings consisting of a reticulogranular pattern (50%), patchy pneumonic infiltrates (30%), and, less commonly, pleural effusions, pulmonary edema, cardiomegaly, and increased pulmonary vascular markings. Persistent fetal circulation or ARDS may develop. Sepsis without localization is noted in 30{endash}–40% of infants. Apnea or hypotension may be initial findings.

Meningitis occurs in less than 10% of infants with earlyonset infection. Patients with meningeal involvement may have seizures, lethargy, coma, and a bulging fontanel, but meningitis may be present without signs of meningeal involvement. These patients cannot be identified by clinical findings; therefore, a lumbar puncture is indicated in every patient with suspected early- or late-onset neonatal sepsis. Late-onset GBS infection is manifest as meningitis in 60% of patients and is predominantly caused by the type III serotype. Additional manifestations of late-onset GBS (also type III). Manifestations of late-onset GBS meningitis are indistinguishable from other causes of neonatal meningitis

DIAGNOSIS. The differential diagnosis of early-onset GBS infection includes hyaline membrane disease; amniotic fluid aspiration syndrome; sepsis from other vertically transmitted ascending infections (E. coli, HSV); and those metabolic (hypoglycemia, hyperammonemia), anatomic (congenital heart disease, diaphragmmatic hernia), or other conditions that produce manifestations of sepsis. The probability of infection increases with the presence of risk factors and colonization in the mother if untreated during labor. Diagnosis of GBS infection is made in the laboratory.

LABORATORY. The diagnosis is established by isolation and identification of the organism from normally sterile sites (blood, CSF, rarely urine, pleural fluid, abscess material, cellulitis aspirates, bone and joint aspirates). The demonstration of

gram-positive organisms in pairs or chains in buffy coat or other normally sterile fluids is evidence of infection, which is most commonly due to GBS. Gram-positive cocci in gastric or tracheal aspirates suggest infection but may represent colonization. Isolation of GBS from skin or mucous membranes indicates colonization and not invasive infection.

Antigen detection of GBS is possible with latex particle agglutination, but the test is less sensitive than cultures and is most useful when there has been prior antibiotic therapy of mother or infant and in abacteremic sepsis. Urine samples may need to be pretreated to remove cross-reacting ABO antigens. Urine samples collected by bag may yield false-positive results in healthy but colonized neonates owing to contamination by GBS organisms, which colonize the perineum or rectum. Thus, a positive urine latex test result is suggestive but not diagnostic of systemic infection. The test should not be performed on asymptomatic newborn infants; the amount of antigen needed for a positive test is associated with signs of infection. Rapid antigen detection tests have been used for screening women at the time of delivery. A recent study showed that only 40% of colonized women would be detected.

CSF should be examined in all patients suspected of having meningitis or sepsis. Other findings may include an increased band count, increased ratio of immature to total white blood cells (> 0.20), neutropenia, thrombocytopenia, leukocytosis, elevated serum C-reactive protein level, and pneumonia or osteomyelitis on roentgenogram. However, before isolation of GBS from blood or CSF, none of these nonspecific clinical manifestations or laboratory tests is diagnostic for GBS and none distinguishes GBS from infection caused by other pathogens.

COMPLICATIONS. The mortality rate for early-onset GBS disease ranges from 10 to 20%; the mortality rate is highest in very low-birthweight infants and in those with septic shock or a delay in instituting antimicrobial therapy. Because of increased awareness, earlier diagnosis and treatment, and the increased use of intrapartum chemoprophylaxis by obstetricians, the incidence and mortality rates from GBS early-onset disease appear to have declined. The mortality rate from GBS-associated persistent fetal circulation has dramatically decreased owing to the use of extracorporeal membrane oxygenation. Neurologic sequelae after meningitis are severe in 20{endash}–30% of cases and include mental retardation, quadriplegia, repeated uncontrollable seizures, hypothalamic dysfunction, cortical blindness, hydrocephalus, bilateral deafness, and hemiplegia. Additional neurodevelopmental sequelae are noted in 15{endash}–25% of patients and include mild mental retardation, mild cortical atrophy, a stable seizure disorder, delay in receptive and expressive speech and language development, and other learning disabilities.

Sequelae of focal infections (arthritis, osteomyelitis) are usually localized and are not as significant as those associated with sepsis and meningitis.

PREVENTION. The Committee on Infectious Diseases of the American Academy of Pediatrics has recommended selective chemoprophylaxis of high-risk, colonized pregnant women with premature labor, fever, prolonged rupture of membranes (>12 hr), or suspected chorioamnionitis as an effective method of preventing early-onset neonatal GBS infection. Colonization is determined at 26{endash}–28 wk of gestation. Intrapartum administration of intravenous ampicillin to colonized women with one or more risk factors reduces the need to treat all mothers (only 4{endash}–5% fulfill all the criteria). Intravenous ampicillin (2 g initially and then 1 g every 4 hr) is given immediately to high-risk women at the onset of labor and is repeated until the infant is born. This protocol reduces both the colonization and infection of neonates. However, a single dose of ampicillin may not prevent early-onset infection if there is chorioamnionitis or insufficient time for therapy before delivery. Recent studies indicate that 73% of women delivering infants with early-onset GBS infection fulfill criteria for intrapartum chemoprophylaxis. An alternative approach is to identify high-risk women at the time of labor with rapid antigen detection of vaginal GBS. Rapid tests can identify heavy maternal colonization within 5 hr and thus select the women who are at greatest risk for delivery of infected infants and in need of chemoprophylaxis with intrapartum ampicillin. However, antigen detection is less sensitive than culture. The risk of early-onset GBS disease is low in full-term infants without risk factors. Nonselective intrapartum chemoprophylaxis is not cost effective. Because there is usually a latent period before disease in infants without risk factors, a single injection of penicillin in the delivery room would reduce the likelihood of early-onset disease. Women with no prenatal care may be given ampicillin during labor or screened with a test for antigen. Penicillin therapy may be indicated for the asymptomatic twin of an infected sibling.

In theory, early- and late-onset GBS disease might be prevented by immunoprophylaxis. Because colonized mothers, and thus infants with GBS infection, often lack type-specific IgG antibody, it has been proposed that active immunization of the mother or possibly passive IgG administration to the newborn infant might prevent GBS disease. Sera containing type-specific antibody facilitate opsonophagocytosis against the individual GBS type in the presence of complement and neutrophils. Passive immune therapy would require development of hyperimmune type-specific GBS sera because the currently available commercial preparations of standard IVIG have variable and potentially low levels of GBS IgG antibody. Type-specific active immunization is possible using purified capsular polysaccharides from type Ia, II, or III strains. Pregnant women without demonstrable antibodies to GBS at 30 wk of gestation respond to injection of type III{endash}–

specific polysaccharide with a significant rise in antibody, which is transferred to cord sera and persists for 1{endash}–2 mo in the infant. Nonetheless, the polysaccharide antigen is not sufficiently immunogenic because only 54% of pregnant women demonstrate an immune response, and conjugate vaccines have now been developed for clinical trials.

TREATMENT. GBS are uniformly sensitive to penicillin G, which is the treatment of choice of confirmed GBS infection. Empirical antimicrobial therapy is initiated with a penicillin (usually ampicillin) and an aminoglycoside until GBS have been differentiated from other bacteria. In vitro, a combination of penicillin and gentamicin provides synergistic bactericidal activity against GBS despite resistance of GBS to aminoglycosides. Some authorities recommend continuation of ampicillin plus gentamicin for several days until there is a good clinical response or the CSF becomes sterile.

GBS demonstrate a minimal inhibitory concentration (MIC) (0.01{endash}–0.4 m{mu}g/mL) for penicillin G that is 4- to 10-fold greater than that of group A streptococci. An inoculum effect (higher GBS colonies per milliliter require more penicillin) may have clinical application because CSF may contain as many as 107{endash}–108 colony-forming units per milliliter. Rarely (4{endash}–6%), GBS demonstrate tolerance (minimal bactericidal concentration >16{endash}–32 times the MIC), which may correlate with delayed killing and recurrent infection. The significance of in vitro tolerance among GBS remains speculative.

GBS are also susceptible to vancomycin, semi-synthetic penicillins, cefotaxime, ceftriaxone, and imipenem. These agents are not superior to penicillin or ampicillin and should not be used to treat documented GBS infection. Penicillin should be used in high doses for the treatment of GBS meningitis, i.e., 300,000 units/kg/24 hr of penicillin G or 300 mg/kg/24 hr of ampicillin. These higher than usual doses are recommended because of a higher than usual MIC, high CSF inoculum size, reports of relapse of GBS meningitis in patients treated with 200,000 units/kg/24 hr of penicillin G, and the relative safety of penicillins in the neonate. CSF should be obtained within 48 hr of therapy of documented meningitis to determine whether persistent infection is present (> 90% are sterile within 36 hr), owing to a high inoculum effect or tolerant GBS. If GBS continue to grow from the CSF, some authorities continue giving a combination of penicillin (or ampicillin) and gentamicin (for synergism) for the duration of treatment (2{endash}–3 wk). Failure to document sterile CSF within 48 hr of therapy may also signify subdural empyema, brain abscess, ventriculitis, suppurative dural sinus thrombosis, or an insufficient dose of a bactericidal antibiotic.

Recurrence or relapse is uncommon, but if either occurs, it is seen within 2{endash}–43 days of therapy (mean 16 days). Prior therapy was usually too short

(<10 days for bacteremia, <14 days for meningitis) with too low a dose of antibiotic. Antibiotic treatment may not eliminate GBS colonization from the mucosal surfaces, and prior infection may not produce protective antibody. Reinfection may result from maternal mastitis, and late complications of brain abscess or endocarditis have been reported. Repeat therapy with higher doses of penicillin, for a longer course, is effective therapy for recurrent GBS infection.

Supportive care of GBS infection. Treatment of hypoxia and shock, DIC, seizures, increased intracranial pressure, and inappropriate antidiuretic hormone are discussed elsewhere. Extracorporeal membrane oxygenation may be an effective adjunctive therapy for full-term or large preterm infants with hypoxia who are unresponsive to conventional mechanical ventilation.

Adjunctive therapy with current IVIG has not been efficacious because of low levels of protective antibody. Hyperimmune IVIG or human monoclonal antibodies would overcome this limitation. Although granulocyte transfusion may be beneficial in neutropenic infants with neutrophil storage pool depletion, there are associated risks (viral infection, pulmonary sequestration, graft versus host disease) and logistic problems. The use of GCSF is under study. It is important to remember that antibody, complement, and phagocytes are required for optimal killing.

Escherichia coli.

E. coli continues to be a principal cause of gram-negative bacillary bacteremia and meningitis in the newborn. For 2 decades, it has been recognized that more than 80% of the strains that cause neonatal meningitis synthesize K1 capsular antigen. Our understanding of pathogenesis and immunity has been advanced, and better antimicrobial agents are now available.

EPIDEMIOLOGY. E. coli are common inhabitants of the intestinal and vaginal flora. E. coli K1 strains have been isolated in 20{endash}–40% of rectal swabs in individuals of all ages. Vertical transmission has been documented in healthy infants and those with E. coli meningitis. High rates of carriage in nursery personnel suggests the probability of nosocomial transmission in some cases of late-onset infections. The prevalence of K1 strains in E. coli meningitis is as high as 88%. In contrast, about 33% of infants with E. coli bacteremia have K1 strains.

Obstetric and/or neonatal risk factors are often present in infants with E. coli infections. These include UTIs during the last month of pregnancy, intrapartum fever, prolonged rupture of the membranes, postpartum endometritis, assisted delivery, prematurity, multiple birth, postmaturity, and congenital abnormalities. Congenital defects include spina bifida, sacrococcygeal teratoma, gastroschisis, duodenal atresia in Down syndrome, galactosemia, and pyruvate kinase deficiency.

E. coli bacteremia and, less commonly, meningitis may complicate NEC. In contrast to infections with GBS, E. coli infections in the newborn infant occur most frequently between 3 days and 2 wk of age.

ETIOLOGY. The bacterial cell wall of E. coli consists of lipid-linked polysaccharide or O antigen. Many strains produce capsular polysaccharides or K antigens, which are associated with virulence and invasiveness. There are more than 150 O antigens and 100 K antigens. The K1, K2, K3, K5, K12, and K13 antigens are present in most isolates from the urinary tract. E. coli K1 strains cause most cases of neonatal bacteremia, neonatal meningitis, and childhood pyelonephritis. The K1 polysaccharide is an a{alpha}-2®{right arrow}8-linked linear homopolymer of N-acetylneuraminic acid, which is identical to group B meningococcal polysaccharide. There is also structural similarity to the embryonic form of the neural cell adhesion molecule (N-CAM).

PATHOGENESIS AND PATHOLOGY. The K1 polysaccharide is a unique virulence factor. Because of its structural identity with N-CAM, the K1 antigen is poorly recognized by the newborn infant's immune system, and the host often exhibits a state of tolerance. Serum antibodies to the K1 capsule, when present, are predominantly of the IgM class and do not cross the placenta.

The capsule provides an antiphagocytic barrier to activation of the alternative complement pathway. Thus, opsonization by antibody and complement-mediated mechanisms is markedly impaired.

On the other hand, the ratio of newborn infants colonized with E. coli K1 to those who become infected is high. Therefore, host defense mechanisms, environmental risk factors, or other virulence factors may play a role. E. coli produce a purulent meningitis with ventriculitis as a common complication.

CLINICAL MANIFESTATIONS. E. coli usually produce bacteremia, sepsis, and meningitis in the newborn infant. Other infections include pneumonia, soft tissue abscesses, UTI, arthritis, osteomyelitis, and ascending cholangitis. The signs are typical of these infections.

DIAGNOSIS. E. coli are identified by isolation from normally sterile body fluids. The K1 strains are easily identified by a latex agglutination test using antisera to group B meningococci.

TREATMENT. E. coli vary in their susceptibility to antibiotics. The choice of antimicrobial agents should be guided by the site of infection, antibiotic sensitivity data, the clinical response, and follow-up culture results.

Coagulase-negative staphylococci (CONS) are currently the most common organisms associated with late-onset infections in neonatal intensive care units. Infections are frequently associated with the use of foreign bodies in very low-birthweight and chronically hospitalized infants.

ETIOLOGY. Staphylococci belong to the family Micrococcaceae and appear microscopically as gram-positive cocci in clusters. CONS are differentiated from Staphylococcus aureus by the latter's ability to produce coagulase. There are 21 species of CONS; 11 are found in human flora. The most common human pathogens are S. epidermidis, S. saprophyticus, and S. hemolyticus. Commercially available kits allow speciation by biochemical determinations, but these are not widely utilized. Laboratories generally report isolates as CONS. Antibiotic susceptibility patterns, slime layer production, biotyping, serologic typing, phage typing, and polypeptide DNA and plasmid analysis are techniques that have been applied to epidemiologic investigations. All these techniques have limitations.

EPIDEMIOLOGY. CONS are ubiquitous and are acquired early in life in essentially all infants, at birth or in the nursery. Skin, respiratory tract, and gastrointestinal tract are commonly colonized. CONS are the most common cause of bacteremia in low-birthweight infants. Approximately 50% of bacteremic infants have central venous catheters in place. Central nervous system shunts are also a risk factor for CONS ventriculitis. The mortality rate from CONS infections is lower than that from GBS and gram-negative enteric infections.

The increased prevalence of CONS infections in neonatal intensive care units has been attributed to the increased survival of very low-birthweight infants, which is associated with prolonged hospitalization, heavy exposure to broad-spectrum antibiotics, and the use of invasive procedures for monitoring and treating unstable infants. Recently, the use of intravenous lipid emulsion has been associated with an increased risk of CONS bacteremia.

PATHOGENESIS. Breakdown of the mucocutaneous barrier is the usual initial step. CONS are able to adhere to prosthetic devices, either by contiguous or bacteremic spread. Although there does not appear to be any phenotypic characteristic of CONS responsible for virulence, S. epidermidis is the most common species colonizing the newborn and associated with neonatal disease. S. epidermidis and S. hemolyticus are more virulent in animal models. Colonization and infection are enhanced by production of a slimelike substance, an exopolysaccharide. Slime-producing strains of CONS are often associated with neonatal disease.

Slime enhances adherence to catheters, inhibits neutrophil chemotaxis and phagocytosis, and may affect resistance to glycopeptide antibiotics. Lack of optimal opsonophagocytosis is the most important immunologic defect in the newborn's defense against CONS infection. Opsonic activity for CONS in premature infants is proportional to gestational age. Other possible virulence factors include cytotoxins, hemolysins, and proteinases.

CONS have been associated with NEC in the newborn infant. Like S. aureus, strains of CONS produce a delta toxin, which has been found in the stools of infants

with NEC. Delta toxin causes lesions resembling NEC in rabbit intestinal loops and may play a role in the pathogenesis of NEC.

CLINICAL MANIFESTATIONS. The manifestations of most CONS neonatal infections are nonspecific. Bacteremia without a focus of tissue damage is associated with a variety of signs, ranging from mild to severe. Respiratory distress, apnea, bradycardia, gastrointestinal abnormalities, thermoregulatory problems, evidence of poor perfusion, and cerebral dysfunction are common. Specific infections caused by CONS include pneumonia, pleural effusions, meningitis, endocarditis, NEC, omphalitis, abscesses, and osteomyelitis.

DIAGNOSIS. Differentiation of CONS in normally sterile biologic fluids from contaminating organisms is a continuing problem for clinicians. Careful collection of specimens for culture and the use of multiple cultures will improve the validity of culture results. Some authors have recommended the use of quantitative cultures; however, low colony counts may occur in infections of the blood and CSF. Specific characteristics of CONS are not helpful in differentiating pathogens from contaminants in any individual case.

TREATMENT. Management of CONS infections involves antimicrobial therapy and, often, a decision regarding the removal of a foreign body. Because most hospital CONS isolates are resistant to penicillin, penicillinase-producing penicillins, and gentamicin and resistance to vancomycin is uncommon, vancomycin is the choice for initial therapy of suspected or proved CONS infections. If the organism is susceptible to penicillin or cephalosporin, these agents should be used to minimize the adverse effects and development of resistance to vancomycin. Vancomycin is nephrotoxic and ototoxic; peak and trough levels should be maintained between 25 and 40 mg/mL and less than 10 mg/mL, respectively. Dosing schedules based on weight and postnatal age have been developed.

Although removal of indwelling catheters or prosthetic devices significantly improves the response to antimicrobial therapy, there is usually a trial of antimicrobial therapy without removal of the foreign body. Infections with slime-producing CONS are less likely to respond, and endocarditis is more difficult to treat without removal of the umbilical venous catheter. If infection persists despite the use of an agent with good in vitro activity, synergistic therapy with rifampin and vancomycin is recommended.

Candida species are a common cause of oral mucous membrane (thrush) and perineal skin infections (diaper dermatitis) in newborn infants. With improved survival of very low-birthweight infants, disseminated fungal infections are occurring more frequently in special care nurseries. The incidence is as high as 5% in very low-birthweight infants.

ETIOLOGY. Candidiasis is caused by members of the genus Candida, which includes 80 different species. C. albicans accounts for 80{endash}–90% of human infections. C. tropicalis, C. parapsilosis, C. lusitaniae, and C. glabrata are less commonly associated with infection in the newborn infant.

Candida has three predominant morphologic forms. Yeast cells (blastospores) are 1.5{endash}–5 m{mu}m in diameter, bud asexually, grow on body surfaces and fluids, initiate invasive lesions, and may cause toxic or inflammatory reactions. Chlamydospores are larger (7{endash}–17 m{mu}m) and are unusual as a form of systemic illness. Hyphae (pseudomycelia) forms are the tissue, rather than the contamination, phase of Candida and are filamentous processes that elongate from the yeast cell. Candida grows aerobically on routine laboratory media but may take several days of incubation.

EPIDEMIOLOGY. C. albicans is commonly isolated from gastrointestinal and vaginal flora of adults. Pregnancy increases the rate of vaginal colonization from less than 20% to about 33%. Approximately 10% of term infants are colonized within the first 5 days of life, but in infants smaller than 1,500 g, fungal colonization rates approach 30%. Early colonization occurs in the gastrointestinal and respiratory tracts. After 2 wk, colonization commonly involves the skin.

Congenital candidiasis has been rarely reported. It occurs as an ascending infection and has been associated with foreign bodies in the genital tract. Postnatal infection most commonly appears as thrush at about 1 wk of age. Monilial diaper dermatitis presents somewhat later with a peak incidence at 3{endash}–4 mo.

Systemic candidiasis is predominantly an infection of very low-birthweight infants with an estimated attack rate of 2{endash}–5%. Term infants exposed to abdominal surgery or prolonged ventilatory support are also at risk. Prolonged intravenous catheterization, the use of intravenous alimentation, and broad-spectrum antibiotic administration are risk factors.

PATHOGENESIS. Overgrowth of Candida on mucocutaneous surfaces and their presence on intravenous catheter tips favor entry and penetration. Clinical infection appears to be related to inoculum size. NEC may provide a mechanism for dissemination. The inability of the newborn infant to localize, control, and eradicate Candida infections appears to be related to the relative impairment of specific and nonspecific host defense mechanisms. Hematogenous spread leads to vasculitis and miliary nodules in many organs. The lungs, kidneys, gastrointestinal tract, heart, and meninges are commonly infected. Yeast and filaments are readily identified.

CLINICAL MANIFESTATIONS. Thrush presents with white, curdlike plaques on the oropharyngeal mucosa. The plaques are adherent to the mucosa and scraped off with some difficulty, leaving an erythematous base. Candida dermatitis is an

erythematous, scaling rash most prominent in the intertriginous areas, with pustules forming along the leading edge and as satellites.

Congenital candidiasis presents as a generalized, intensely erythematous eruption in the first 12 hr of life. The rash may desquamate and become pustular. It contains fungi and is associated with fungal "colonies," which are visible as small yellow-white lesions on the placenta and umbilical cord. Preterm infants frequently have systemic disease characterized by pneumonia, leukocytosis, shock, and a high mortality rate. Full-term infants usually have disease localized to the skin.

The manifestations of systemic infection vary in acuteness and severity. Fungemia may be asymptomatic or may be associated with sepsis and septic shock. Either respiratory tract or gastrointestinal signs may be present. Severe apnea and bradycardia, temperature instability, generalized erythema, and hyperglycemia may be noted.

Vascular disease ranges from vasculitis of the aorta or vena cava to endocarditis. Infected thrombi in vessels and the right atrium are not uncommon. Renal involvement may be subclinical or may present with involvement of the upper or lower urinary tract. Upper tract involvement is manifested as flank mass, hypertension, renal failure, renal abscesses, papillary necrosis, and fungal balls in the collecting system with obstruction and hydronephrosis.

Central nervous system candidiasis may involve the meninges, ventricles, or cerebral cortex with abscess formation. Clinical manifestations of central nervous system disease may be subtle or not apparent. Endophthalmitis may occur in up to 50% of very low-birthweight infants with systemic candidiasis. It begins as chorioretinitis, which may extend to the vitreous. Cotton ball exudates are typical of Candida retinal pathologic conditions.

DIAGNOSIS. Isolation of fungi from cultures of normally sterile body fluids is the basis for diagnosis of invasive candidiasis. Occasionally, buffy coat smears of blood may show yeasts, allowing a preliminary diagnosis. Skin scrapings of generalized rashes in very low-birthweight infants with suspected systemic candidiasis should be examined microscopically. Because cultures of blood and CSF are often intermittently positive, multiple samples should be obtained. CSF cultures are positive in 33% of infants with systemic infection. Cultures should be taken from peripheral veins to differentiate true-positive cultures from contaminated catheter. Urine specimens for culture must also be obtained carefully to differentiate perineal colonization. There are no satisfactory antigen detection tests for clinical use. Serologic tests are under investigation but presently unavailable.

It is important to distinguish between catheter-associated transient candidemia and disseminated candidiasis. The former is characterized by positive blood cultures, owing to contamination of in situ intravascular catheters but no evidence of focal or

disseminated disease, and may be treated by removing the catheter. Disseminated candidiasis is characterized by involvement of one or more organ systems.

Ultrasonography is useful for localization of Candida infection in the cardiovascular, renal, and central nervous systems. Radiographs of the chest may reveal fungal balls. Biochemical analysis of the blood should be performed in patients with suspected sepsis to assess renal and hepatic status.

TREATMENT. Amphotericin B is the drug of choice for systemic candidiasis. The drug is active against both yeast and mycelial forms. The initial dosage ranges from 0.5{endash}–1.0 mg/kg/24 hr intravenously. Because of individual variability, determination of serum levels is recommended to avoid drug accumulation. Amphotericin B should be diluted in 5% dextrose in water without electrolytes to a concentration of less than 0.2 mg/mL and administered over 4{endash}–6 hr. The duration of therapy varies widely according to clinical response and drug toxicity. The total recommended dose is 20{endash}–30 mg/kg. Nephrotoxicity is fairly common in the newborn infant and generally presents with oliguria, azotemia, and hyperkalemia. Some clinicians add flucytosine orally in a dose 100{endash}–150 mg/kg/24 hr divided every 6 hr. Flucytosine shows some synergism with amphotericin B and yields good levels in CSF. Fungi develop resistance when flucytosine is used alone. Patients must be observed for bone marrow, gastrointestinal, and hepatotoxicity.

Indwelling catheters should be removed if possible. Infected intracardiac and intravascular thrombi usually must be resected, but resolution without surgery has been described.

V. Plan and organizational structure of the lesson.

Serial №	**The main periods of lesson, their functions and contents**	**Educational aims in links of learning**	**Methods of control**	**Methodical materials for control, imaging, directory materials**	**Distribution of time in minutes**
	Preparatory stage				
1	Organizing measures				3 minutes
2	Setting of educational aims and motivation			p.I “Actuality of theme”	12minutes
3	Control of secondary knoweleges and practice level:		Individual verbal questioning	p.II ”Educational aims” Tables, pictures,	25 minutes
	5. Etiology of inflammatory diseases in newborn infants	α2	Fase-to-fase interlocution Control by	structural schemes Pharmaceutical preparations,	
	6. The main pathogenesis links of septic diseases in newborn infants	α2	the second level tests Solving of	slides. Questions for individual inquiry.	
	7. Clinical classifica-	α2	typical the	The second level	

	tion of inflammatory diseases in newborn infants 8. Clinical and diagnostical features of different inflammatory diseases in newborn infants	 α2	second level tasks	tests The third level tests The second level tasks	
	5.Clinical and diagnostical features of inflammatory diseases in preterm and full-term newborn infants 6.Laboratory and instrumental diagnostic of septic diseases in newborn 7.Differential diagnostic of different inflammatory diseases in newborn infants 8.Differential diagnostic of sepsis in newborn 9.Complications of septic diseases in newborn infants 10.Principes of treatment newborn infants with inflammatory diseases 11.Prevention of septic diseases in newborn infants 12.Reabilitation of infant, who was ill with neonatal sepsis	α2 α2 α2 α2 α2 α2 α2	Control by the third level tests		
4	**The main stage** Formation of professional practices and skills: 10. To conduct clinical examination of newborn infant with septic disease, to capture methods of medical histories gathering 11. To conduct clinical examination of infant, to reveal the main symptoms of inflammatory diseases 12. To formulate and to prove initial diagnosis 13. To compose plan of laboratory and instrumental examination of patient 14. To interpret results of laboratory and instrumental examination 15. To establish differential diagnostic between inflammatory diseases with the same	 α3 α3 α3 α3 α3	Method of forming practices: Practical professional traning, solving of the typical third level tasks and tests	Algorithms for creation practical skills. Algorithms for creation professional abilities. Patients Medical histories List of medical prescriptions. The third level tests The third level tasks Imitational games Equipment: Instructions(on cards), orders of	115 minutes

	clinical manifestations 16. To give recommendations of regime and nutrition to infant with septic disease 17. To compose the plane of patient treatment 18. To determine the medical tactics in septic complications	α3 α3 α3		Ukrainian Ministry of Public Health (protocols of review and treatment). Situational atypical tasks of the third level. Algorithms of the first aid giving	
5 6	**Final stage** Control and correction of professional skills and practices Sizing up the lesson		Analysis of clinical work results. Solving of atypical tasks and tests of the third level.	Results of clinical work. Situational atypical tasks of the third level.	25 minutes
7	Home task (basic and additional literature about the topic)		Estimation of clinical work.	Approximate card for one's own work with literature	

Questions for elementary level of knowledges control

1. Which of physiological features of newborn infants helps to development of septic diseases in it?
2. Etiology of pyoinflammatory diseases of skin and hypodermic tissue.
3. Clinical course of infectional diseases of skin and hypodermic tissue (pemphigus, exfoliative dermatitis, phlegmon of newborn, mastitis of newborn, catarrhal and festering omphalitis, candidosis of skin).
4. Clinical manifestation of inflammatory diseases of umilical wound.
5. Principles of local pyoinflammatory diseases' treatment.
6. To count risk factors of newborn sepsis' development
7. To count the main clinic form of sepsis.
8. Features of sepsis' course in newborn.
9. Features of sepsis' course in premature newborn.
10. Which clinic manifestations of immunologic insufficiency in patients with sepsis?
11. Diagnostic criteria of sepsis and means of laboratory investigation.
12. Differential diagnostic between immunodeficiency disorders, intranatal infections, genetic defects of metabolism, pathology of endocrine system.
13. To invite principles of treatment of sepsis in newborn.
14. Principes of prophylaxis of pyoseptic diseases in newborn infants.
15. Dispensary observation at infants, who was ill with sepsis.

Examples of tests and tasks:

1.Child 5 days of life, take place the hyperemia, the infiltration of umbilical wound, purulent discharge from umbilical wound, the umbilical vein is palpated as tension bar. Follows symptoms appeared during the next day of life: stiff neck, tonic abduction of eyeglobes, retraction of the big fontanel, pulsation of an angle of a mouth, refusal of meal, cerebral scream. In the routine blood test is leucotsytosis, deviation to the left, acceleration of a blood sedimentation rate. In a bacterial sowing from umbilical wound the St.aureus allocated. Establish the preliminary diagnosis:

A Hypoxic CNS injury , acute period, hypertensive hydrocephalic syndrome, convulsive syndrome, severe course

B. Purulent omphalitis. Thrombophlebitis of an umbilical vein

C. Subarachniodal hemorrhage. Purulent omphalitis

D. Postnatal staphylococcal umbilical sepsis. Septicopyemia. Purulent omphalitis. Purulent meningitis. Thrombophlebitis of umbilical vein.

E The complicated purulent meningitis.

2. Child 5 days of life, take place the hyperemia, the infiltration of umbilical wound, purulent discharge from umbilical wound, the umbilical vein is palpated as tension bar. Follows symptoms appeared during the next day of life: stiff neck, tonic abduction of eyeglobes, retraction of the big fontanel, pulsation of an angle of a mouth, refusal of meal, cerebral scream. In the routine blood test is leucotsytosis, deviation to the left, acceleration of a blood sedimentation rate. In a bacterial sowing from umbilical wound the St.aureus allocated. What test allows diagnosing purulent meningitis?

A Lumbar puncture

B. The developed analysis of a blood

C. Neurosonography

D. Bacteriological blood analysis

E. Echo - encephalography

3. Child 5 days of life, take place the hyperemia, the infiltration of umbilical wound, purulent discharge from umbilical wound, the umbilical vein is palpated as tension bar. Follows symptoms appeared during the next day of life: stiff neck, tonic abduction of eyeglobes, retraction of the big fontanel, pulsation of an angle of a mouth, refusal of meal, cerebral scream. In the routine blood test is leucotsytosis, deviation to the left, acceleration of a blood sedimentation rate. In a bacterial sowing from umbilical wound the St.aureus allocated. Name the most comprehensible variant of debut antibacterial therapy

A. Cephasolinum, azlocillinum

B. Ampiox, gentamycinum

C. Oxacillinum, gentamycinum

D. Cephasolinum

E. Oxacillinum, rovamycin

4. Child 5 days of life, take place the hyperemia, the infiltration of umbilical wound, purulent discharge from umbilical wound, the umbilical vein is palpated as tension bar.. Follows symptoms appeared during the next day of life: stiff neck, tonic abduction of eyeglobes, retraction of the big fontanel, pulsation of an angle of a mouth, refusal of meal, cerebral scream. In the routine blood test is leucotsytosis, deviation to the left, acceleration of a blood sedimentation rate. In a bacterial sowing from umbilical wound the St.aureus allocated. Select an adequate dosage of antibiotics indicated in this case

A. Oxacillinum 100 mg/kg; gentamycinum 3 mg/kg

B. Oxacillinum 150; mg/kg, gentamycinum 3 mg/kg

C. Oxacillinum 100; mg/kg , gentamycinum 5 mg/kg

D Oxacillinum 150 mg/kg; gentamycinum 5 mg/kg

E. Oxacillinum 100 mg/kg; gentamycinum 7 mg/kg

5. In newborn child, 1 day of life, was born in 37 week of grstational age with weight 1800g an absence of a physiological erythema, marbing and paleness of skin has appear, hepatoslenomegaly. RDS of III degree, convulsive readiness, protrusion of the big fontanel, stiff neck, purulent conjunctivitis. The acute salpingo-oophoritis is diagnosed for mother in 3 trimester of pregnancy. Establish the preliminary diagnosis:

A.Antenatal sepsis: Septicopyemia. Purulent meningitis.Pneumonia. Purulent conjunctivitis.

B. Natal trauma of CNS. Purulent conjunctivitis

C. Intrauterine infection. Conjunctivitis

D. Pneumopathy.. RDS III. Intrauterine oligotrophy

E .Intranatal sepsis. Hematosepsis

6. In newborn of five days of life in survey the hyperesthesia, the compelled pose is taped with restriction of movement in the upper right extremity, pain in a palpation of t right brachium, edema of the right humeral joint, right sided oppression of Moro reflex, downstroke of appetite, flaccidity, hypodynamia, paleness of skin,. In routine blood test the hyperleucocytosis, neutrophilosis, anemia admitted. What disease do similar signs characterize?

A. Kerer paralysis

B. Epiphyseal osteomyelitis

C. Paralysis of Duchen-Erb

D. Fracture of a humeral bone

E. Traumatic epiphisiolysis of humeral bone.

7. In child of 6 day of life who was born in 35 weeks of gestational age with weight 2100 the vesiculopustulosis diagnosed. To 7 day of life on background of umbilical wound physiological wetting the infiltration and hyperemia of umbilical ring has appeared. To 19 day of life the cuticularization of umbilical wound has not stepped. From this day signs of an intoxication accrue, oppression of CNS. In bacterial crop the St.aureus allocated. Select an optimal antibiotic:

A. Rovamycin

B. Ampicillin
C. Oxacillin
D. Gentamycin
E. Carbenicillin

8. In child of 6 day of life who was born in 35 weeks of gestational age with weight 2100 the vesiculopustulosis diagnosed. To 7 day of life on background of umbilical wound physiological wetting the infiltration and hyperemia of umbilical ring has appeared. To 19 day of life the cuticularization of umbilical wound has not stepped. From this day signs of an intoxication accrue, oppression of CNS. In bacterial crop the St.aureus allocated. Select an optimal immunopreparation

A .Antistaphilococcal immunoglobulin
B. Native plasma
C. Thymalin
D. Levamisol
E. Immunoglobulin human normal

9. In a child of 8 days of life on the right breech the purple - and cyanotic spot with dimensions of 3x5 cm occur, protruding above the surface of skin, dense and painful by a touch. According to mother information child became languid, sucks badly, belching, has a fever. What is the probable diagnosis?

A. Pseudofurunculosis of Figner
B. Adiponecrosis
C. Exfoliative dermatitis of Ritter
D. Postinjectional abscess
E. Phlegmon of newborn.

10. In a child of 8 days of life on the right breech the purple - and cyanotic spot with dimensions of 3x5 cm occur, protruding above the surface of skin, dense and painful by touch. According to mother information child became languid, sucks badly, belching, has a fever. What volume of antibacterial therapy needs to be administrated?

A. 2 antibiotics in therapeutical doses
B. 1 antibiotic in therapeutical dose
C. 1 antibiotic in maximal dose
D. 2 antibiotics in maximal dose
E. There is no necessity in administration of antibiotics

11. In a child of 8 days of life on the right breech the purple - and cyanotic spot with dimensions of 3x5 cm occur, protruding above the surface of skin, dense and painful by touch. According to mother information the child became languid, sucks badly, belching, has a fever. Determine the range of topical therapy

A. Disclosing of a wound by alternating cuts within the limits of healthy tissues
B. Application of bandages with hypertonic salt solutions
C. Application the bandages with oinment of Vishnevsky
D .Disclosing by one cut

E. Using of UHV

12. In newborn of 5 day of life a vesicles on the skin of abdomen and extremities filled with serous and purulent liquid has appeared. The general state of the child has not changed Establish the diagnosis:

A. Syphilitic pemphigus
B. Pemphigus of newborns, the malignant form
C. Exfoliative dermatitis of Ritter
D. Pemphigus of newborn. Simple form
E. Physiological ecdysis

13. In newborn of 5 day of life a vesicles on the skin of abdomen and extremities filled with serous and purulent liquid has appeared. The general state of the child has not changed. Prescribe the treatment:

A. Immunotherapy, topical therapy
B. Antibiotic, topical therapy
C. 2 antibiotics, topical therapy
D. General UVI of skin
E. Topical therapy, general UVI of skin

14. In newborn of 5 day of life a vesicles on the skin of abdomen and extremities filled with serous and purulent liquid has appeared. The general state of the child has not changed. What etiology of these rashes?

A. Streptococcus
B. St.aureus
C Treponema pallidum
D. Herpes simplex virus
E. Listerias

15. In newborn of 14 day of life the infiltration and hyperemia of umbilical ring admitted, serous and purulent allocations from umbilical wound. Administration of antibiotic during the 7 days and the intensive lavage of umbilical wound with using of 3 % solution of Hydrogenium peroxide, 70 % medical alcohol, 5 % solution of a potassium permanganate were ineffective. Name the most probable diagnosis.

A. Umdilical sepsis
B. Incomplete umbilical fistula, purulent omphalitis
C. Complete umbilical fistula, purulent omphalitis
D Purulent omphalitis
E. Complete urinary fistula, purulent omphalitis

16. In newborn of 14 day of life the infiltration and hyperemia of umbilical ring admitted, serous and purulent allocations from umbilical wound. Administration of antibiotic during the 7 days and the intensive lavage of umbilical wound with using of 3 % solution of Hydrogenium peroxide, 70 % medical alcohol, 5 % solution of a potassium permanganate were ineffective. What is the further tactics?

A Intensifying of topical therapy
B.Continuation of prescribed therapy

C. Intensifying of antibacterial therapy
D .Changing of antibiotics
E. Consultation of surgeon

17.In newborn with weight 1900g, the signs of an intoxication take place., RDS III, anemia, trombocytopenia, leucocytosis with deviation to the left, on X-ray the pneumonia with fine centers. What variant of pneumonia course is expected?

A .Lingering
B. Acute
C. Chronic
D. Fulminant
E. Subacute

18. In newborn with weight 1900 g, the signs of an intoxication take place, RDS III, anemia, trombocytopenia, leucocytosis with deviation to the left, on X-ray the pneumonia with fine centers. Select an optimal variant of treatment:

A. 1 antibiotic, immunostimulators, liquid infusion, physiotherapy
B. 2 antibiotics, respiratory therapy, physiotherapy
C. 2 antibiotics, passive immunotherapy, respiratory therapy,liquid infusion, physiotherapy
D. immunotherapy , respiratory therapy, liquid infusion
E. 2 antibiotics, respiratory therapy, passive immunotherapy.

19. In newborn with weight 1900 g, the signs of an intoxication take place, RDS III, anemia, trombocytopenia, leucocytosis with deviation to the left, on X-ray the pneumonia with fine centers. What parameters will define the necessary volume of respiratory therapy?

A. Gas blood test, pH of blood
B. Silverman score
C. Dowence score
D. Frequency of respiration
E. Color of skin

20.In newborn child of 3 day of life due to hyperbilirubinemia the catheter in an umbilical vein fixed. The catheter functioned during the 2 days To the 6 day of life the signs of coloenteritis admitted. To the 8 day the pneumonia diagnosed, to the 10 day the purulent meningitis. Classify sepsis by the entrance hiluses:

A. Pulmonary
B. Umbilical
C Cryptogenic
D. Intestinal
E. Iatrogenic

Tasks.

1. A 1-month-old is noted to have eosinophilia, during a routine-screening. Other blood datas is normal. Which of the following most commonly causes increased eosinophilia in the peripheral blood smear?

Some common causes of eosinophilia in the peripheral blood smear include asthma, recurrent urticaria, infantile eczema, serum sickness, angioneurotic edema, helminth infections, collagen vascular disease, and some neoplasms. Allergic rhinitis can cause eosinophilia in nasal secretions, but usually does not cause dramatic peripheral eosinophilia.

2. In newborn of 5 day of life a vesicles on the skin of abdomen and extremities fi lled with serous and purulent liquid has appeared. The general state of the child has not changed. Trombocytopenia, leucocytosis with deviation to the left anemia take place.

What etiology of these rashes?

Prescribe the treatment to the patient

Early-onset GBS disease is associated with immature host defense mechanisms among low-birthweight infants and exposure to heavily colonized maternal genitourinary tract sites (ascending vertical transmission through ruptured amniotic membranes). GBS may cause local inflammation of intact membranes, causing subsequent weakness and rupture of amniotic fluid membranes, thus initiating premature labor. Recurrence or relapse is uncommon, but if either occurs, it is seen within 2{endash}–43 days of therapy (mean 16 days). Prior therapy was usually too short (<10 days for bacteremia, <14 days for meningitis) with too low a dose of antibiotic. Antibiotic treatment may not eliminate GBS colonization from the mucosal surfaces, and prior infection may not produce protective antibody. Reinfection may result from maternal mastitis, and late complications of brain abscess or endocarditis have been reported. Repeat therapy with higher doses of penicillin, for a longer course, is effective therapy for recurrent GBS infection.

3. Newborn child was hospitalized with mothers complaints at worsening of appetite, brings up, limpness, one-time temperature increase, weeping of umbilical wound during last few days. Bacterial inoculation from the umbilical wound is: St.aureus, St.epidermalis. Blood datas is normal.

Determine diagnosis.

What is pathogenesis of infant’s illness?

Festering omphalitis take place. Rarely, inhalation of infected amniotic fluid may produce pneumonia and sepsis in utero, manifested by fetal distress or neonatal asphyxia. Exposure to pathogens at delivery and in the nursery or community is the mechanism of infection after birth.

The physiologic manifestations of the inflammatory response are mediated by a variety of proinflammatory cytokines, principally TNF, interleukin-1 (IL-1), and IL-6, and by-products of activation of the complement and coagulation systems. Studies in newborn infant are limited, but it appears that some cytokine production may be diminished, which is consistent with an impaired inflammatory response. However, elevated levels of IL-6, TNF, and platelet-activating factor have been reported in newborn infants with neonatal sepsis and necrotizing enterocolitis (NEC). IL-6 appears to be the cytokine most often elevated in neonatal sepsis.

4. In newborn of 8 day of life with hypothermia the signs of spotted rush occurs (Candida detected). Then, the pneumonia with impoverished auscultative signs and the rich mucopurulent sputum was diagnosed. The sclerema and icterity of skin take place. In the routine urine analysis the erhythrocyturia, cylindruria, leukocyturia, proteinuria detected.

Determine diagnosis.

Prescribe the treatment to this patient.

Candida sepsis, septicopyemia take place. Amphotericin B is the drug of choice for systemic candidiasis. The drug is active against both yeast and mycelial forms. The initial dosage ranges from 0.5{endash}–1.0 mg/kg/24 hr intravenously. Because of individual variability, determination of serum levels is recommended to avoid drug accumulation. Amphotericin B should be diluted in 5% dextrose in water without electrolytes to a concentration of less than 0.2 mg/mL and administered over 4{endash}–6 hr. The duration of therapy varies widely according to clinical response and drug toxicity. The total recommended dose is 20{endash}–30 mg/kg. Nephrotoxicity is fairly common in the newborn infant and generally presents with oliguria, azotemia, and hyperkalemia. Some clinicians add flucytosine orally in a dose 100{endash}–150 mg/kg/24 hr divided every 6 hr. Flucytosine shows some synergism with amphotericin B and yields good levels in CSF. Fungi develop resistance when flucytosine is used alone. Patients must be observed for bone marrow, gastrointestinal, and hepatotoxicity.

5. Newborn 6 days of life, take place the hyperemia, the infiltration of umbilical wound, purulent discharge from umbilical wound, the umbilical vein is palpated as tension bar. Follows symptoms appeared during the next day of life: stiff neck, tonic abduction of eyeglobes, retraction of the big fontanel, pulsation of an angle of a mouth, refusal of meal, cerebral scream. In the routine blood test is leucotsytosis, deviation to the left, acceleration of a blood sedimentation rate. In a bacterial sowing from umbilical wound the St.aureus allocated.

Establish the preliminary diagnosis.

Prescribe etiotropic treatment.

Postnatal staphylococcal umbilical sepsis. Septicopyemia. Purulent omphalitis. Purulent meningitis take place. Thrombophlebitis of umbilical vein. Treatment of neonatal sepsis may be divided into antimicrobial therapy for the suspected or known pathogen and supportive care. Fluids, electrolytes, and glucose should be monitored carefully with correction of hypovolemia, hyponatremia, hypocalcemia, and hypoglycemia and limitation of fluids if there is inappropriate antidiuretic hormone secretion. Shock, hypoxia, and metabolic acidosis should be identified and managed with inotropic agents, fluid resuscitation, and mechanical ventilation. Adequate oxygenation of tissues should be maintained because ventilatory support is frequently necessary for respiratory failure caused by congenital pneumonia, persistent fetal circulation, or adult RDS (shock lung). Refractory hypoxia and shock may require extracorporeal membrane oxygenation, which has reduced mortality rates in full-term infants with septic shock and persistent fetal circulation. Hyperbilirubinemia should be monitored and treated with exchange transfusion because the risk of kernicterus

increases in the presence of sepsis and meningitis. Parenteral nutrition should be considered for infants who cannot sustain enteral feedings.

Because neutrophil storage pool depletion has been associated with a poor prognosis, a number of clinical trials of polymorphonuclear replacement therapy have been conducted, with variable results. Sepsis that is unresponsive to antibiotics with persistent neutropenia may be an indication for granulocyte transfusion. The use of granulocyte-macrophage colony{endash}–stimulating factor (GM-CSF) is under investigation. Treatment with intravenous immunoglobulins (IVIG) containing specific antibodies is currently under clinical investigation. Currently, granulocyte transfusion, granulocyte colony{endash}–stimulating factor (G-CSF), and IVIG are experimental therapies of undetermined value.

6. In an infant of 5 days of life on the right breech the purple - and cyanotic spot with dimensions of 3x5 cm occur, protruding above the surface of skin, dense and painful by a touch. According to mother information child became languid, sucks badly, belching, has a fever.

What is the probable diagnosis?

What volume of therapy needs to be administrated?

Phlegmon of newborn. It's needed to provide seurgical, antibacterial and topical terapy.

7. In child of 7 day of life who was born in 35 weeks of gestational age with weight 2100 the vesiculopustulosis diagnosed. To 8 day of life on background of umbilical wound physiological wetting the infiltration and hyperemia of umbilical ring has appeared. To 19 day of life the cuticularization of umbilical wound has not stepped. From this day signs of an intoxication accrue, oppression of CNS.

Identify the most probable causative agent of newborns affection.

Select an optimal antibiotic

St.aureus. GBS are uniformly sensitive to penicillin G, which is the treatment of choice of confirmed GBS infection. Empirical antimicrobial therapy is initiated with a penicillin (usually ampicillin) and an aminoglycoside until GBS have been differentiated from other bacteria. In vitro, a combination of penicillin and gentamicin provides synergistic bactericidal activity against GBS despite resistance of GBS to aminoglycosides. Some authorities recommend continuation of ampicillin plus gentamicin for several days until there is a good clinical response or the CSF becomes sterile.

8. In worn child of 8 day of life the necrotic phlegmon, destructive pneumonia, purulent otitis admitted. This state is accompanied by a serious toxicosis and the hyperthermia. In routine blood test are anemia, trombocytopenia, hyperleucocytosis.

What are the late manifestations of neonatal sepsis?

What volume of therapy needs to be administrated in case of DIC?

Late manifestations of sepsis include signs of cerebral edema and/or thromboses, respiratory failure as a result of acquired respiratory distress syndrome (ARDS), pulmonary hypertension, cardiac failure, renal failure, hepatocellular disease with

hyperbilirubinemia and elevated enzymes, prolonged prothrombin time (PT) and partial thromboplastin time (PTT), septic shock, adrenal hemorrhage with adrenal insufficiency, bone marrow failure (thrombocytopenia, neutropenia, anemia), and disseminated intravascular coagulation (DIC). DIC may complicate neonatal septicemia. Platelet counts, hemoglobin, PT, PTT, and fibrin split products should be monitored. DIC may be treated by management of the primary sepsis, but if bleeding occurs, DIC may be treated with fresh frozen plasma, platelet transfusions, or whole blood.

Metohodical materials to support basic stage class.

Professional algorythm of patient's management for practical skills and abilities forming.

№	Task	Sequence of implementation	Remarks and warnings related to self-control
1	To conduct examination of neborn infant with septic disease.	1. To conduct gathering of complaints and disease and obstetric anamnesis.	Pay attention to features of disease course, under-lying factors, concomi-tant diseases etc. To establish the availability of risk factors which facilitate disease occurrence.
		2. To conduct patient's examination.	To assess patient general condtion, position in bed, color and humidity of skin and mucouse, presence of hemorrhages and pyoinflammatory components on the skin, and extremities swelling. To pay a regard to presence of haemor-rhages, bleeding from mucouses, umbilical wound, nasal bleedings, melena and so on.
		3. To investigate cardiovascular system of the patient (palpation, percussion).	To pay a regard to rhythm of pulse, it tension and size on both hands, apex shove, it properties, margins of absolute and relative cardiac dullness, it changes, HR(tachi-or

		4. To investigate the pulmonary system (percution, bronchophony).To conduct lungs auscultation. 5. To investigate the system of digestion. 6. To investigate the urinary tracts. 7. To investigate the nervous system.	bradicardia, extrasystole),BP. To pay regard to heart tones weakening or amplifying, appearance of murmurs and additional III, IV tones. To pay attention to features of percussion and auscultation. Presence of apneustic breath, character of wheezes during the auscultation. Presence of emesis, belches, swellings, fast decline of weight, signs of enterocolitis or peritonitis. Presence of edemas, anuria. Signs of depression or hyperexcitability, crumps.
2	To formulate the initial diagnosis.	1.To formulate the initial diagnosis 2. To substantiate all the components of preliminary diagnosis based on complaints,anamnesis, and examinations.	Taking the classification as a starting point to formulate the inintial diagnosis of pyoinflammatory disease and to subtantiate each component of it.
3	To evaluate the parameters of additional laboratory investigations.	1. To evaluate the blood count data. 2. To conduct Apt's test in the preasens of melena. 3. To evaluate the bleeding time, clotting time, platelete count, clot retraction, platelet aggregation tests(using activators), thrombin time, prpthrombin index, APTT(Activated Partial	To pay attention to the signs of anemia, leucocytosis, changing of formula, elevation of sedimentation rate. To pay attention to bleeding time, clotting time, platelete count, clot retraction, platelet aggregation tests(using activators), thrombin time, prpthrombin index, APTT(Activated Partial

		Thromboplastin Time), ACT, fibrinogen, tests to assessing the fibrinolytic mechanims. 4. To evaluate the results of bacterial investigation. 5. To evaluate the results of instrumental patient's investigation.	Thromboplastin Time), ACT, fibrinogen, tests to assessing the fibrinolytic mechanims. To pay attention to the US of internals and brain, to ECG and X-ray of thoracal organs.
4.	To conduct differential diagnosis.	1.Consistently to find out common signs in complaints,life and disease anamnesis, the data of examination, data of laboratory and instrumental tests in patient and in similar states. 2.To find differences among complaints, information of life and disease anamnesis,examination data, information about the laboratory and instrumental methods in similar nosology. 3.To find out the differrences to excluding similar diseases from the list of probable diagnoses. 4. To conduct differenttial diagnostics according to the above mentioned algorithm among all of nosologies are having the similar signs, among other pyoinflammatory diseases. 5. Taking into account the impossibility to exclude the diagnosis of pyoinflammatory disease	Special attention must be paid to differential diagnosis among the intranatal infections, respiratory distress syndrome in premature, thrombopenia, inherited coagulopathy, jaundice, natal trauma.

		from the list of probable diagnoses to draw a conclusion about most probability of such diagnosis.	
5.	To formulate the final clininical diagnosis.	11. To formulate the final clininical diagnosis 12. Based on initial diagnosis, additional investigations data, conducted differential diagnosis to substantiate all elements of the final clininical diagnosis.	Being based on modern classification of pyoinflammatory diseases to formulate a concluding clininical diagnosis, complications of disease and presence of concomitant diseases.
6.	To prescribe treatment for patients.	1.To prescribe not medicinal treatment 2.To prescribe the medicinal treatment.	Expressly to specify the regimen and detailzed nutrition according to pyoinflammatory disease. Taking into account gestational age, severity of patient state, the stage of disease, the presence of complications and concomitant pathology, to prescribe modern medicinal treatment in accordance to the standards of pyoinflammatory diseases therapy.

Materials of control for conclusive classes stage:

1. In newborn child of 3 days of life in physiological department of maternity hospital in survey the vesiculitis and the purulent conjunctivitis diagnosed. Mother is healthy. Children in the ward are healthy. What is the further tactic?

A. Immediate excerption
B. Immediate transferring to newborns pathology department
C. Transferring to newborns pathology department in age of 5 days
D. Administration of topical therapy in the maternity hospital
E. Transferring to observational department

2. In newborn child of 3 days of life in physiological department of maternity hospital in survey the vesiculitis and the purulent conjunctivitis diagnosed. Mother is healthy. Children in the ward are healthy. What is the probable source of infection?

A. Personnel of newborns department
B. Mother of newborn child
C. Newborns in the ward.
D. Postnatal department
E. Iatrogenic interventions

3 In newborn of 10 days of life the osteomyelitis caused by Pyocyanic rod was diagnosed. What is the dose of carbenicilline?
A. 50-100 mg/kg
B. 30-40 mg/kg
C. 3-4 mg/kg
D. 100-150 mg/kg
E. 300-400 mg/kg

4.In newborn of 6 day of life with hypothermia the signs of coloenteritis occurs (Klebsiella detected).Then, the pneumonia with impoverished auscultative signs and the rich mucopurulent sputum is diagnosed. The sclerema and icterity of skin take place. In the routine urine analysis the erhythrocyturia, cylindruria, leukocyturia, proteinuria detected. What most probabaly ethiology of sepsis?
A. Streptococcus
B. Staphilococcus
C. Klebsiella
D. Pyocyanic rod
E. coli

5.In newborn of 6 day of life with hypothermia the signs of coloenteritis occurs (Klebsiella detected).Then, the pneumonia with impoverished auscultative signs and the rich mucopurulent sputum is diagnosed. The sclerema and icterity of skin take place. In the routine urine analysis the erhythrocyturia, cylindruria, leukocyturia, proteinuria detected. Specify an initial combination of antibiotics:
A. Carbenicillin, linkomycin
B. Ampicillin, oxacillin
C. Cephasolin, oxacillin
D. Ampicillin, gentamycin
E. Gentamycin, tobramycin.

6. In newborn of 6 day of life with hypothermia the signs of coloenteritis occurs (Klebsiella detected).Then, the pneumonia with impoverished auscultative signs and the rich mucopurulent sputum is diagnosed. The sclerema and icterity of skin take place. In the routine urine analysis the erhythrocyturia, cylindruria, leukocyturia, proteinuria detected. Choose the variant of patient’s feeding:
A. Breast feeding
B. Single feeding of adapted mixture with probe
C. Single feeding of breast milk with probe
D. Feeding from the bottle with adapted mixture
E. Feeding from the bottle with breast milk

7. In newborn of 6 day of life with hypothermia the signs of coloenteritis occurs (Klebsiella detected). Then, the pneumonia with impoverished auscultative signs and the rich mucopurulent sputum is diagnosed. The sclerema and icterity of skin take place. In the routine urine analysis the erhythrocyturia, cylindruria, leukocyturia, proteinuria detected..

What preparation is more fit to this case?

A. Antistaphylococcal plasma 10-15 mg/kg

B. Antiklebsiellic plasma 10-15 mg/kg

C. Antipyocyanic plasma10-15 mg/kg

D. Native plasma 10-15 mg/kg

E. Immunoglobulin human normal 1,5-2 doses.

8. In worn child of 8 day of life the necrotic phlegmon, destructive pneumonia, purulent otitis admitted. This state is accompanied by a serious toxicosis and the hyperthermia. In routine blood test are anaemia, trombocytopenia, hyperleucocytosis. Specify the ethiology of sepsis:

A. Staphylococcus

B. Streptococcus

C. Klebsiella

D. Pyocyanicrod

E. Campylobacter

9. In worn child of 8 day of life the necrotic phlegmon, destructive pneumonia, purulent otitis admitted. This state is accompanied by a serious toxicosis and the hyperthermia. In routine blood test are anemia, trombocytopenia, hyperleucocytosis. Specify the variant of sepsis course.

A Fulminant

B. Subacute

C. Lingering

D. Chronic

E. .Acute

10. In worn child of 8 day of life the necrotic phlegmon, destructive pneumonia, purulent otitis admitted. This state is accompanied by a serious toxicosis and the hyperthermia. In routine blood test are anemia, trombocytopenia, hyperleucocytosis. Classify sepsis according to entrance hiluses:

A. Dermal

B. Otogenic

C. Pulmonary

D. Cryptogenic

E. Iatrogenic

11. In newborn to 6 day of life on the right breech has appeared a crimsonly and cyanochroic spot up to 6cm in diameter and prominented above a surface of skin, dense and painful by touch. The condition of child gradually worsens. Determine the volume of local therapy.

A To put cuts in alternated lines within the limits of healthy tissues
B To put longitudinal cuts
C Application of a physiotherapy
D Application of bandages with a solution of Furacilinum
E Application of bandages with a normal saline solution.

12. In worn child in the age of 6 days on different sites of skin there are follow signs are observed: erythema, flaccid bubbles, erosive surfaces, cracks, exfoliation of false skin. The baby looks like scalded of boiled water. Nikolsky sign is positive. The general condition of child is serious. In examination the anxiety, hyperesthesia, febrile temperature. What is the most probable diagnosis?

A. Pseudofurunculosis of Figner
B. Phlegmon of newborn
C. Exfoliative dermatitis of Ritter
D. Pemphigus of newborn
E. Epidermolisis

13. To 5 day of life in the child who was born in time, with weight of 3200g, the body temperature has risen up to 37,5 began to take a mamma torpently. The child has been enclosed to a breast of mother to 3 day because of her postnatal endometritis. Objectively: child is active. On a skin of chest, stomach and hips the superficial flaccid bubbles 10 by number, diameter 5 - 10mm and with muddy contents are found out. Some from them have collapsed, thus the bright - pink surface was naked. On the part of internal bodies any changes are not present. In what department is necessary to direct the child for the subsequent intensive care?

A. Surgical
B. Observational
C. Pathology of newborns
D. Infectious
E. Reanimation

14. In child examination in the age of 2 weeks on the face and chest the small bubbles with a hyperemia around found out. The staining after Right of cellular elements from these bubbles has revealed the presence of eosinocytes. What from diagnoses are most probable?

A. Toxic erytheme
B. Heat rash
C. Pseuofurunculosis
D. Vesiculopustulosis
E. Ostiofolliculitis

15. In a girl to 7 day of life the enlargement of right mamma has appeared. In palpation right mamma is dense and child cries. The skin in a place of infiltration is bloodshote. The appetite is reduced. From channels of mamma the pus excretes. What is the most authentic pathology takes place?

A. Gynecomastia

B. Mastitis of newborn
C. Necrotic phlegmon
D. Sepsis of newborn
E. Transitional sexual crisis

16. In newborn child to third day of life on the thorax a painful spot with precise borders has appeared, red and dense, hot by touch, painful in palpation. Within several hours it has considerably increased in size, next day the color became cyanotic and crimson and there was a ramollissement in center. What is the most probable diagnosis?

A. Necrotic phlegmon of newborns
B. Pemphigus of newborn
C. Exfoliative dermatitis of Ritter
D. Pseudofurunculosis
E. Erysipilatous inflammation of newborns

17. In prematurely birth child on hip skin the vesicular rashes revealed. The general condition of child is unchanged. With what infectious agent it is possible to connect these changes?

A. Staphylococcus
B. Acyanotic spirochete
C. Streptococcus
D. Mycoplasma
E. Listeria

18. Child 20 days of life. Was born from the first pregnancy with a toxicosis of 2 half, the anhydrous period is 12 hours. Body weight in birth is 2900g, blood allocation from umbilical wound were marked. To 20 day vesicular and pustular rush appeared, and body temperature is increased. The child has been hospitalized. In hospitalization the state is serious. On a skin the pustular rush, crusts. In umbilical wound a hemorrhagic crust. In percussion on the right in subscapular area is an obtusion. In auscultation there is weakened respiration. Cardiac sounds are muffled, 160 per minute. The stomach is inflated, the liver is under edge of a costal arch on 4cm and lien on 1cm. Stool 5 - 6 times per day is liquid and yellow. What tests first of all are necessary to conduct in this case?

A. Bacteriological tests from locuses
B. Proteinogramme
C. Immunogramme
D. Coagulogramme
E. Routine blood analysis

19. In the child of 8 days of life on the right breech the crimson and cyanochroic stain in sizes of 3 x 5sm detected. The stain is above a surface of skin, dense and painful by touch. Mother informed that the child became flaccid, badly sucks, belchs and in a fever. What volume of antibacterial therapy must be administrated?

A. 2 antibiotics in the maximal doses

B. 1 antibiotic in a therapeutic dose
C. 1 antibiotic in the maximal dose
D. 2 antibiotics in therapeutic doses
E. There is no necessity for administration of antibiotics

20. In newborn of 5 day of life a vesicles on the skin of abdomen and extremities filled with serous and purulent liquid has appeared. The general state of the child has not changed. What etiology of these rashes?

A. Streptococcus
B. St.aureus
C Treponema pallidum
D. Herpes simplex virus
E. Listerias

Materials of the medical support for students' self prepapation: a reference chart for organization of students' independent work with educational literature.

Tasks	Instructions
To study the etilogy, epidemiology and risk factors of pyoinflammatory diseases in newborn inants.	- To enumerate basic etiologic factors of pyoinflammatory diseases in newborn infant; - Epidemiological links of pyoinflammatory diseases in newborn infant; - Features of immunologic reactions in newborn infant; - Risk factors of inflammatory pathology in newborn infant.
To study clinical manifestations of skins and subcutaneous fats diseases in newborn infant.	To select clinical symptoms, which can prove the probable diagnosis of pemphigus, exfoliative dermatitis, phlegmon of newborn, mastitis of newborn, catarrhal and festering omphalitis.
To study etiology, links of pathogenesis, pathomorphology of sepsis in newborns.	- etiology, features of causal organism, its dependency on infections period; - pathogenetic changes in sepsis; - risk factors of neonatal sepsis; - pathomorphology of sepsis.
To study clinic criteria of sepsis	- characteristic of early and late sepsis; - clinical manifestation of sepsis;

	- clinical manifestation of septi-copyemia with characteristic of festering focus, features of clinic, questions of differential diagnostic of hematogenous osteomyelitis, neonatal meningitis.
To study the main complications of sespsis	-septic shock; -characteristic features
To study diagnostic criteria of sepsis	To make investigational plan of newborn with sepsis
To study pathognomic changes of additional investigative methods	To recapitulate the main diagnostical criteria of sepsis according to the data of additional investigational methods
To conduct differential diagnostics, to establish a concluding diagnosis	To substantiate the basic components of diagnosis in accordance to modern classification, and to conduct a differential diagnosis.
To study main strights of neonatal sepsis' treatment.	a) ensuring of hemorrhagic stability and tissues oxigination; b) antibacterial therapy, starting scheme of antibacterial therapy; c) modulation of microorganisms reactivity; d) anticoagulant therapy; local treatment of festering seats.
To study the main questions of prophylaxis of pyoinflammatory diseases and sepsis in newborn infants	Prophylactic measures in prenatal and natal periods
To study methods of dispensary observations at newborn infants , which were endured sepsis	Observations of experts, divisional paediatrics, terms of grafting.

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