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Current course of measles in adults (a literature review)

Yu. Yu. Riabokon*^{1,A,E,F}, S. O. Bilokobyla^{1,2,B,D}, O. V. Riabokon^{1,B,C,D}

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Measles is a highly contagious acute infectious disease of viral etiology. Thanks to the widespread use of measles vaccine in the European Region in the early 2000s, WHO set a goal to achieve measles elimination. An essential feature of measles during the period of elimination was the predominance of cases among adults.

The purpose of the work is to analyze the literature data on the peculiarities of the current course of measles in adults.

According to the WHO, in 2017–2018 in Europe, including Ukraine, there was a significant increase in the number of people with measles. The rise in the incidence of measles in modern conditions is characterized by a change in the genotypes of circulating viruses. The data of modern medical literature show that a significant feature of measles outbreaks in recent years is the predominance of cases among adults, the incidence of measles among medical workers who were vaccinated against measles. The clinical picture of measles in adults remains typical; however, unlike measles in children, it is characterized by a greater incidence of complications.

The development of pneumonia and encephalitis is the most severe and life-threatening. Pneumonia is a frequent complication of measles in adults over 20 years of age, the incidence of which in adults, according to different studies, ranges from 14 to 66 %, but the most patients need oxygen therapy. The risk of measles encephalitis occurs during the rash onset and mortality rate depends on the age of patients in this complication: 25 % in adults versus 5 % in children. In adult patients with measles, liver damage is recorded much more often than in children, with the prevalence of cytolytic syndrome, sometimes with the development of jaundice, but is characterized by a benign clinical course. In the literature, there are reports of enteritis and pancreatitis development in patients with measles. Data on the course of measles in pregnant women warrant special attention due to such adverse effects as abortions, premature births, and stillbirths. Measles is a controlled infection, therefore vaccination, including adults, is the main focus in the fight against this disease.

Conclusions. In modern conditions, there is a high incidence of measles in adults, primarily due to the low level of community immunity. The prevalence of adults among measles patients is an important feature of this infection outbreak in recent years. The clinical picture of measles in adults retains typical symptoms, but the course is characterized by a high risk of a wide range of complications, the most severe of which are pneumonia and measles encephalitis. It is possible to achieve success in the fight against measles through the effective vaccination coverage.

Key words:

measles, diagnosis, complications.

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Сучасний перебіг кору в дорослих (огляд літератури)

Ю. Ю. Рябоконт, С. О. Білокобила, О. В. Рябоконт

Кір – висококонтагіозне гостре інфекційне захворювання вірусної етіології. Завдяки широкому застосуванню вакцинації проти кору в Європейському регіоні на початку 2000-х років ВООЗ поставила за мету елімінацію кору, тобто припинення місцевої циркуляції вірусу. Суттєвою особливістю кору в період її елімінації стало переважання дорослих серед тих, хто захворів.

Мета роботи – проаналізувати літературні дані щодо особливостей сучасного перебігу кору в дорослих.

За даними ВООЗ, у 2017–2018 роках у країнах Європи, зокрема в Україні, відзначено істотне зростання хворих на кір. Підйом захворюваності на кір у сучасних умовах характеризується зміною генотипів вірусів, які циркулюють. Дані сучасної фахової наукової літератури показують, що суттєвою особливістю спалахів кору в останні роки є переважання серед хворих дорослих, зокрема і медичних працівників, які щеплені проти кору. Клінічна картина кору в дорослих залишається типовою, але, на відміну від кору у дітей, вирізняється більшою частотою розвитку специфічних ускладнень.

Найтяжчим і загрозливим для життя пацієнтів ускладненням є розвиток пневмонії та енцефаліту. Пневмонія – часте ускладнення кору в дорослих, які старші за 20 років, частота розвитку в дорослих, за даними різних дослідників, коливається від 14 до 66 %, однак більшість пацієнтів потребують проведення оксигенотерапії. Ризик виникнення корового енцефаліту виникає в період появи висипу, при розвитку цього ускладнення летальність має залежність від віку хворого: 25 % у дорослих проти 5 % у дітей. У дорослих значно частіше, ніж у дітей, реєструють ураження печінки з переважанням цитолітичного синдрому, іноді навіть із появою жовтяниці, але характеризується доброякісним перебігом. Є також повідомлення про розвиток ентериту, панкреатиту у хворих на кір. Заслужують на особливу увагу дані щодо перебігу кору у вагітних: зафіксовані такі несприятливі наслідки, як аборт, передчасні пологи та мертвонародження. Кір – керована інфекція, тому головним напрямом боротьби з цією недугою є вакцинація, зокрема й дорослого населення.

Висновки. У сучасних умовах високий рівень захворюваності на кір у дорослих передусім пов'язаний із низьким рівнем популяційного імунітету. Переважання дорослих серед хворих на кір є суттєвою особливістю спалаху цієї інфекції в останні роки. Клінічна картина кору в дорослих зберігає типові ознаки, але перебіг характеризується високим ризиком ускладнень та їхнім широким спектром, найтяжчими є пневмонія та коровий енцефаліт. Досягти успіхів у боротьбі з кором можливо за умови проведення ефективної вакцинації.

Ключові слова:

кір, діагностика, ускладнення.

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Ключевые слова:

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С. 697–701**Современное течение кори у взрослых (обзор литературы)**

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Корь – высококонтагиозное острое инфекционное заболевание вирусной этиологии. Благодаря широкому применению вакцины против кори в Европейском регионе в начале 2000-х годов ВОЗ поставила цель достичь элиминации кори. Существенной особенностью кори в период элиминации стало преобладание взрослых среди заболевших.

Цель работы – проанализировать литературные данные об особенностях современного течения кори у взрослых.

По данным ВОЗ, в 2017–2018 годах в странах Европы, в том числе и в Украине, отмечено значительное увеличение числа больных корью. Подъем заболеваемости корью в современных условиях характеризуется изменением генотипов циркулирующих вирусов. Данные современной медицинской литературы показывают: существенной особенностью вспышек кори в последние годы является преобладание взрослых среди заболевших, отмечается заболеваемость медицинских работников, которые привиты против кори. Клиническая картина кори у взрослых остается типичной, однако, в отличие от кори у детей, имеет большую частоту развития осложнений. Наиболее тяжелым и угрожающим жизни пациентов осложнением является развитие пневмонии и энцефалита. Пневмония является частым осложнением кори у взрослых старше 20 лет, частота развития которой у взрослых, по данным разных исследований, колеблется от 14 до 66 %, однако большинство пациентов нуждаются в проведении оксигенотерапии. Риск возникновения коревого энцефалита возникает в период появления сыпи, при развитии данного осложнения летальность зависит от возраста пациентов: 25 % у взрослых против 5 % у детей. У взрослых значительно чаще, чем у детей, регистрируют поражение печени с превалированием цитолитического синдрома, иногда с развитием желтухи, однако характеризуется доброкачественным течением. В литературе есть сообщения о развитии энтерита, панкреатита у больных корью. Особого внимания заслуживают данные о течении кори у беременных, при котором зафиксированы такие неблагоприятные последствия, как аборт, преждевременные роды, мертворождения. Корь является управляемой инфекцией, поэтому главным направлением в борьбе с этим заболеванием является вакцинация, в частности, взрослого населения.

Выводы. В современных условиях высокий уровень заболеваемости корью взрослых связан с низким уровнем популяционного иммунитета. Преобладание взрослых среди заболевших корью – существенная особенность вспышки этой инфекции в последние годы. Клиническая картина кори у взрослых сохраняет типичные признаки, однако течение характеризуется высоким риском осложнений и широким их спектром, из которых наиболее тяжелыми являются пневмония и коревой энцефалит. Достичь успехов в борьбе с корью можно при условии проведения эффективной вакцинации.

Measles is a highly contagious infection of viral etiology with a significant risk of developing severe complications. Prior to the mandatory immunization, measles was exclusively a childhood infection and fatal cases of this infection were recorded between 5 million to 8 million in the world annually. The period before the start of the vaccination was characterized by the rise and fall of morbidity, high mortality, a higher proportion of infected children, cyclical changes in the annual dynamics. The development of specific immune prophylaxis of measles and its widespread introduction since 1967 allowed to reduce the incidence by 50 times and mortality rate by 2 times, however, the main determinants of the epidemic process remained [1,2].

Due to the widespread use of measles vaccine in the European region in the early 2000s, the WHO launched a global immunization campaign against measles aiming for a reduction in the local circulation of measles virus eliminating it by 2010 [3]. The elimination period was characterized by a further decrease in measles and variations of the main determinants of the epidemic process. During this period, due to the stable high collective immunity, quantitative changes in the parameters of the epidemic process transformed into qualitative. First of all, measles has been stopped considering as a childhood infection, epidemic centers have become predominant with isolated cases, seasonal factors have almost ceased to influence the epidemic process manifestation in the annual dynamics [2,4].

Aim

The purpose of the work is to analyze the literature data on the peculiarities of the modern course of measles in adults.

Despite some progress in addressing the issue of the measles elimination in the European region, in particular in Ukraine, the epidemic process remains rather intense, which does not allow the elimination of this infection [5]. Cyclical epidemic and local measles outbreaks suggest the accumulation of susceptible individuals as a consequence of immune prophylaxis defects in the previous years resulting in a decrease in postvaccinal immunity. In recent years, there have been several epidemic outbreaks of measles, in particular, 2005–2006, 2012–2014, 2017–2018 years. Serological studies in Ukraine regarding the definition of the most vulnerable adults among the population made it possible to allocate patients from 16 to 30 years, since only 78.1 % of the examined persons had immunity against measles, which coincided with the high percentage of this age group among patients with measles [6].

Due to the high contagiousness of measles, the level of collective immunity should be very high due to vaccination coverage of ≥ 95 % of the population. This will provide a sufficient level of community immunity to stop the circulation of endemic viruses and prevent their recurrence in case of spreading [5]. Taking into account the official definition of the term “elimination” [7] for verifying the measles elimination in the European Region, WHO is invited to apply the following criteria:

- the absence of endemic measles and rubella cases in all Member States for a period of at least 36 months from the last known case, due to complete interruption of endemic virus transmission;
- the presence of high-quality surveillance system that is sensitive and specific enough to detect, confirm and classify all suspected cases;
- genotyping evidence that supports the interruption of endemic transmission.

For timely diagnosis of measles, suspicious clinical cases with symptoms that meet the criteria for clinical diagnosis of measles should be considered: fever, maculo-papular rash, cough, drowsiness, conjunctivitis. All suspected cases have to be investigated and classified based on clinical, laboratory and epidemiological data as one of the following [8]:

- laboratory confirmed case of measles: a suspected case which meets the laboratory criteria for measles case confirmation;

- epidemiologically confirmed case of measles: a suspected case which has not been adequately tested by laboratory and which was in contact with a laboratory-confirmed measles case 7–18 days before the onset of rash;

- clinically compatible case of measles: a suspected case which has not been adequately tested by laboratory and has not been epidemiologically linked to a confirmed measles case.

In Ukraine, the system of laboratory confirmation of measles cases was introduced in 2005. Patients with suspected measles were laboratory confirmed in 76.9 % of cases during the epidemic threshold increase in 2006. Epidemiological surveillance of this infection continues with the increase in the measles incidence. Reducing this indicator against the backdrop of 100 % laboratory confirmation of measles cases will be considered effective [9].

According to the WHO, in 2017–2018 in Europe, in particular in Ukraine, there was a significant increase in measles patients. The increase in measles morbidity in modern conditions is characterized by a change in the genotypes of circulating viruses with the predominance of the B3, D8 and D9 genotypes, in contrast to the predominance of the genotype D6 in the early 2000's [10, 11]. It should be noted that the genotype B3 is imported into European countries from Africa, located to the south of the Sahara, where its circulation is endemic. Thus, since 2016, in Belgium, France, Italy, Romania, Bulgaria, Portugal, and the United Kingdom along with the circulation of the D8 genotype, a significant number of patients with the B3 genotype of measles virus have been identified [12, 13]. From 2005–2006, in Europe, there were also sporadic cases of measles due to another imported virus D4 genotype. This genotype is endemic for India, Eastern and Southern Africa, and the Middle East [14]. The effectiveness of post-vaccinal immunity against measles in relation to the level of viruses with different genotypes neutralization by post-vaccine antibody response is still an open question [4, 15].

An important feature of the measles outbreaks in recent years is the prevalence among adult patients in the typical clinical picture of measles. In Germany, a percentage of adult patients with measles was 52 % [16], in Italy, 73% of measles patients were older than 15 years [17], in Belgium, 50 % of patients were over 15 years old [18]. The predominance of adults among patients with measles is noted not only in European countries. Thus, in Sri Lanka, the proportion of patients between 12 and 29 years old was 73.3 % [19], and in Japan, older adults aged 15 to 29 years accounted for 45 % [20] of the total number of patients with measles. In addition, a large number of nosocomial transmission of infection was noted among healthcare workers, especially in those cases when measles patients came to hospitals in the prodromal period of the disease, as well as in cases of severe complications with an atypical course [12, 17]. Analyzing cases of measles in healthcare

workers, it was found that cases of measles also occurred in previously vaccinated individuals [21].

Statistical data on the incidence of measles in different age groups of patients varies in different studies, which is probably due to the analysis of hospitalized patients. At the same time, indications for hospitalization vary around the world. However, almost all studies demonstrate the dependence of complications frequency and their spectrum on patients' age. Children of the first year of life and adults often have a complicated course of the disease [10, 18]. In Ukraine [10], during the outbreak of measles in 2017–2018, the incidence of severe cases among hospitalized children of the first year of life was 16,7 %, at the age of 1–2 years it was 23.1 %, at the age of 2–5 years – 17.8 %, it was the lowest in the age group of 6–11 years, and the highest it was in the age group of children older than 12 years – 21.3 %. It should be noted that 82.9 % of complications in children were associated with respiratory system [10].

To date, mechanisms of the complications development in patients with measles are studied. The risk for the development of measles complications correlates with the immunosuppression severity, which develops in patients with measles. However, measles is paradoxically associated with the induction of a strong virus-induced specific immunity which is life-long [22]. Mechanisms of immunosuppression remain insufficiently cleared. A suppression of hemopoiesis, violations of lymphocytes proliferation and immunological memory, destruction of the epithelial barrier, etc. are considered by researchers among key links [22–25].

Pneumonia is one of the frequent and severe complications of measles with the rate of development, according to various authors, varying from 14 to 66 % [18, 26, 27]. The literature suggests that pneumonia is a frequent complication of measles in adults older than 20 years, but the frequency of pneumonia in adult patients with measles varies according to different researchers. At sporadic incidence of measles, the authors recorded a high incidence of cases – 57.1 % (8 out of 14) with the development of pneumonia in adults with measles [28]. During the outbreak of measles, Spanish researchers diagnosed pneumonia in 15.3 % of patients [29], Italian authors – in 26 % of patients [30], and French researchers reported the development of pneumonia in 20.6 % of hospitalized adults, the proportion of pneumonia cases increased with age, reaching 28.8 % in adults over 30 years of age [31]. In another French study [32], the development of pneumonia was noted in 31% of adult patients with measles, 72 % of whom needed oxygen therapy. In Ukraine, in 2017–2018, the analysis of measles complications in the military showed the development of pneumonia in 20 % of cases, while in the cohort study patients with measles had a mild-to-moderate course [14]. All while, the researchers noted that pneumonia was suspected in these patients with measles based on the presence of decreased breath sounds in the lower lung fields in the absence of wheezing, and confirmation of it required not only a chest X-ray examination in a number of cases, but also a computer tomography [14]. At the same time, the frequency of pneumonia in children was 4.5 % during the period of measles outbreak in 2017–2018, while the vast majority of these children was over 12 years old [10].

Measles encephalitis is primary and occurs during the period of rash in 1–3 per 1000 infected persons. The

pathogenetic mechanisms of this complication development have not been fully understood, but onset at the early phase suggested a primary viral invasion of neurological cells, which was confirmed by detection of measles virus RNA in the cerebrospinal fluid followed by chemokine induction and lymphocytic infiltration [33]. The mortality rate reaches 15 % in measles encephalitis and is dependent on patients' age: measles encephalitis-associated mortality is 5 % in children and 25 % in adults. One in four patients endures severe postencephalitic neurological damage [33].

The liver involvement in measles is most common among children older than 15 years of age and adults. In the examination of 140 patients with measles, the development of hepatitis manifested by a cytolytic syndrome without clinical symptoms was observed only in 1.4 % of patients aged 15 and 17 years [10]. In modern scientific literature there is little information about the liver damage in adults with measles, but they all indicate a high incidence of hepatitis in adult measles patients [14,34–36]. Analysis of the course of measles in 65 adults in the 1980s allowed the authors to show the dependence of hepatitis frequency on the disease severity [35]. In the 1990s, Mexican researchers analyzing the course of measles in 201 adults recorded hepatitis in 45 % of patients [36]. In conditions of the current course of measles, the development of hepatitis in adult patients, most authors note much more often the liver damage [14,34]. In the work of French researchers [34], the analysis of measles course in 80 adult patients with a mean age of 30.1 years showed 81 % of hepatitis patients with ALT elevation and in some patients up to a significant level, namely 5 times more than normal in 22.2 % and 10 times more – in 6.2 % of patients. Development of hyperbilirubinemia was noted in 4 % of patients. However, there was no link between the hepatitis incidence and the severity of measles course or the development of bacterial complications in this work. Based on this, the authors considered the development of hepatitis in adult patients with measles as a manifestation of the disease, but not its complication [34]. In the study [14] included examinations of 30 soldiers with measles, a cytolytic syndrome was observed in 60 % of patients, while the severity of measles course was mild-to-moderate.

In the severe course of measles in adults, other gastrointestinal complications are recorded, so, enteritis occurs in 8 % of patients [14]. In the literature, there are a few reports of pancreatic lesion. According to [37], pancreatitis was observed in 1.1 % of patients, and according to [32] – in 2.5 % of adult patients with measles. There is report of Mexican scientists about gastrointestinal complication such as upper gastrointestinal bleeding in 13 % of measles patients [36].

Increasing the incidence of measles among adults leads to a more frequent occurrence of the disease in pregnant women. It is known that measles virus has no teratogenic effect, but measles in pregnant women increases the risk of premature birth and the development of complications [38]. Observations of recent years demonstrated spontaneous abortions or stillbirths in pregnant women with measles [20]. The analysis of the measles course in 4 pregnant women revealed hepatological complication in one case and pulmonary complications and premature births in the other patients [18]. Some authors also reported about complications in pregnant women with measles such as a

miscarriage, stillbirth, low birth weight, preterm birth prior to 37 weeks gestation [14].

Etiotropic treatment of measles is not developed. In the modern scientific literature, there are some reports about the efficacy of ribavirin and high doses of vitamin A in the treatment of patients with severe and complicated course of measles [39,40]. In a few reports about measles meningoencephalitis, researchers described an empirical use of acyclovir in the treatment of this severe complication, but this did not influence the disease outcome [10].

Measles is a managed infection, so vaccination coverage including the adult population (especially under the age of 30 years) is the most important in this disease control [41–43]. The WHO Strategic Advisory Group on Immunization, after a detailed analysis of scientific data on the biological and technical capabilities of measles elimination, concluded that global measles elimination is biologically justified and cost-effective. The measles should be eliminated by vaccination and integrated surveillance of fever and rash [41,42].

Conclusions

1. In modern conditions, in the period of measles elimination in the European region, there is a high incidence of measles in adults due to the low level of community immunity and changes in virus strains currently circulating.

2. The prevalence of adults among measles patients is an important feature of this infection outbreak in recent years. The clinical picture of measles in adults retains typical signs, but the course is characterized by a high risk of a wide range of complications, the most severe of which are pneumonia and measles encephalitis.

3. It is possible to achieve success in the fight against measles through the effective vaccination coverage at least 95 % of the population including adults.

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