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CARDIOVASCULAR DISEASES

(«INTERNAL MEDICINE». MODULE 2)

Topics for self-education of students

PART 2

The executive task force for students of medical faculty of 5th cource

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Cardiovascular diseases («Internal Medicine». Modul 2). Topics for self-education of students. Part 2=Серцево-судинні захворювання («Внутрішня медицина». Модуль 2). Теми для самостійної роботи студентів. Ч. 1 : The executive task force for students of 5th course of medical faculty / A. E. Berezin. – Zaporizhzhia : ZSMU, 2018. – 135 p.

The executive task force is provided for students of 5th courses of medical faculties for helping to study of some topics in the fields of cardiovascular diseases incorporated into the discipline «Internal Medicine». There is the information about the most important topics regarding diagnosis of cardiac diseases.

Content

List of abbreviations

ANP	atrial natriuretic peptide
AR	aortic regurgitation
BNP	brain natriuretic peptide
BP	blood pressure
DCM	dilated cardiomyopathy
ECG	electrocardiogram
EF	ejection fraction
HF	heart failure
LV	left ventricle
MR	mitral regurgitation
NT-proBNP	N-terminal brain natriuretic peptide
OHCM	obstructive hypertrophic cardiomyopathy
PE	pulmonary thromboembolism
RA	right atrial
RCM	restrictive cardiomyopathy
RV	right ventricle
SVT	supraventricular tachycardia
WPW	Wolf-Parkinson-White

1. **Topic 5. Practical skills for the topic №9 «Myocardities and cardiomyopathies»**

After implementation into routine clinical practice the endomyocardial biopsies diagnosis of myocarditis could be established during life of the patients. Multiple infectious etiologies (Table 1) have been implicated as the cause of myocarditis, with the most common being viral, specifically, Coxsackie B. In the majority of patients, active myocarditis remains unsuspected because the cardiac dysfunction is subclinical, asymptomatic, and self-limited.

Table 1: Causes of Myocarditis

Main reasons	Type of causes	Examples
Infectious	Viral	Coxsackie virus, echovirus, HIV, Epstein-Barr virus, influenza, cytomegalovirus, adenovirus, hepatitis (A and B), mumps, poliovirus, rabies, respiratory synctial virus, rubella, vaccinia, varicella zoster, arbovirus
	Bacteria	Cornyebacterium diptheriae, Streptococcus pyogenes, Staphylococcus aureus, Haemophilus pneumoniae, Salmonella spp., Neisseria gonorrhoeae, Leptospira, Borrelia burgdorferi, Treponema pallidum, Brucella, Mycobacterium tuberculosis, Actinomyces, Chlamydia spp., Coxiella burnetti, Mycoplasma pneumoniae, Rickettsia spp.
	Fungi	Candida spp., Aspergillus spp., Histoplasma, Blastomyces, Cryptococcus, Coccidioidomyces
	Parasites	Trypanosoma cruzii, Toxoplasma, Schistosoma, Trichina
Noninfectious	Drugs causing hypersensitivity reactions	Antibiotics: sulfonamides, penicillins, chloramphenicol, amphotericin B, tetracycline, streptomycin
		Antituberculous: isoniazid, para-aminosalicylic acid
		Anticonvulsants: phenindione, phenytoin, carbemazepine
		Anti-inflammatories: indomethacin, phenylbutazone
		Diuretics: acetazolamide, chlorthalidone, hydrochlorothiazide, spironolactone
		Others: amitriptyline, methyldopa, sulfonylureas
	Drugs not causing hypersensitivity reactions	Cocaine, cyclophosphamide, lithium, interferon alpha
	Nondrug causes	Radiation, giant-cell myocarditis

Endomyocardial biopsy is essential for definite diagnosis of idiopathic myocarditis. However, since endomyocardial biopsy is guided by fluoroscopy, whether or not the diseased myocardium is biopsied depends on chance, and this may lead to

misdiagnosis. If the endocardial surface represents changes indicative of stages of myocarditis, staging of myocarditis and targeted cardioscope-guided biopsy could be used for accurate histological diagnosis. Histologic evidence of myocarditis following traumatic death is identified in 1 to 3 percent of autopsies, suggesting that the frequency of myocarditis is underestimated by analyzing data only from symptomatic patients

Pathogenesis

Infection by cardiotropic viruses prompted the initial hypothesis that the viral infection was responsible for myocardial injury. However, several investigators noted that cardiac dysfunction increased after the eradication of the infective agent and speculated that the pathogenesis may be due to the immunologic responses initiated by the virus. Support for this theory comes initially from the work of Woodruff, who noted that the histologic evidence of cardiac injury in Coxsackie B infection occurred only after the virus was no longer detectable in the myocardium. Subsequently, demonstration of T-lymphocyte and macrophage infiltration, perforin granules, and a variety of cytokines known to depress myocardial contractility in endomyocardial biopsies of patients with active carditis strengthened the concept of immune-mediated injury. Furthermore, immunosuppressive therapy in animal models attenuated inflammation-with improved survival, less cellular infiltrate, and less necrosis. The specific immune responses that lead to the myocardial injury are incompletely defined. A murine model of myocarditis induced by coxsackie B has provided some insight into immunologic sequence of events. Following infection with coxsackie B3 virus, macrophages are present in the infiltrate until day 8. After macrophage activity decreases, both effector (CD8) and helper (CD4) T cells are identified within myocardial lesions. At peak infiltration, some murine strains showed a predominance of CD8-positive cells while in others CD4 cells predominate, suggesting participation of both humoral- and cell-mediated immune responses. In human subjects, T-lymphocyte and macrophage infiltration characterizes the immunohistochemical picture, whereas B lymphocytes and natural killer cells are absent. T-lymphocyte subset analysis of human serum does not demonstrate consistency in dominance of CD4 or CD8 cells. The

mechanisms of injury when lymphocytes infiltrate the myocar-dium are unknown. In the murine model, messenger ribonucleic acid (m-RNA) of perforin, the pore-forming protein mediating cytotoxicity, was identified in cytoplasmic granules of in-filtrating cells by in situ hybridization. Similarly, biopsy samples from patients with active myocarditis contain perforin granules in infil-trating cells, implying that direct cytotoxicity can occur. Alternatively, release of cytokines such as interleukin-1, inter-leukin-6, interleukin-8, and tumor necrosis factor alpha may cause reversible depres-sion of myocardial contractility without resulting in cell death. Therefore, the effect of T cell-mediated immune injury may be either irreversible as a result of cell death through cytotoxicity (perforin) or reversible as a result of injury mediaed by cyto-kines. A marked reduction in myocardial cell damage is noted in T cell-depleted mice inoculated with encephalomyocarditis virus. Antiheart antibodies in the serum of pa-tients with myocarditis have been reported but may reflect nonspecific myocardial damage. When serum from patients with myocarditis was screened for autoantibo-dies, high-titer immunoglobulin G (IgG) with cardiac specificity was detected in 59 percent of patients with myocarditis and in none of the normal samples. Antibodies with specificity for contractile and energy-transport proteins have been identified. In sera from patients with active myocarditis, Western immunoblotting demonstrated reactivity of a fraction that includes antibody to the heavy chain of cardiac myosin. In a murine myocarditis model, cardiac myosin antibodies are observed following cox-sackie B virus infection. Moreover, injection of cardiac antimyosin antibodies with-out infection results in myocarditis that is histologically similar to that seen following coxsackie B3 virus infection. The role of viral infection has been deemphasized fol-lowing the popularization of the immune injury hypothesis. Viral infection is the trig-ger for the immune response that is deleterious. Attempts to culture virus from human myocardial tissue generally have been unsuccessful. Only a single case report of Coxsackievirus identified in a myocardial biopsy specimen in an adult has been de-scribed. However, identification of viral genomic fragments in myocardial samples by in situ hybridization and polymerase chain reaction from patients with myocarditis and dilated cardiomyopathy have been reported. These genomic fragments may not

be capable of replicating as intact cardiotropic virus but probably serve as a persistent source of antigen to drive the deleterious immune responses. In addition to the tropism of the virus, host immune responses play an important role in determining the severity of the clinical disease. When quantitative peripheral T- and B-lymphocyte populations were analyzed in patients with dilated cardiomyopathy and myocarditis, no consistent changes were detected. However, immunologic assays demonstrate a reduction in the function of natural killer cells, antibody-dependent cellular cytotoxic cells, and suppressor cells and an increase in circulating levels of interleukin-1 and tumor necrosis factor alpha. These immunoregulatory defects may predispose the host with a high antigenic load to develop immune responses that are not modulated by the natural inhibitory immunoregulatory mechanisms. In addition to chronic inflammatory immune mechanism or persistent viral infection, apoptotic cell death may be another mechanism by which myocarditis can result in cardiomyopathy. Several different viruses have been reported to be triggers for apoptosis.

The association between acute myocarditis and dilated cardiomyopathy has been recognized for the past two centuries. However, the link between these two diseases remains circumstantial. Autoreactive antibodies and interleukin-2 receptors are identified commonly in both patients with myocarditis and those with dilated cardiomyopathy. Serologic titers to cardiotropic viruses are more common in patients with cardiomyopathy than in normal subjects. Viral genomic material can be detected more frequently by polymerase chain reaction (PCR) in patients with dilated cardiomyopathy versus other cardiac diseases. Animal models of myocarditis can progress to dilated cardiomyopathy, as can patients with clinically suspected or biopsy-proven myocarditis. However, the percentage of patients with idiopathic dilated cardiomyopathy that represent the end stage of an active myocarditis is unknown.

Cardiomyopathy is literally defined as a "disease of heart muscle." Goodwin first proposed a clinicopathological classification of cardiomyopathy designed to assist in the differential diagnosis of heart failure in 1964 and further modified it in 1972. Categories included dilated (congestive, fibrotic), hypertrophic, and restrictive categories, and their use has proven valuable in identifying etiological factors, deter-

mining prognosis, and planning treatment. Nonetheless, some have considered even this system too complex; in 1970, it was suggested that the cardiomyopathies were in danger of being classified into oblivion. Certainly, any attempt to classify any disease into subcategories should remain as simple as possible. At the same time, it is absolutely essential that any classification be meaningful if it is to be useful.

WHO's first proposal to classify cardiomyopathies and thus develop "order from chaos" was published in 1968; this document suggested that the term "idiopathic cardiomegaly" be used for cardiomyopathies. This definition was easily applicable in developing countries but did nothing to facilitate an understanding of heart muscle disease in either these developing countries or in more medically sophisticated societies. In 1980, WHO/ISFC followed this initial effort by recommending that cardiomyopathies be divided into "cardiomyopathy," in which the causes were unknown, and "specific heart muscle diseases," in which a definite etiology could be identified.

Specific cardiotoxic agents such as viruses and chemicals produce heart muscle disease and dysfunction and thus by definition, cardiomyopathy. In 1982, only 10 345 deaths in 410 000 days of hospital care were attributed to cardiomyopathy; this illustrates the difficulty of applying this nomenclature generally.

WHO/ISFC now suggests that the cardiomyopathies be "defined as diseases of the myocardium associated with cardiac dysfunction" and that they be "classified by the dominant pathophysiology, or, if possible, by etiologi-cal/pathogenetic factors." Thus, cardiomyopathies would be pathophysiologically classified as dilated, hypertrophic, restrictive, and arrhythmogenic right-ventricular cardiomyopathies. The term "specific cardiomyopathies" is now used to describe heart muscle diseases that are associated with specific cardiac or systemic disorders." Disease categories include ischemia, valvular heart disease, inflammatory cardiomyopathy, metabolic cardiomyopathy, general system disease, muscular dystrophies, neuromuscular disorders, sensitivity and toxic reactions, and peripartal cardiomyopathy.

It is not clear why the WHO/ISFC definition of cardiomyopathy was ever restricted to heart muscle diseases of unknown cause. All cardiomyopathies have causes, regardless of whether the specific etiology can be identified. The limitations of

this initial restriction have been recognized and removed. However, it is now just as unclear why the use of the term "cardiomyopathy" should be restricted only to heart muscle disease associated with cardiac dysfunction. While the clinicopathological classification of dilated, hypertrophic, and restrictive cardiomyopathy is useful in formulating differential diagnoses and selecting therapeutic regimens, the classification only recognizes the advanced stages of the cardiomyopathic process.

The classification process must remind both clinician and clinical investigator that cardiomyopathy is present before the cardiac anatomy and physiological function are altered and that the cardiomyopathic process begins with the first diseased myocardial cell(s), which in 1996 and beyond may be subject to therapeutic salvage or treatment. Yet, the WHO/ISFC definitions would not permit recognition of the process of geometric remodeling in a hypertensive individual's heart as cardiomyopathic. A parallel situation using coronary artery disease as the disease process would be the failure to recognize that the heart of a 45-year-old, overweight, smoking, hypercholesterolemic man with a strong family history of coronary artery disease is likely to be atherosclerotic until myocardial infarction has occurred.

Cardiomyopathy and clinical heart failure are closely linked. However, heart failure is but one possible clinical outcome of cardiomyopathy. The recognition of latent cardiomyopathy may well allow therapeutic intervention designed to delay or prevent the development of clinical heart failure. For example, the realization that latent or early cardiomyopathy may be present in the hypertensive individual, despite the absence of symptoms or clinical evidence of cardiac dysfunction, should be a strong indicator for antihypertensive therapy to prevent the development of advanced hypertensive cardiomyopathy that would lead to clinical heart failure.

The listing of specific cardiomyopathies is too limited to reflect current understanding of the causes of heart muscle disease. Surprisingly, there is no category to cover heredofamilial cardiomyopathy. Although this etiological consideration of a genetic basis overlaps categories such as neuromuscular disorders, the absence of such a category ignores the vast amount of progress in understanding the molecular biological basis of cardiomyopathy. Also missing from the classification scheme is a

category of hyperergopathic cardiomyopathy (cardiomyopathy of overwork, pathological hypertrophy, cardiac remodeling). This hypertrophic process occurs in virtually all the other cardiomyopathies, once sufficient myocardial damage results from the initial insult. Finally, the classification does not include the descriptive category "idiopathic." Clearly, certain patients presenting with heart failure cannot be specifically diagnosed regarding the etiology of the underlying cardiomyopathy, nor should the treating physician apologize for using the term "idiopathic." In fact, use of the term should encourage investigators to explore possible new etiologies and develop better tests for those already identified.

WHO/ISFC now defines ischemic cardiomyopathy as "a dilated cardiomyopathy with impaired contractile performance not explained by the extent of coronary artery disease or ischemic damage." This would appear to represent a contradiction in terms; if myocardial dysfunction cannot be explained by the extent of ischemia, how, then, can the etiology be attributed to ischemia? The intent of the original description by Burch et al in 1970 was not to limit the definition of ischemic cardiomyopathy to unexplained factors but rather to define the disease as heart muscle damage resulting from inadequate perfusion of the myocardium relative to metabolic demands, usually due to obstructive changes in the coronary circulation. Myocardial ischemia produces biochemical abnormalities and significant resultant cellular dysfunction even when ischemia is not prolonged or severe enough to produce myocardial necrosis in the well-described processes of myocardial hibernation and stunning. Technically, ischemic cardiomyopathy begins with the onset of excessive cellular anaerobiosis and eventually encompasses a broad spectrum of disease.

Although many cases of cardiomyopathy are clearly pluricausal (eg, is-chemia and diabetes mellitus), the WHO/ISFC classification does not allow for such multiple etiologies. Again, analogous to the pathogenesis of atherosclerosis, multiple risk factors may be present for the development of cardiomyopathy.

As recommended previously, cardiomyopathy should be defined simply as diseases of heart muscle. The natural progression of the disease should be recognized by establishing potential (latent), early, and advanced clinical categories. The knowled-

geable physician will understand that the pathophysiological process is a continuum and that the final expression may be characterized as dilated, hypertrophic, nondilated, none-hypertrophic (restrictive), and so forth. Thus the presence of clinical dysfunction represents a late stage in the development of cardiomyopathy, and therapeutic emphasis should be on prevention or early interruption of the pathophysiological process. The classification scheme also should emphasize that the cardiomyopathies may be multifactorial.

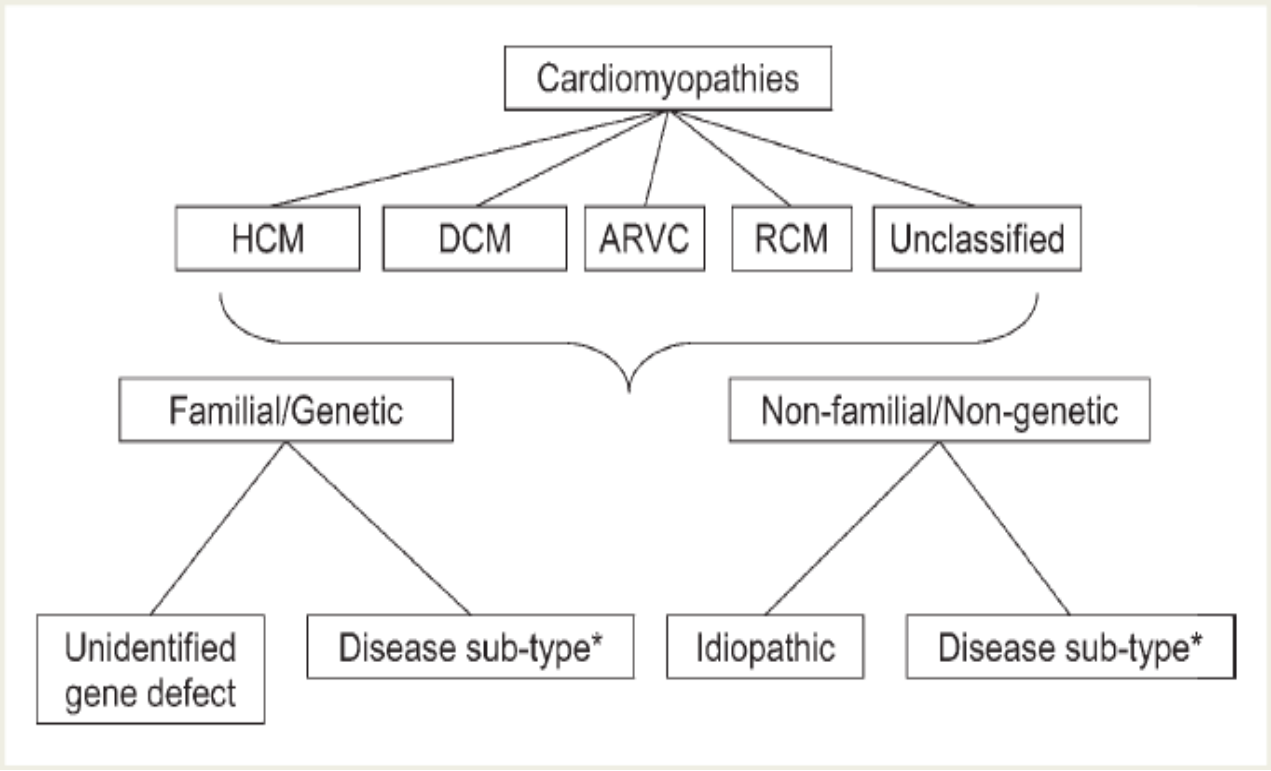
At least three additional categories should be added to the classification scheme: heredofamilial, hyperergopathic (overwork), and idiopathic. On the one hand, these represent recognition of the vast progress made in understanding the basis and progression of many cardiomyopathies and, on the other, allow for the classification of cardiomyopathies that have eluded the diagnostic and investigative processes. The process of progression should be reemphasized among the etiological/pathogenetic factors. For example, ischemic cardiomyopathy begins with the first episode of myocardial ischemia (clinically apparent as angina or silent) and ends with terminal heart failure or sudden death.

Progress reclassifying the cardiomyopathies has been slow. The current WHO/ISFC Task Force is certainly to be congratulated for making substantive changes and for recognizing that the classification process is dynamic. Nevertheless, it is time now to finish the course and remove the remaining stumbling blocks the current classification places in the way of the investigation, diagnosis, and treatment of this important group of diseases. The treatment of asymptomatic and early myocardial dysfunction has already been shown to benefit patients. Ideally, we will soon be conducting clinical trials to investigate the treatment of specific cardiomyopathies rather than the end-stage processes of heart failure and sudden death.

When the classification system for cardiomyopathies was originally con-ceived, the lack of knowledge about the underlying cause and pathophysiology of different types of cardiomyopathy was recognized, but there was an implicit assumption that they were distinct entities. Cardiomyopathies were defined as primary myocardial disorders of unknown cause; heart muscle disorders of known aetiology or associated

with systemic disorders were classified as secondary or specific heart muscle diseases. With the passage of time, the distinction between primary and secondary heart muscle disease has become increasingly tenuous, as the aetiology of previously idiopathic disorders has been discovered. Recently, an expert committee of the American Heart As-sociation proposed a new scheme in which the term primary is used to describe diseases in which the heart is the sole or predominantly involved organ and secondary to describe diseases in which myocardial dysfunction is part of a systemic disorder. However, the challenge of distinguishing primary and secondary disorders in this way is illustrated by the fact that many of the diseases classified as primary cardiomyopathies can be associated with major extra-cardiac manifestations; conversely, pathology in many of the diseases classed as secondary cardiomyopathies can predominantly (or exclusively) involve the heart.

The contemporary classification of cardiomyopathies are reported Figure 1.



Notes: ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy

As many cardiomyopathies are caused by mutations in genes that encode various cardiac proteins, an alternative approach is to reclassify cardiomyopathies ac-

cording to the causative genetic defect. However, in clinical practice the pathway from diagnosis to treatment rarely begins with the identification of an underlying genetic mutation; more usually, patients present with symptoms or are incidentally found to have clinical signs or abnormal screening tests. Even when the genetic defect is known in a family, the identification of clinically relevant disease in gene-carriers still requires the demonstration of a morphological phenotype. Thus, we believe that a clinically oriented classification system in which heart muscle disorders are grouped according to ventricular morphology and function remains the most useful method for diagnosing and managing patients and families with heart muscle disease.

The cardiomyopathies are an important and complex group of heart muscle diseases with multiple etiologies and heterogeneous phenotypic expres-sion. Awareness and knowledge of these diseases in both the public and medical communities have historically been impaired by periodic confusion surrounding definitions and nomenclature. Therefore, formal and systematic classifications have traditionally been viewed as useful exercises promoting greater understanding of the heart muscle diseases. Indeed, a multitude of such cardiomyopathy classifications have been advanced over the years by individual investigators and consensus panels sanctioned by medically related organizations such as the World Health Organization (WHO).

By virtue of these novel insights into the morphological and functional expression of the heart muscle diseases, older entrenched disease definitions and classifications are no longer relevant. In particular, the popular clinical classification for cardiomyopathies of "hypertrophic-dilated-restrictive" poses major limitations by mixing anatomic designations (ie, hypertrophic and dilated) with a functional one (ie, restrictive) into the same construct, and this classification probably should be abandoned. An example of confusion in nomenclature caused by "mixed phenotypes" arises with regard to hypertrophic cardiomyopathy (the most common of the purely genetic cardiomyopathies), given that this disease may appear in 2 or all 3 of the categories. Hypertrophic cardiomyopathy is characterized by left ventricular hypertrophy, is usually restrictive in the sense that impaired diastolic filling is a common and impor-

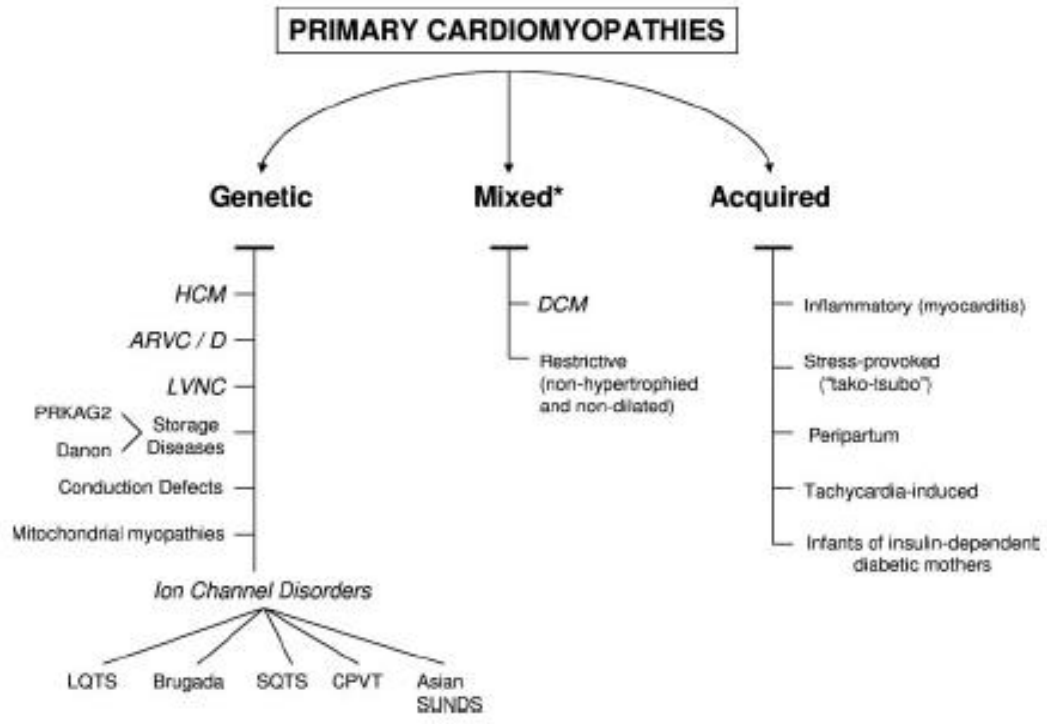
tant disease component, and furthermore may evolve into a dilated phase with systolic dysfunction as part of a remodeling process. Similarly, amyloid and other infiltrative cardiomyopathies do not adopt uniformly static phenotypic expression, and as part of their natural history they may evolve from a nondilated (often hyperdynamic) state with ventricular stiffness to a dilated form with systolic dysfunction and heart failure.

In addition, it is often difficult to reliably distinguish dilated from nondilated forms of cardiomyopathy given that quantitative assessments of ventricular chamber size represent a continuum and patients can vary widely in their degree of cavity enlargement (often deviating only slightly from the upper limits of normal). Indeed, such ambiguities may also arise with regard to some rare and/or newly identified cardiomyopathies for which few quantitative cardiac dimensional data are available. In other conditions, such as stress (tako-tsubo) cardiomyopathy and the transient cardiomyopathy in infants of diabetic mothers, the dynamic remodeling that occurs with clinical recovery substantially changes (and normalizes) cardiac morphology. Finally, the pure form of restrictive (nonhypertrophied) cardiomyopathy is extraordinarily rare and should not be confused with the myriad of myocardial diseases that have a component of restrictive physiology, usually with associated left ventricular hypertrophy (such as hypertrophic cardiomyopathy).

The proposed definition of cardiomyopathies offered by the AHA expert consensus panel is as follows: "a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction, which usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation, due to a variety of etiologies that frequently are genetic. Cardiomyopathies are either confined to the heart or are part of generalized systemic disorders, and often lead to cardiovascular death or progressive heart failure–related disability." This definition of cardiomyopathies, similar to that reported by the European Society of Cardiology (ESC), under the auspices of the Working Group on Myocardial and Pericardial Diseases, excludes myocardial involvement secondary to coronary artery disease, systemic hypertension, and valvular and congenital heart disease. Primary cardiomyopathies (ie, those solely

or predominantly confined to heart muscle) are shown in the Figure 2 from the AHA classification.

Figure 2: AHA classification model for primary cardiomyopathies



Notes: (disease processes solely or predominantly confined to the working myocardium). These conditions are segregated according to their genetic or nongenetic acquired etiologies in accord with contemporary definitions.

*Regarded as predominantly nongenetic on the basis of current knowledge, ie, familial disease has been reported in only a minority of cases. ARVC/D indicates arrhythmogenic right ventricular cardiomyopathy/dysplasia; CPVT, cate-cholaminergic polymorphic ventricular tachycardia; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LQTS, long QT syndrome; LVNC, left ventricular noncompaction; SQTS, short QT syndrome; and SUNDS, sudden unexplained nocturnal death syndrome.

Clinical Presentation of myocarditis and cardiomypathies.

The clinical manifestations of myocarditis are variable. Most patients have a self-limited disease, whereas others present in profound cardiogenic shock. The most obvious symptom suggesting myocarditis is an antecedent viral syndrome. Flu-like symptoms occur in approximately 60 percent of patients.Chest pain may occur in up

to 35 percent of patients and may be typically ischemic, somewhat atypical, or pericardial in character. Occasionally patients will present with a clinical syndrome identical to an acute myocardial infarction, with left ventricular asynergy, electrocardiographic evidence of injury or Q waves, and ischemic cardiac pain. In this syndrome, at autopsy, the coronary arteries are widely patent, although viral coronary arteritis has been reported. Coronary vasospasm has also been associated with acute myocarditis. Patients may present with syncope or palpitations with atrioventricular (AV) block or ventricular arrhythmia. Complete AV block is common with some patients presenting with Stokes-Adams attacks. The complete heart block is generally transient and rarely requires a permanent pacemaker. Sudden cardiac death can be the initial presentation of myocarditis in some patients, presumably from complete heart block or ventricular tachycardia. In a 20-year review of sudden death among Air Force recruits, 20 percent had myocarditis documented at autopsy. In some patients with refractory ventricular arrhythmias, endomyocardial biopsy or autopsy has revealed myocarditis. Systemic or pulmonary thromboembolic disease is also associated with myocarditis. A familial tendency for the development of myocarditis may be present. In one report, a suppressor cell defect was detected, predisposing to development of active myocarditis. Patients with peripartum cardiomyopathy have a high frequency of myocarditis on endomyocardial biopsy. The immunoregulatory changes during and following pregnancy may heighten susceptibility to viral myocarditis, and exposure to trophoblastic antigens may predispose to immune-mediated myocardial injury. Patients with new-onset left ventricular dysfunction given the diagnosis of idiopathic dilated cardiomyopathy may actually have active myocarditis despite the absence of clinical signs and symptoms of acute infection.

Neither the AHA nor the ESC presentations represent comprehensive guides that dictate precise, clinical diagnostic strategies for each of the cardiomyopathies. Nevertheless, the ESC promotes their document as an improved "clinically oriented" classification with "utility for "everyday practice," which serves as an improved guide for diagnosis emphasizing specific morphological and functional phenotypes. However, on close inspection, the ESC and AHA do not differ substantially in this regard be-

cause both in fact rely on specific structural disease states (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy/dysplasia) as the basis for the classification.

The hypertrophic cardiomyopathy (HCM) has been defined by the presence of myocardial hypertrophy in the absence of haemodynamic stresses sufficient to account for the degree of hypertrophy and systemic diseases such as amyloidosis and glycogen storage disease. The aim of this distinction was to separate conditions in which there is myocyte hypertrophy from those in which left ventricular mass and wall thickness are increased by interstitial infiltration or intracellular accumulation of metabolic substrates. In everyday clinical practice, however, it is frequently impossible to differentiate these two entities using non-invasive techniques such as echocardiography or magnetic resonance imaging. One approach to this conundrum is to include the histological demonstration (on myocardial biopsy) of myocyte hypertrophy in the definition of HCM; unfortunately, the patchy and complex nature of most myocardial pathologies means that this distinction can only be reliably made at postmortem. In order to provide a common starting point for clinical investigation, the presence of intramyocardial storage material is not an exclusion criterion for HCM in this classification scheme. Instead, hypertrophic cardiomyopathies are simply defined by the presence of increased ventricular wall thickness or mass in the absence of loading conditions (hypertension, valve disease) sufficient to cause the observed abnormality.

Inevitably, this approach will be controversial, but it reflects the terminology that is already in use in paediatric practice and avoids the circular arguments and contradictions that arise when trying to confine the term HCM to one narrow phenotype and aetiology (i.e. sarcomere protein disease). The potential inaccuracy (in a pathological sense) of the term ‘hypertrophic’ in some clinical settings is, in our view, outweighed by a shift in the clinical emphasis towards the development of appropriate diagnostic strategies based on clues from the history, physical examination, and non-invasive investigations.

The working group considered at some length the issue of cardiac amy-loid, historically regarded as an exemplar of restrictive cardiomyopathy (RCM), in spite of the fact that, in strict morphological terms, it frequently fails to fulfil most of the features listed in previous definitions. The arguments for continuing with this convention are that interstitial (rather than intracellular) accumulation of amyloid protein precludes use of the term ‘hypertrophy’ and that, unlike other causes of myocardial thickening, amyloid has distinct features on electrocardiography and cardiac imaging that suggest the diagnosis. The counterargument is that the logic of a morphological classification dictates that increased ventricular wall thickness caused by amyloidosis should be listed as HCM. The final consensus was that amyloidosis should be listed in the differential diagnosis of both HCM and RCM, acknowledging that this still leaves a degree of nosological ambiguity.

Left ventricular hypertrophy in the absence of hypertension and valve disease occurs in approximately 1:500 of the general population. Many individuals have familial disease with an autosomal dominant pattern of inheritance caused by mutations in genes that encode different proteins of the cardiac sarcomere. The majority of patients with sarcomeric protein gene mutations have an asymmetrical pattern of hypertrophy, with a predilection for the interventricular septum and myocyte disarray. Left ventricular cavity size is usually diminished and fractional shortening typically higher than normal. Progression to left ventricular dilatation and systolic failure occurs in a minority of patients (up to 10% in some series). All patterns of hypertrophy are consistent with the diagnosis of sarcomeric protein disease, but concentric hypertrophy is more frequent in patients with metabolic disorders such as Anderson–Fabry disease, mitochondrial cytopathy, and glycogen storage disease. Additional diagnostic clues in these patients include the inheritance pattern (X-linked, autosomal recessive) and the presence of signs and symp-toms of multi-system disease. Athletic training to national or international level is associated with physiological changes in left ventricular morphology that can be confused with a pathological phenotype, but myocardial thickness similar to those seen in patients with HCM are rare (less than 2% of male athletes). In the young, HCM is often associated with congenital syndromes, inherited

metabolic disorders, and neuromuscular diseases. In familial cases, various patterns of inheritance are observed; autosomal disorders that present in the young include Noonan and LEOPARD syndrome (dominant) and Friedreich's ataxia (recessive)

DCM is defined by the presence of left ventricular dilatation and left ventricular systolic dysfunction in the absence of abnormal loading conditions (hypertension, valve disease) or coronary artery disease sufficient to cause global systolic impairment. Right ventricular dilation and dysfunction may be present but are not necessary for the diagnosis.

The prevalence of DCM in the general population is unknown, but it clearly varies with age and geography. At least 25% of patients in Western populations have evidence for familial disease with predominantly autosomal dominant inheritance. Familial disease should also be suspected when there is a family history of premature cardiac death or conduction system disease or ske-letal myopathy. Autosomal dominant forms of the disease are caused by muta-tions in cytoskeletal, sarcomeric protein/Z-band, nuclear membrane and intercalated disc protein genes. X-linked diseases associated with DCM include muscular dystrophies (e.g. Becker and Duchenne) and X-linked DCM. DCM may also occur in patients with mitochondrial cytopathies and inherited metabolic disorders (e.g. haemochromatosis). Examples of acquired causes of DCM include nutritional deficiencies, endocrine dysfunction, and the administration of cardiotoxic drugs

DCM can occur at a late stage following cardiac infection and inflammation. In contrast to active or fulminant myocarditis, which is by definition, an acute inflammatory disorder of the heart, often with preserved left ventricular size, inflammatory DCM is defined by the presence of chronic inflammatory cells in association with left ventricular dilatation and reduced ejection fraction; histology and/or immunocytochemistry are, therefore, necessary for the diagnosis. A proportion of individuals with inflammatory DCM have persistence of viral proteins in the myocardium; viral persistence can also be observed in the absence of inflammation

Ischemic cardiomyopathy is defined as a dilated cardiomyopathy in a patient with known coronary disease, specifically a patient with a prior history of infarct or a

greater than 70 percent narrowing of a major epicardial artery. Compensatory mechanisms to improve stroke volume result in myocyte hypertrophy, ventricular dilatation, and activation of the sympathetic nervous system. Remodeling of the left ventricle and a decrease in ejection fraction occur in 15 to 40 percent of patients within 12 to 24 months following an anterior wall infarct3 and in a smaller percentage following an inferior infarction. In the Framingham study, 14 percent of men developed congestive heart failure (CHF) within 5 years of a first myocardial infarction4 and half were dead within 5 years. Prognosis in ischemic heart failure is known to be worse than in other forms of cardiomyopathy, presumably due to the superimposed risk of ongoing ischemic events. Aggressive coronary revascularization in instances of significant heart failure may be justified and may achieve a survival benefit without necessarily affecting functional improvement.

The first presentation of IDC may be with systemic embolism or sudden death, but patients more typically present with signs and symptoms of pulmonary congestion and/or low cardiac output, often on a background of exertional symptoms and fatigue for many months or years before their diagnosis. Intercurrent illness or the development of arrhythmia, in particular atrial fibrillation, may precipitate acute decompensation in such individuals. Increasingly, IDC is diagnosed incidentally in asymptomatic individuals during routine medical screening or family evaluation of patients with established diagnosis

The World Health Organization (WHO) and World Heart Foundation define cardiomyopathies as heart muscle diseases of unknown etiology and classify them according to hemodynamic and pathophysiologic criteria. Although this definition differentiates primary cardiomyopathies from other pathologic processes that disturb myocardial function-such as ischemic, hypertensive, valvular, and congenital heart diseases-the WHO classification, despite recent modifications, remains controversial. The clinicopathologic classification scheme initially proposed by Goodwin is similar and includes dilated or congestive, hypertrophic, and restrictive forms. Restrictive cardiomyopathy refers to either an idiopathic or systemic myocardial disorder characterized by restrictive filling, normal or reduced left ventricular (LV) and right ventri-

cular (RV) volumes, and normal or nearly normal systolic (LV and RV) function. Thus, the clinical and hemodynamic picture thus simulates constrictive pericarditis and is characterized by elevated venous pressure with prominent X and Y descents, a small or normal sized LV, and pulmonary congestion.

Restrictive left ventricular physiology is characterized by a pattern of ventricular filling in which increased stiffness of the myocardium causes ventricular pressure to rise precipitously with only small increases in volume. Restrictive cardiomyopathy (RCM) has always been difficult to define because restrictive ventricular physiology occurs in a wide range of different pathologies. In this classification system, restrictive cardiomyopathies are defined as restrictive ventricular physiology in the presence of normal or reduced diastolic volumes (of one or both ventricles), normal or reduced systolic volumes, and normal ventricular wall thickness. Historically, systolic function was said to be preserved in RCM, but is rare for contractility to be truly normal. Restrictive physiology can occur in patients with end-stage hypertrophic and DCM but we do not believe that these entities require their own sub-category.

Restrictive cardiomyopathy may be noninfiltrative or infiltrative and oc-curs with or without obliteration; infiltration may be interstitial (e.g., amyloid, sarcoid) or cellular (e.g., hemochromatosis). Restrictive cardiomyopathy has assumed importance in clinical cardiology for several reasons. First, these myocardial disorders epitomize diastolic heart failure; thus, abnormal ventricular diastolic compliance and impaired ventricular filling constitute their central pathophysiologic components and congestion and elevated diastolic pressure are their major clinical and hemodynamic manifestations. Second, the hemodynamic and clinical manifestations may mimic those produced by constrictive pericarditis, which, in contrast to restrictive cardiomyopathy, is a surgically curable disorder. Accordingly, its lack of recognition may have dire consequences. Third, restrictive cardiomyopathy may present with interventricular conduction delays, heart block, or skeletal muscle disease, often making the diagnosis difficult. Fourth, diagnostic criteria for restriction are not universally accepted, and the morphologic spectrum overlaps with hypertrophic cardiomyopathy challenges our traditional concepts of classification.3 Finally, a comprehensive echo

Doppler assessment has become an important, noninvasive means of detecting the pathophysiology, morphology, and prognosis of the restrictive cardiomyopathies

The exact prevalence of RCM is unknown but it is probably the least common type of cardiomyopathy. RCM may be idiopathic, familial, or result from various systemic disorders, in particular, amyloidosis, sarcoidosis, carcinoid heart disease, scleroderma and anthracycline toxicity. Familial RCM is often characterized by autosomal dominant inheritance, which in some families is caused by mutations in the troponin I gene; in others, familial RCM is associated with conduction defects, caused by mutations in the desmin gene (usually associated with skeletal myopathy). Rarely, familial disease can be associated with autosomal recessive inheritance (such as haemochromatosis caused by mutations in the HFE gene, or glycogen storage disease), or with X-linked inheritance (such as Anderson–Fabry disease).

Restrictive ventricular physiology can also be caused by endocardial pa-thology (fibrosis, fibroelastosis, and thrombosis) that impairs diastolic function. These disorders can be sub-classified according to the presence of eosinophilia into endomyocardial diseases with hypereosinophilia [now grouped under hypereosinophilic syndromes (HES)] and endomyocardial disease without hypereosinophilia [e.g. endomyocardial fibrosis (EMF)]. Parasitic infection, drugs such as methysergide, and inflammatory and nutritional factors have been implicated in acquired forms of EMF. Fibrous endocardial lesions of the right and/or left ventricular inflow tract cause incompetence of the atrioventricular valves. Isolated left ventricular involvement results in pulmonary congestion and predominant right ventricular involvement leads to right heart failure.

EMF should be distinguished from endocardial fibroelastosis, occurring in early childhood, characterized by thickening of mural endocardium mainly of the left ventricle, secondary to proliferation of fibrotic and elastic tissues. It is often associated with congenital malformations and some data suggest an aetiologic role for viral infection, in particular, mumps virus.

The restrictive cardiomyopathy is not necessarily a primary disease of heart muscle. Irrespective of the etiology, terminology, or the nature of myocardial process,

the ventricles are small (generally <110 mL/m^2), and stiff, restricting ventricular filling. Despite normal (or near normal) systolic function, ventricular diastolic, jugular, and pulmonary venous pressures are increased. Typically, LV filling pressures exceed RV filling pressures by more than 5 mmHg, but equalization of the diastolic pressures and a "square root" dip and plateau of early diastolic pressures of the RV and LV may be seen if the compliances of these chambers are similarly affected. Importantly, the hemodynamics of constrictive pericarditis may be simulated. Moreover, elevated atrial pressures produce symptoms of systemic and pulmonary venous congestion (dyspnea, orthopnea, edema, abdominal discomfort), and relatively underfilled ventricles are responsible for reduced cardiac output and fatigue. In patients with restrictive cardiomyopathy as part of a systemic disorder, cardiac symptoms may dominate or overshadow symptoms referable to other organ systems. Patients with constrictive cardiomyopathy generally have lower RV systolic pressures (<40 mmHg) and an RV end-diastolic pressure greater than one-third of the pressure RV systolic pressure as opposed to patients with restrictive cardiomyopathy but these differences are far from absolute.

Unlike HCM, DCM, and RCM, arrhythmogenic right ventricular cardiomyopathy (ARVC) is defined histologically by the presence of progressive replacement of right ventricular myocardium with adipose and fibrous tissue often confined to a ‘triangle of dysplasia’ comprising the right ventricular inflow, outflow, and apex. While these pathologic abnormalities can result in functional and morphological right ventricular abnormalities, they also occur in the left ventricle, producing a DCM phenotype, or can be present in the absence of clinically detectable structural changes in either ventricle. For the purposes of this classification, ARVC is defined by the presence of right ventricular dysfunction (global or regional), with or without left ventricular disease, in the presence of histological evidence for the disease and/or electrocardiographic abnormalities in accordance with published criteria.

Although uncommon (estimated prevalence 1:5000), ARVC is a frequent cause of sudden death in young people in some areas of Europe. Autosomal recessive forms of ARVC (e.g. Naxos and Carvajal syndromes caused by mutations in genes encod-

ing plakoglobin and desmoplakin, respectively) are recognized, but the majority of cases are caused by autosomal dominantly inherited mutations in genes encoding plakophilin 2 and other proteins of the desmosome of cardiomyocytes. Mutations in TGF-ß and Ryanodine receptor genes may be associated with an ARVC phenotype.

Left ventricular non-compaction (LVNC) is characterized by prominent left ventricular trabeculae and deep inter-trabecular recesses. The myocardial wall is often thickened with a thin, compacted epicardial layer and a thickened endo-cardial layer. The population prevalence of isolated LVNC is not known, but it is reported in 0.014% of consecutive echocardiograms. In large paediatric series, LVNC is reported to be the commonest cause of unclassified cardiomyopathies. LVNC is frequently familial, with at least 25% of asymptomatic relatives having a range of echocardiographic abnormalities. Genes in which causative mutations have been identified include G 4.5 encoding taffazin (X-linked), alpha dystrobrevin, ZASP, actin, lamin A/C and a locus on chromosome 11 p 15.

Stress-induced cardiomyopathy—also known as Takotsubo cardiomyopathy, apical ballooning syndrome, or ampulla cardiomyopathy—is an acute, reversible condition characterized by LV systolic dysfunction generally involving the mid and apical segments. Recently Takotsubo cardiomyopathy was being reported in the section “Cardiomyopathy”, but noq this disease is referred as acute ischemia-induced heart failure. Transient left ventricular apical ballooning syndrome or takotsubo cardiomyopathy is characterized by transient regional systolic dysfunction involving the left ventricular apex and/or mid-ventricle in the absence of obstructive coronary disease on coronary angiography. Patients present with an abrupt onset of angina-like chest pain, and have diffuse T-wave inversion, sometimes preceded by ST-segment elevation, and mild cardiac enzyme elevation. Originally described in Japan, the condition is reported in Caucasian populations in Europe and North America. Most reported cases occur in post-menopausal women. Symptoms are often preceded by emotional or physical stress. Norepinephrine concentration is elevated in most patients and a transient, dynamic intraventricular pressure gradient is reported in 16% of cases. Left ventricular function usually normalizes over a period of days to weeks and

recurrence is rare. The same kind of reversible myocardial dysfunction is occasionally encountered in patients with intracranial haemorrhage or other acute cerebral accidents (neurogenic myo-cardial stunning).

1.1. Mastering the skills of interpretation of blood tests in the field of the topic (acute phase reactants, total protein and proteins' fractions).

Laboratory findings are generally not diagnostic. Sixty percent of patients will have an elevated erythrocyte sedimentation rate and 25 percent an elevated white blood cell count. Elevated titers to cardiotropic viruses may be present. However, a fourfold rise in IgG titer over a 4- to 6-week period is required to document acute infection. Elevated IgM antibody titer may denote an acute infection more specifically than a rise in IgG antibody titer. Unfortunately, a rise in antibody titer documents only the response to a recent viral infection and does not indicate active myocarditis. Abnormalities in peripheral T- and B-lymphocyte counts have been reported, but these findings have not been consistent and cannot be used as diagnostic adjuncts. Increase in the MB band of CPK is observed in approximately 12 percent of patients. Troponin levels may also increase.

Endomyocardial biopsy is the critical test to confirm the diagnosis. Endomyocardial biopsy techniques enable the repetitive sampling of the human myocardium with minimal discomfort and minor morbidity. Right ventricular myocardial specimens can be obtained by accessing the right internal jugular or femoral vein. Intravascular biopsy of the left ventricle is infrequently performed due to the higher morbidity associated with this approach. The right ventricular bioptome is positioned under fluoroscopy or echocardiography to sample the interventricular septum. As the myocarditis can be focal, a minimum of four to six fragments are obtained. Sampling error is reduced by less than 5 percent. Using the Stanford bioptome, typical samples are 2 to 3 mm in maximal diameter and 5 mg in wet weight. Samples are processed, paraffin-imbedded, sectioned, and stained with hematoxylin-eosin and trichrome. Special stains are employed if other diagnoses are considered.

Several investigators have performed endomyocardial biopsies in patients with unexplained congestive heart failure and/or ventricular arrhythmia. The percentage of

patients with biopsies interpreted as myocarditis varied widely, primarily owing to the different diagnostic criteria for active myocarditis used by the investigators. This variability of endomyocardial biopsy criteria prompted a meeting of cardiac pathologists to reach a consensus on the pathologic definition of myocarditis, now known as "the Dallas criteria." Active myocarditis was defined as "an inflammatory infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of the ischemic damage associated with coronary artery disease." Examination of a minimum of four to six fragments from each patient is required for interpretation. The term borderline myocarditis is applied when the inflammatory infiltrate is too sparse or myocyte injury is not demonstrated. Repeat biopsy is then suggested. A high frequency of active myocarditis is confirmed by repeat biopsy in patients whose initial histologic samples demonstrated borderline myocarditis. When right ventricular endomyocardial biopsy has failed to establish the diagnosis, sampling the left ventricle may improve diagnostic yield (Fig. 2).

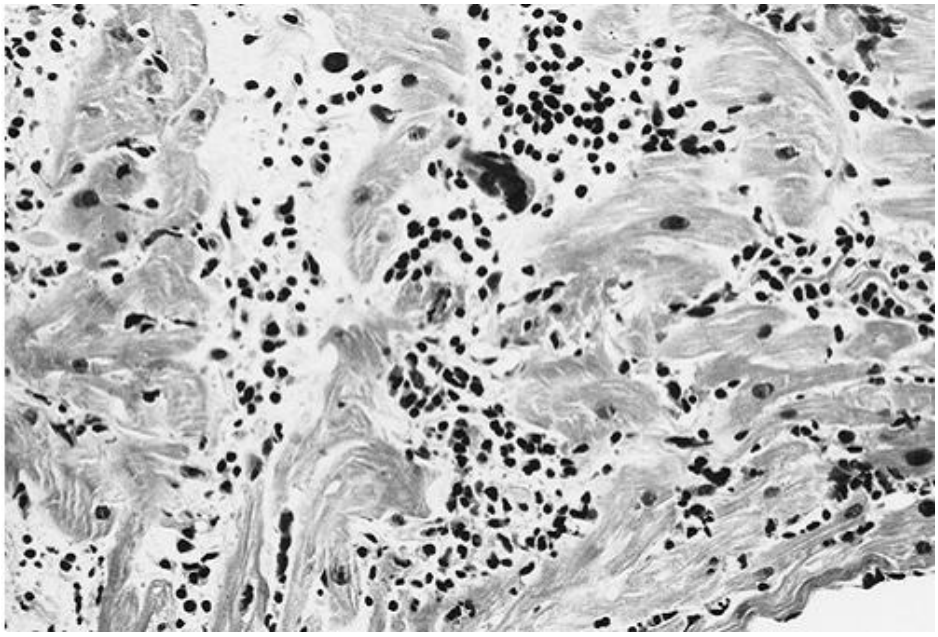


Figure 2. Photomicrograph showing extensive interstitial infiltrates of lymphocytes and myocytes with focal myocyte necrosis (×60).

Endomyocardial biopsy must be applied as quickly as possible to maximize the diagnostic yield. Biopsies in patients with peripartum cardiomyopathy have the high-

est yield when performed early after onset of symptoms. Resolution of active myocarditis has been documented within 4 days of initial biopsy, with progressive clearing over several weeks on serial biopsy. Progression of active myocarditis to dilated cardiomyopathy has been documented when serial biopsies are performed. Newer molecular biology techniques are being applied to the analysis of endomyocardial tissue for the detection of viral nucleic acid. The usefulness of PCR amplification of viral genomic material from endomyocardial tissue in children with suspected myocarditis was shown in a study that found PCR amplified viral product in 67 percent of the children studied.

Although technetium-99m-pyrophosphate scintigraphy has proved useful in the detection of myocarditis in a murine model, it has not been effective in diagnosing myocarditis in humans. Imaging with gallium 67, an inflammation-avid radioisotope, has shown promise as a screening method for active myocarditis, with a specificity and sensitivity of 83 percent and a negative predictive value of 98 percent in biopsy-proven myocarditis. Indium 111-labeled antimyosin antibody scans can be used to detect myocyte necrosis. Application of this technique in patients with myocarditis has demonstrated a sensitivity of 83 percent, a specificity of 53 percent, and a positive predictive value of a normal scan of 92 percent. In those patients who were antimyosin antibody-positive and biopsy-negative, the possibility of inflammation undetected by biopsy has been considered. Antimyosin imaging, however, detects myocyte injury independent of etiology, and noninflammatory causes of heart muscle injury in young patients may cause false-positive scans. The usefulness of scintigraphy in diagnosing myocarditis is limited by low specificiy, radiation exposure, and expense Tissue alterations associated with myocarditis may be identifiable using magnetic resonance imaging (MRI). Preliminary results suggest that myocardial inflammation may induce abnormal signal intensity of the myocardial walls. Use of T2-weighted images to visualize tissue edema has been described in several case reports of patients with active myocarditis. More recently, contrast media-enhanced MRI has been used to characterize myocardial changes in myocarditis. The MRI imaging contrast agent gadopentetate dimeglumine accumulates in inflammatory lesions. It is a

hydrophilic agent that accumulates in the extracellular space of water-containing tissues. Gadolinium increases the signal of T1-weighted images. A total of 19 patients with clinically suspected myocarditis and 18 normal subjects underwent contrast-enhanced MRI. Global relative enhancement was higher in patients than controls. Contrast MRI also visualized the area of inflammation and the extent of inflammation and may prove to be a valuable technique in both the diagnosis and monitoring of disease activity. Despite the promise of noninvasive techniques, endomyocardial biopsy remains the diagnostic standard

1.2. Mastering the skills of ECG and echocardiogramms' interpretation in the field of the topic.

The electrocardiogram most frequently shows sinus tachycardia. Diffuse ST-T-wave changes, prolongation of the QTc interval, low voltage, and even an acute myocardial infarct pattern has been noted in some patients with myocarditis. Conduction delay is common, with left bundle branch block identified in 20 percent of patients. Cardiac arrhythmias are frequently observed in patients with myocarditis, including complete heart block, supraventricular arrhythmias-especially in the presence of congestive heart failure or pericardial inflammation, and ventricular arrhythmias. Echocardiography can reveal left ventricular systolic dysfunction in patients with a normal-sized left ventricular cavity. Segmental wall motion abnormalities may be observed. Wall thickness may be increased, particularly early in the course of the disease, when inflammation is fulminant. Ventricular thrombi are detected in 15 percent of those studies. Echocardiographic findings in active myocarditis can mimic restrictive, hypertrophic, or dilated cardiomyopathy.

The cardiac silhouette on the chest radiograph may be normal or moderately enlarged. The ECG typically shows decreased voltage, a pseudoinfarction pattern, left axis deviation; arrhythmias and conduction disturbances may predominate the clinical course. The M-mode echocardiogram may reveal symmetrical wall thickness involving the right and left ventricles, a small or normal LV cavity, variable (but often depressed) systolic function, left atrial enlargement, and a small pericardial effusion. Digitized M-mode tracings may reveal decreased rates of systolic wall thickening and

diastolic wall thinning and increased isovolumic relaxation time, especially in the early stages.

Two-dimensional echo findings include thickening of the ventricular myocardium, the interatrial septum and valves (especially the AV valves), enlarged papillary muscles, and dilated atria and inferior vena cava. LV wall thickness is an important prognostic variable; in one study, patients with biopsy-proven myocardities having a mean wall thickness 15 mm had a median survival of 0.4 years, whereas patients with a mean wall thickness 12 mm had a median survival of 2.4 years. Highly reflective echoes producing a granular or sparkling appearance and occurring in a patchy distribution are characteristic echocardiographic findings but are neither sensitive nor specific; concentric hypertrophy, as occurs in hypertension or aortic stenosis, may produce a uniformly speckled or echolucent appearance of the myocardium; and idiopathic hypertrophic cardiomyopathy may display a patchy, granular sparkling. Although they correlate with wall thickness, granular echoes may not be seen. Importantly, their recognition is subjective and is affected by ultrasound instrument.

Doppler studies may show the restrictive pattern of LV filling-i.e., a transmitral E/A ratio 2 without respiratory variation, transmitral diastolic deceleration time <150 ms, and an isovolumic relaxation time 70 ms. The RV filling pattern is often abnormal. The systolic-todiastolic pulmonary venous flow ratio is <1 and atrial reversals increase with inspiration in the pulmonary and hepatic veins. However, the earliest sign of amyloid cardiomyopathy is impaired LV relaxation, manifest by an E/A ratio <1, and increased isovolumic relaxation and transmitral diastolic deceleration times. The severity of combined systolic and diastolic abnormalities can be determined with an echo Doppler index using isovolumic contraction and relaxation and ejection times. In addition, Doppler has shown utility in prognosis; a deceleration time <150 ms and an increased E/A transmitral ratio are strong predictors of cardiac death. Abnormalities of LV filling are also demonstrated with the LV time-activity curve from radionuclide ventriculography.

Based on stored electrogram data from HCM patients experiencing ap-propriate implantable cardioverter-defibrillator discharges, ventricular tachycar-dia/fibrillation

appears to be the primary mechanism most commonly responsible for sudden death in HCM, although a number of other mechanisms may also be involved. No particular symptom complex has been shown to be reliably associated with subsequent sudden death in HCM with the exception of recurrent or exertional syncope, particularly in the young. Furthermore, patients with or without subaortic obstruction may die suddenly, and some patients appear to tolerate marked outflow obstruction for virtually their entire lives without adverse consequences. Indeed, the presence or magni-tude of the outflow gradient has not been independently associated with increased risk for sudden death. However, other disease variables have been associated with an increased likelihood of sudden death. The most important of these proposed risk factors include the following: prior cardiac arrest or sustained ventricular tachycardia, "malignant" genotype or family history of premature HCM death, multiple-repetitive (or prolonged) bursts of nonsustained ventricular tachycardia on ambulatory ECGs, massive degree of left ventricular hypertrophy (wall thickness, 30 mm). A hypotensive blood pres-sure response to exercise may also be informative regarding risk but is encum-bered by a low positive predictive accuracy and is much more powerful as a negative predictor of outcome.

The ECG in patients with IDC may be remarkably normal, but abnor-malities ranging from isolated T wave changes to septal Q waves in patients with extensive left ventricular fibrosis, prolongation of atrioventricular (AV) conduction, and bundle branch block may be observed. Sinus tachycardia and supraventricular arrhythmias are common, in particular atrial fibrillation. Approximately 20-30% of patients have non-sustained ventricular tachycardia and a small number present with sustained ventricular tachycardia.

An echocardiogram is essential for the diagnosis of IDC. In patients with poor echo windows other imaging modalities such as radionuclide scans and magnetic resonance may be useful. Recently suggested echocardiographic criteria for IDC are shown in the adjacent box. When making the diagnosis of IDC it is important to take into account sex and body size. The most widely applied criteria in family studies are based on the Henry formulae, with a left ventricular cavity dimension of >112% of

predicted normal values used to define left ventricular enlargement and a shortening fraction of <25% defining abnormal systolic function. These criteria have some limitations, in particular the use of only short axis dimensions and a relatively low specificity in young patients, but they are practical and reproducible

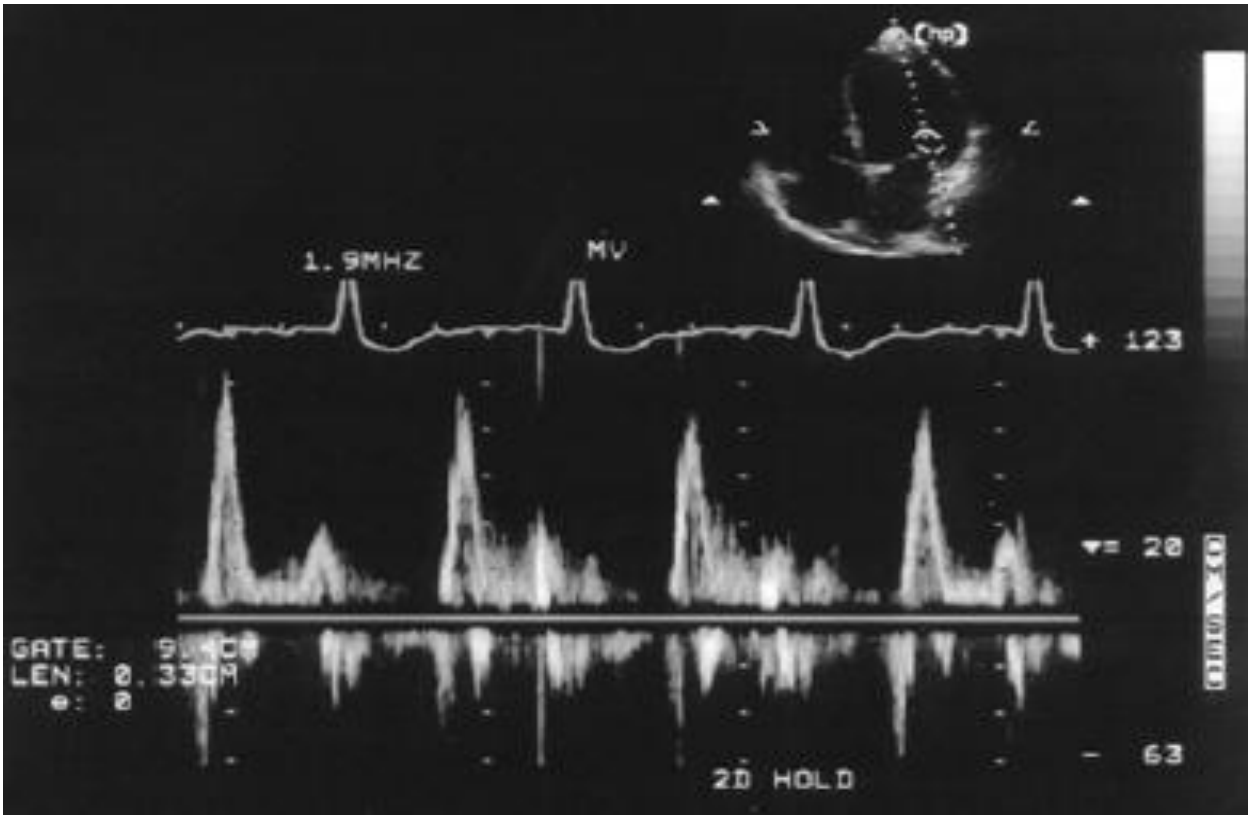
Recently, Doppler techniques (spectral Doppler, color M-mode, and Doppler tissue imaging) have assumed an important role in characterizing the nature of transvalvular filling and in clinically distinguishing between constrictive pericarditis and restrictive cardiomyopathy. In the normal subject, the early filling wave (E) of mitral flow is greater than the late, atrial systolic wave (A), and neither change significantly with respiration. In contrast, the E and A velocities of tricuspid valve flow increase slightly with inspiration. The deceleration time of the LV early diastolic wave ranges from 150 to 240 ms, and the LV isovolumic relaxation time ranges from 70 to 110 ms. Pulmonary venous flow is generally biphasic, with a dominant wave during systole (S) and a smaller wave during diastole (D); respiratory changes are minimal and atrial systolic reversals are generally small. Hepatic vein flow consists of a larger S and smaller D wave with small reversals (Vr and Ar) after each wave, respectively. With expiration, S and D waves decrease and Vr and Ar increase. Doppler tissue imaging (DTI) shows a prominent longitudinal axis velocity in early diastole (Ea >8 cm/s) and a smaller velocity after atrial contraction (Aa). The slope of early diastolic LV filling on color M-mode (Vp) is >45 cm/s.

In the patient with restrictive cardiomyopathy, mitral valve flow shows an increased E/A ratio (>2) with a short (<150 ms) deceleration time and a short (<70 ms) isovolumic relaxation time (a "restrictive" pattern of filling) without respiratory variation (Fig 3).

The tricuspid valve flow shows an increased E/A ratio without respiratory variation, a shortened deceleration time, and a short isovolumic relaxation time that shortens further with inspiration. The S/D ratio of pulmonary venous flow is <1, atrial reversals are increased, and there is little respiratory variation. The S/D ratio of hepatic venous flow is <1 and prominent reversals are seen during inspiration. Doppler tissue

imaging shows a striking decrease in Ea (<8 cm/s) and the propagation velocity on color M-mode is <45 cm/s.

Figure 3: Doppler record of mitral inflow velocity from a patient with idiopathic restrictive cardiomyopathy



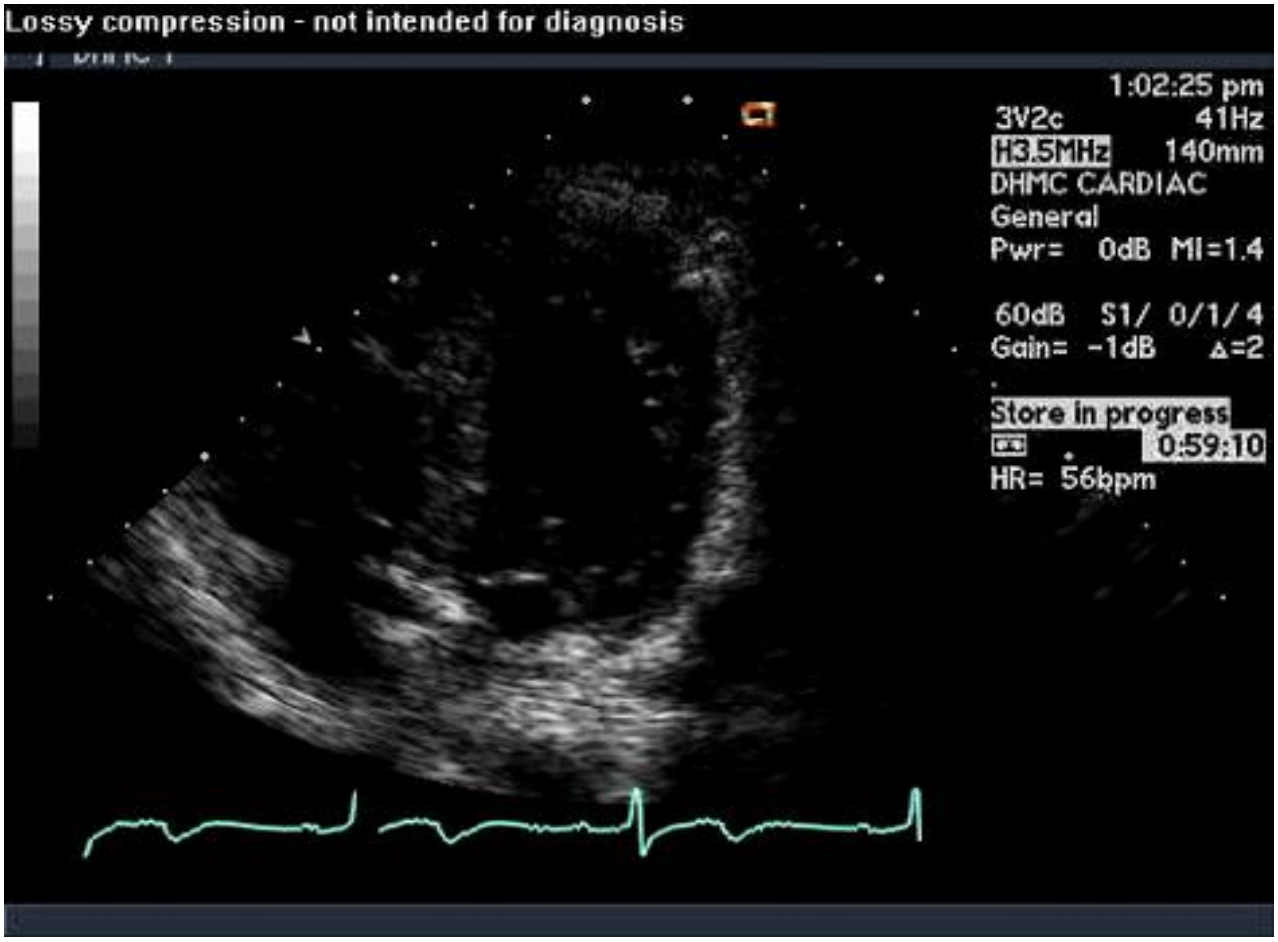
However, measurements of LV filling-such as the peak filling rate, time to peak filling, and various filling fractions-require careful attention to technical detail. The need for stable heart rates, the lack of venous flows, and the inability to observe the influence of respiration on cardiac blood flows are important limitations of the radionuclide ventriculographic technique. Magnetic resonance imaging (MRI) and computed tomography (CT) are useful for accurately assessing pericardial thickness; a pericardium >4.0 mm thick can distinguish the two entities Recent preliminary data suggest that constrictive pericarditis is associated with severe autonomic dysfunction that involves all segments of the autonomic nervous system, whereas in restrictive cardiomyopathy the autonomic dysfunction is localized to the parasympathetic effe-

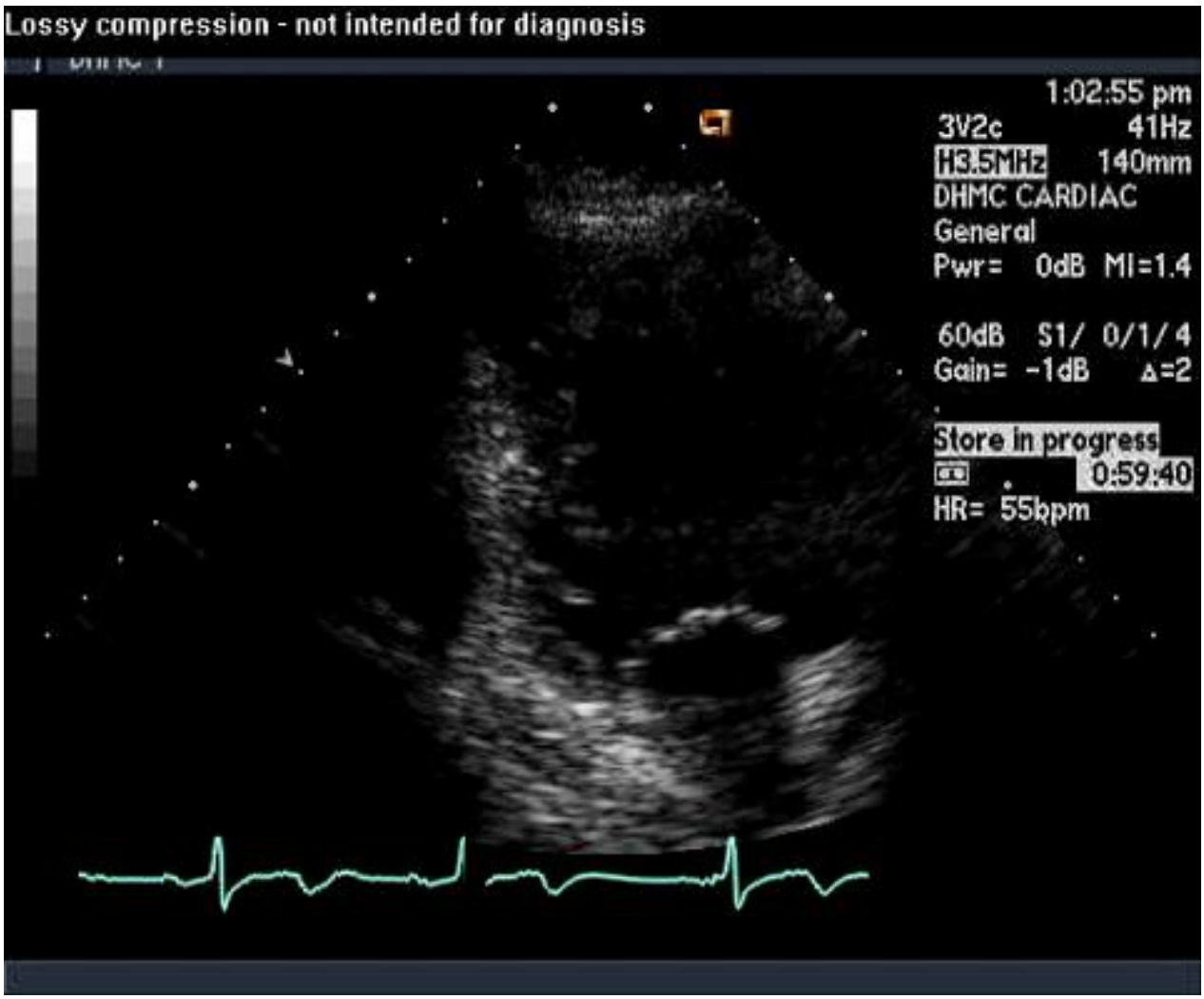
rent pathway. Invasive hemodynamics may be helpful, and occasionally a histologic diagnosis is necessary.

It is important to remember that clinical and laboratory testing, including imaging and pathologic studies, may produce results consistent with mixed constrictive pericarditis and restrictive cardiomyopathy; indeed, the two entities may coexist [for example, after mediastinal irradiation or after coronary artery bypass grafting (CABG)]. In these cases, a decision to treat conservatively or surgically explore a patient requires experienced clinical judgment.

Echocardiography is essential for detecting of non-compact cardiomyopathy (Fig.4).

Figure 4: Echogramms of non-compaction left ventricle





In some patients, LVNC is associated with left ventricular dilatation and systolic dysfunction, which can be transient in neonates.

It is not clear whether LVNC is a separate cardiomyopathy, or merely a congenital or acquired morphological trait shared by many phenotypically distinct cardiomyopathies. LVNC occurs in isolation and in association with congenital cardiac disorders such as Ebstein's anomaly or complex cyanotic heart disease and some neuromuscular diseases.

Echocardiography is recommended to differentiate Takotsubo (stress-induced) cardiomyopathy at the early stages. Associated electrocardiographic abnormalities suggest ischemia or myo-cardial injury, but occur in the absence of obstructive epicardial coronary artery disease. The majority of patients present after an acute emotional or physical stressor, which implicates a catecholamine surge in the pathophysi-

ology. Stress-induced cardiomyopathy mimics an acute coronary syndrome and is estimated to account for approximately 1–2% of all presentations with symptoms of myocardial infarction. The in-hospital mortality rate is lower than that for myocardial infarction. Long-term survival is similar to that of an age-matched and gender-matched population. The diagnosis of stress-induced cardiomyopathy in the patient in this case was confirmed by the presence of all four Mayo Clinic diagnostic criteria: transient contractile dysfunction of the mid-LV segments with or without apical involvement, extending beyond a single epicardial vascular distribution; absence of obstructive coronary disease or angiographic evidence of acute plaque rupture; new electrocardiographic abnormalities (either ST-segment elevation, T-wave inversion, or both) or elevated cardiac troponin; and the absence of a pheochromocytoma or myocarditis.

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2. Topic 6. Подготовка к практическому занятию №10 «Infective endocardities. Pericardities».

Infection remains the number one killer worldwide. Nevertheless, it is the expectation that bacterial infections can be eliminated with antibiotics. Unfortunately, there remain infections due to bacteria that are difficult to detect and difficult to reach, because of minimal blood supply, with even the most potent of antibiotics. One of the diseases in this category is infections that initiate on the inner lining of a vital organ, the heart. These infections are referred to as endocarditis since they involve the endocardium, the inner lining of the heart and valves. The initial site of infection is generally in areas exposed to mechanical trauma or prosthetic device. Unfortunately the damage to the heart if not treated can be fatal and often survival requires surgical replacement of one of the valves. Despite the tremendous array of antibiotics and the marked increase in potency of these drugs to eradicate bacterial infection, the efficacy of treating the relatively a vascular lining of the heart or its valvular apparatus often eludes the desired effect. This is further complicated by the changing substrate for bacterial endocarditis, namely, artificial valves and devices and the increasing number of individuals who are imuno-suppressed because of drug use, human immuno deficiency virus infections or other debilitating conditions. Endocarditis due to bacteria and other agents remains a continuing threat as well as a challenge in terms of diagnosis, management and treatment. Despite advances in medical and surgical treatments, infective endocarditis continues to be an important clinical problem. It has an in-hospital mortality of 10–20%, and many patients will require valve surgery during long-term follow-up. The di-agnosis is difficult since it is based on a constellation of findings and none of the clinical findings alone is pathognomonic. Unequivocal diagnosis is often made only at surgery or autopsy.

Infective endocarditis (IE) may give rise to numerous extracardiac, cardiac, and valvular findings, including infected thrombi (vegetations), sequelae of local tissue destruction, and systemic manifestations including vasculitis, emboli, and ischemic events. This is an appropriate term as the causal organisms may be bacterial, fungal,

rickettsial, or even viral or mycoplasmal. Traditionally a distinction between acute and subacute infective endocarditis was made depending upon the severity and rate of disease progression. This reflected an organism's virulence and the presence of underlying cardiac disease. With antimicrobial treatment these clinical divisions have little pathologic significance, and it is preferable to think in terms of active, healing, and healed infective endocarditis. The disease is now probably best described by its anatomical location and the organism involved. Infective endocarditis may arise in normal hearts with normal valves, or more commonly in patients with abnormal cardiac anatomy. The most common preexisting cardiac valvular lesions are left-sided ones, including aortic stenosis (especially the congenitally bicuspid aortic valve), aortic insufficiency, and mitral insufficiency. Valves damaged by rheumatic fever continue to be the most common type of predisposing cardiac valvular abnormality in developing countries. However, in developed countries degenerative or age-related diseases, including mitral valve prolapse, degenerative aortic stenosis, and mitral annular calcification are becoming a more predominant background for infective endocarditis.

Other important predisposing conditions are congenital heart diseases, including ventricular septal defect, patent ductus arteriosus, coarctation, transposition of the great arteries, tricuspid and pulmonary atresia or stenosis, and tetralogy of Fallot. Hypertrophic cardiomyopathy and prosthetic grafts or valves may also predispose to infective endocarditis. For infective endocarditis to occur there are usually three features - valvular thrombus, circulating bacteria, and bacterial growth on the valve. Hearts may develop valvular thrombus due to abnormal flow and anatomy. Thrombus may develop due to regurgitant jet lesions, on contact surfaces, or other areas of mechanical trauma. It should be realized that many phenomena of modern medicine, including prolonged intubation, immunosuppression, chemotherapy, complex surgical procedures, and increased use of antimicrobial agents might contribute to increased susceptibility to develop infective endocarditis. Other predisposing conditions include immunodeficiency, alcoholism, malnutrition, and diabetes. Intravenous drug use

(IVDU) may give rise to a repetitive bacteremia and is an important risk factor for infective endocarditis

Intravascular and intracardiac catheters and devices have proliferated and now include pacemakers, defibrillators, indwelling heart catheters, grafts, and valve or non-valve prostheses. These foreign bodies may be the nidus for infection and may also lead to thrombus formation on a neighboring structures or heart valves. Insertions of catheters, pacemakers, and cannulas are routine procedures in modern medical therapy for resuscitation, feeding, hemodynamic monitoring, and therapy of disease. Lines or catheters may contuse, tear, penetrate, perforate, tangle, or thrombose the intracardiac structures. Biofilms of infecting organisms and extracellular matrix may form on the surface of lines or devices and serve as a protective environment for the infective organisms.

The most common catheter- or line-related lesions involve the right atrium, right ventricle, pulmonary, and tricuspid valves. These lesions are rarely important unless they are infected. The catheter lesions are located on the atrial side of the tricuspid valve or on the ventricular side of the pulmonary valve. The lesions usually follow the line of the catheter and the catheter may be surrounded by thrombus which chronically may organize and fibrose. Infections in defibrillators and pacemakers may occur anywhere along the electrode and are not limited to the tricuspid valve. Pacemakers and defibrillators may have infection involving either the lead or the pouch, and Staphylococci are the most common pathogens involved. Fungal infection may also be seen. Septic and bland pulmonary emboli may complicate pacemaker/defibrillator infection. If the device has been in place for some time, lead extraction is usually impossible and open-heart surgery may be necessary.

At surgery or autopsy examination of hearts, valves, and vascular prostheses, clinical suspicion that the patient has infective endocarditis may or may not be present. The presence of unexpected but suspicious valvular lesions should prompt a proper workup for infective endocarditis. Before immersion of the heart or resected valve in fixative, a thorough examination should be made to visualize all the valves and perivalvular structures. Sterile instruments should be used if a suspicious lesion is

encountered. Since the proper approach is to assume that all valvular thrombi are infected until proven otherwise (this is the author's personal practice), portions of the thrombus should be submitted for culture. Swabs of the lesions are not recommended. Cultures should never be interpreted in isolation. Pre-mortem or pre-operative blood cultures should be consulted. Microscopy of the valve or thrombus to confirm the presence of microorganisms is essential. Special stains are useful to detect microorganisms; however, treatment with antimicrobial agents has changed the utility of these stains. Gram stain is useful to detect bacteria, but after a few weeks of antimicrobial treatment the organisms may not stain. Therefore silver stains should always be performed not only to detect fungi but also to detect bacteria that have lost their positive Gram staining, yet still can be detected with silver stain of their cell walls. Care must be exercised with silver stain interpretation as this stain also highlights cellular debris and some intracellular organelles. Giemsa stain is useful to detect rickettsial organisms, which may not stain with the other stains. Correlating the blood culture result with cultures of the tissues and vegetation is essential. Communication with the clinicians may save much frustration if the special stains are negative and the organism is known from prior cultures. This is common in patients who have received prior antimicrobial agents. In culture-negative infective endocarditis, the common culprit organisms include Eikenella, Brucella, Neisseria, fungi, Chlamydia, acid-fast bacilli, or right-sided endocarditis, where the lungs filter out the organisms. HACEK (Hemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella) organisms may be particularly difficult to grow. Clinical history and history of treatment and exposures may be very relevant. Electron microscopy, im-munofluorescence, polymerase chain reaction (PCR), or other molecular tech-niques may be contributory in the search for these often culture negative organ-isms. Studies have suggested that PCR may be a better diagnostic tool than cul-ture, especially after antimicrobial therapy, but there remains concern about false positives and background contamination. Pathological diagnosis of healed infective endocarditis can be difficult, as the findings may be nonspecific and organisms frequently cannot be found. The diagnosis can only be made with confidence when the gross and microscopic features are typi-

cal, and there are collaborative clinical findings. This is quite common in patients with adequate preoperative antibiotic treatment.

On gross examination, infected thrombi of variable size, commonly known as "vegetations," are detected along the lines of valve closure or at the low pressure end of jet lesions. They are usually gray, pink, or brown and are often friable. They may be single or multiple and may affect more than one valve. Common sites are usually on the downstream side of the intracardiac high-velocity flow jets, such as the atrial side of the mitral valve or the left atrial endocardium in cases of mitral insufficiency, the ventricular side of the aortic valve, the ventricular septum or the anterior mitral leaflet in cases of aortic insufficiency, or on the right ventricular endocardium in ventricular septal defects. Infection may also involve the intima of a blood vessel distal to a coarctation or involve the pulmonary artery side of an infected patent ductus arteriosus. Left-sided valve lesions are more common than right-sided lesions except for cases related to interventional devices, catheters, or intravenous drug use. Vegetations may be located anywhere on the valve cusp or leaflet or endocardial surface. In fact this is an important distinguishing feature to note, as valve thrombi associated with nonbacterial thrombotic endocarditis (NBTE) and those related to rheumatic fever do not have this variability in location, and are usually along the lines of valve closure. Libman Sacks lesions in lupus patients may be on both sides of the valve. Thrombi from nonbacterial thrombotic endocarditis, rheumatic fever, Libman Sacks, are not associated with valve destruction. The valve structures may also manifest destructive lesions leading to perforations, defects, aneurysms, erosions, and chordal ruptures. The amount of thrombus and destruction may completely mask the underlying predisposing valve disease. Thrombi may obstruct the valvular orifice, creating stenosis, but valvular insufficiency is a much more common complication. Chordae may rupture resulting in flail leaflets. Leaflet or cusp aneurysms bulge toward the flow surface and may resemble "windsocks," and IE is the most common cause for leaflet aneurysm or diverticulum. If the aneurysm tip ruptures, the valve may become severely regurgitant due to cusp or leaflet defects. On microscopic examination, the appearance of the vegetation depends upon both the virulence and destructiveness of the

organism and the duration of the infection. Early in the disease course there are fibrin, neutrophils, and clumps of organisms . With therapy the organisms may calcify, and the thrombi organize from the base. Organizing thrombus may show no easily recognizable organisms and only show acute and chronic inflammation with neovascularization and fibroblastic proliferation. With thrombus organization giant cells may be seen. If giant cells are prominent one should consider serology for Coxiella or fungi. Pathological changes in the infected valve tissue depend on the chronicity or duration of the infection, the virulence of the organism and the status of the original valve itself. Electron microscopy, immunofluorescence, polymerase chain reaction or molecular techniques are contributory in the search for organisms

Fungal endocarditis is usually encountered when there are preexisting risk factors such as intravenous drug use, prior cardiac surgery, immunosuppression, intravenous hyperalimentation, antibiotic therapy, long-term venous catheters, pacemakers, defibrillators, and other intravascular devices. Fungi may infect either native or prosthetic valves. The common organisms are Candida and Aspergillus. Classical clinical manifestations of bacterial IE are often absent. Fungal infected thrombi are usually quite large and friable. Valve orifice obstruction leading to clinical valve stenosis may occur if the size of the thrombus is large. Embolic events are not unusual and blood cultures are often negative. The organs receiving the emboli frequently develop abscesses.

Patients with Whipple disease have been reported to have symptoms of cardiovascular disease in 58% of cases. However, at autopsy 79% have gross evidence of cardiac involvement, and of these 53% have valvular disease. The mitral valve is the most common valve affected, with the aortic and tricuspid valves also reported to be involved at times. There are periodic acid Schiff reaction (PAS)-positive macrophages on light microscopic examination and bacilliform organisms on electron microscopy. Polymerase chain reaction performed on blood may be helpful for diagnosis. The organism is a Gram-positive actinomycete, Tropheryma whippelii. The infection may lead to fibrosis and chronic inflammation giving rise to a valve with similar appearance to a post-rheumatic one. The deposits may be nodular and are often not calci-

fied. Similar pathological changes are found in the myocardium, endocardium, and pericardium. History of gastrointestinal disorder should be questioned for, as the diagnosis is usually made by small intestinal biopsy.

With successful medical treatment of infective endocarditis the infected vegetations may organize and the thrombi may form calcific valve nodules. De-structive sequelae of the infection are common. The valve may have defects at the edges or central defects forming irregular perforations. Around the holes or perforation there may be brown nodules of organisms that eventually form fibrocalcific nodules. The destruction of the valve tissue may lead to defects at the margins resulting in poor valve coaptation. Distinguishing a post- infective endocarditis perforation from a congenital accessory orifice may be difficult. In atrioventricular valves congenital orifices should have surrounding chordae, while a post- infective endocarditis perforation would not. Fenestrations, an age-related finding, are also confused with perforations. These fenestrations are located laterally on the valve cusps near the commissures and always beyond the line of valve closure. Chordae may rupture resulting in flail leaflets and valve regurgitation. The ruptured chords may knot and calcify along with the organizing infected thrombi. The valve itself may thicken and the chords may fuse. All these are significant contributors to chronic valve regurgitation. Ventricular papillary muscles may rupture for multiple reasons due to infective endocarditis. The infection may extend from an adjacent chord and cause myocardial necrosis and rupture. A coronary arterial embolus may cause a myocardial infarct with papillary muscle rupture, similar to any acute myocardial infarct. Finally an embolus may lead to a myocardial abscess with local tissue destruction.

Extension of the valve infection into surrounding structures predicts a higher mortality, higher risk of significant heart failure, and the need for cardiac surgery. In the early stage, perivalvular abscess is largely composed of inflammatory infiltrate, but at later stages necrosis and cavitation usually develop leading to destruction of perivalvular tissue. Perivalvular abscess is not a static complication but is progressive and can evolve into serious perivalvular complications including perivalvular leak, fistula and pseudoaneurysm. These perivalvular complications may develop in spite

of early valve surgery. Perivalvular leak due to annular abscess may be seen with native valve IE (aortic more than mitral), but are especially common adjacent to infected valve pros-theses. Although a perivalvular leak may be technically related to poor tissues, suture unraveling, suture tissue cut-through, and other technical matters, it is important to keep the possibility of infective endocarditis in mind with all perivalvular leaks. These leaks may cause clinically significant congestive heart failure and sometimes hemolysis. Extension of an active valve infection to adjacent cardiac structures is common, including infected lesions where adjacent valves come in contact or are contiguous—such as from the aortic valve to the base of anterior mitral leaflet, from the posterior leaflet mitral valve to the left atrial endocardium, and from the aortic valve to the ascending aorta. Jet lesions as a result of valvular insufficiency may cause infected endocardial lesions to form along the path of the regurgitant jet. Infections may also extend from the mitral and aortic valves to the valve annuli. This complication is considerably more common in the aortic position as compared to the mitral. This may manifest as an aortic root abscess, or the mitral annulus or mitral annular cal-cification (MAC) may become infected. Mitral annular calcification is a common finding in the hearts of elderly patients. It is considered to be an age-related finding, but it probably represents degenerative changes in the mitral annulus. It is associated with mitral valve disease, especially mitral valve prolapse due to myxomatous/floppy mitral valve. Uncommonly the calcium extends onto the leaflet, producing a mass and the calcium may undergo liquefactive necrosis and grossly mimic infective endocarditis. Mitral annular calcification may ulcerate giving rise to thrombus deposition with potential for embolization and infection. If infected, there is usually leaflet perforation and myocardial abscess formation. If the infection spreads into the lateral atrioventricular groove, the circumflex coronary artery may thrombose because of distortion from the local effects of the infection, and development of arteritis. Annular abscesses may also erode into to the pericardial surface, producing fibrinous or suppurative pericarditis and hemopericardium with tamponade. Aortic root abscesses may become a significant source of embolic material and they may compress adjacent structures around the aortic root. If the proximal coronary arteries are

distorted, myocardial ischemic sequelae may result. The formation of annular abscess is not an end event. Rather these structures are progressive with potential formation of perforations or fistulas. Due to the central position of the aortic valve, infection of this valve may form fistulas with practically any chamber. Each aortic cusp and sinus has its own propensity for fistula formation and complication. Infection in the left aortic cusp or sinus may spread through the aortic wall and cause pericarditis or tamponade, or a fistula may extend into the left atrium. Infection of the posterior (non-coronary) aortic cusp or sinus may cause a fistula to either the left or right atrium. Infection of the right aortic cusp or sinus may cause a fistula to the right atrium, and the right ventricle or right ventricular outflow tract. An aorto-right ventricular fistula is possible due to the presence of the atrioventricular component of the interventricular septum. Extension into the myocardium and the conduction system may be found when the infection involves the valve ring or annulus. Fistulas and abscesses are important problems particularly with prosthetic infective endocarditis, as discussed below. Involvement of the coronary arteries may be due to distortion from an aortic root abscess or they may become directly infected by local extension through the coronary ostia or by formation of mycotic aneurysms. The latter may occur in normal arteries but also may be superimposed pattern or on an underlying atherosclerotic plaque. Mycotic aneurysms may thrombose and are a source of infected emboli that may seed the myocardium leading to myocardial abscesses. Myocardial abscesses may also form as a result of local valvular infective endocarditis extension into the adjacent myocardium. Aortic root abscesses and myocardial abscesses may impinge upon or destroy the conduction system in the areas of the atrioventricular node and His bundle. Clinically this manifests as a progressively worsening degree of heart block and may be an important clinical sign that treatment is failing or disease is progressing. Extension of infection to the pericardial space may lead to hemopericardium and tamponade or to pericar-ditis. Fibrinous pericarditis is a common finding with infective endocarditis, but the pericardium may also become infected, leading to suppurative pericarditis

Infection of valve prostheses may manifest early after surgery or long after hospital discharge. Both bacterial and fungal organisms are important causes of prosthetic infective endocarditis. Valvular bioprostheses have vegetation, cusp thrombi, destruction, erosion, and perforation similar to native valves. With infection of mechanical prostheses, the actual prosthesis usually remains intact and the infection is mainly in the sewing ring and surrounding tissues. The thrombi on a mechanical prosthesis or bioprosthesis may interfere with normal function, as the prosthesis may become dysfunctional with disc or cusp immobility. Peripheral emboli are not uncommon. In any prosthesis, sewing ring and perivalvular tissue infection is common, and the valve prosthe-sis may dehisce or become loose when the surrounding tissues develop necrosis. Annular abscess and fistulas are much more common with prostheses, as compared to native valves. It is a disturbing and memorable experience to image a near totally dehisced valve prosthesis by echocardiography and for the surgeon to be able to remove such a valve prosthesis from the patient without much need for dissection. Sutures, pledgets, as well as the aortotomy site may become infected. A large perivalvular leak results in severe perivalvular regurgitation and heart failure, but even a small perivalvular leak can be significant due to the development of severe hemolysis. Destruction of the adjacent tissues may lead to intracardiac fistulas, conduction system destruction and arrhythmias, and coronary artery inflammation and thrombosis. The mortality of prosthetic IE remains high, with or without surgery, and perivalvular complications can develop despite surgery. Fungal infection of valve prosthesis is a surgical indication due to near total mortality without surgery

Pericardities

The pericardium is a closed, fibroserous membrane sac in the middle mediastinum posterior to the sternum and the second to sixth costal cartilages and anterior to the fifth to eighth vertebrae. During embryologic development, the heart invaginates the sac, based on a pedicle of the great vessels, cavae, and pulmonary veins. A layer of the serous sac becomes densely adherent to the myocardium, forming the visceral pericardium or epicardium. This layer envelops the entire heart apart from a bare area on the posterior aspect of the left atrium between the pulmonary veins in the oblique

sinus. The visceral layer reflects back on itself and is continuous with the parietal pericardium. This reflection forms a second cleft between the great vessels and the left atriumв the transverse sinus.

The parietal pericardium consists of an outer fibrous layer composed of multiple layers of collagen, aligned in different directions, interspersed with elastin fibrils. This fibrous layer has ligamentous attachments with the central tendon of the diaphragm inferiorly, the sternum anteriorly by the superior and inferior sternopericardial ligaments, and the pleural membranes laterally. The inner layer of the parietal pericardium is a serous mesothelial membrane, with microvilli, to aid fluid secretion. The normal pericardium contains about 50 mL of pale serous fluid to minimize friction and restrict excessive cardiac motion. The fluid is low in protein and has a relatively high proportion of albumin, consistent with a transudate. The pericardium is innervated by branches via the phrenic nerve. This may explain the perception of pericardial pain in the left shoulder tip. Arterial supply to the pericardium is via the internal (thoracic) mammary arteries and multiple branches of the bronchial, esophageal, and phrenic arteries. Venous drainage is via the azygous system.

Acute Pericarditis

Inflammation of the layers of the pericardium from any of a myriad of causes yields a common clinical syndrome termed acute pericarditis. The causes of acute pericarditis are listed in Table 8.1. The classical symptom complex represents an important differential diagnosis in the assessment of chest pain presentations. However, the relatively common finding of pericardial inflammation at autopsy suggests that the majority of cases are subclinical.

Acute pericarditis classically presents with progressive, often severe, chest pain over hours. This mechanical pain is typically postural, being worse on lying supine and relieved by sitting forward. It is often pleuritic and aggravated by coughing, motion, and swallowing. It is described as sharp, stabbing, or knifelike in character. The pain may radiate to the neck or shoulder in the region of the trapezius ridge and less frequently to the arms and back and even left shoulder, making differentiation from coronary ischemic pain more difficult. There is often a low-grade fever asso-

ciated with viral and idiopathic pericarditis, whereas purulent pericarditis is associated with very high fevers and systemic sepsis. In strain curve shifts to the right; during normal daily living, it exerts very little constraining effect to filling. Similarly, abrupt changes in cardiac volume superimposed on a chronically dilated heart will move the pericardium into the steep portion of the pressure - volume curve, and a constrictive effect on cardiac filling will be observed.

Table 2.

An etiology of acute pericarditis

I. **Idiopathic**

II. **Infectious** Bacterial, Tuberculous, Viral: *Coxsackie, Influenza, HIV, etc.* Fungal, Rickettsial, Mycoplasma, Leptospira, Listeria, Parasitic, Other

III. **Vasculitis/Connective Tissue Disease:** Rheumatoid Arthritis, Rheumatic Fever, SLE, Scleroderma, Sjogren's Syndrome, Reiter Syndrome, Ankylosing Spondylitis, Wegener's Granulomatosis, Giant Cell Arteritis, Polymyositis (Dermatomyositis), Behcet Syndrome, Familial Mediterraneun Fever, Dermatomyositis, Polyarteritis, Churg-Strause Syndrome

IV. **TTP**, Leukoclastic Vasculitis, Other

V. **Diseases in Adjacent Structures:** myocardial infarction, aortic dissection, pneumonia, pulmonary embolism, empyema

VI. **Metabolic Disorders:** Uraemic, Dialysis-Related, Myxoedema, Gout, Scurvy

VII. **Neoplastic**

A. *Secondary* (Metastatic, or Direct Spread): Carcinoma, Lymphoma, Carcinoid, Other

B. *Primary* Mesothelioma, Sarcoma, Fibroma, Lipoma, Other

VIII. **Trauma**

Direct:

1. Pericardial Perforation: Penetrating Injury, Esophageal or Gastric Perforation
2. Cardiac Injury: Cardiac Surgery, Percutaneous Procedures

Indirect

Radiation, Non-Penetrating Chest Injury

IX. **Association with Other Syndromes**

Post-Myocardial and Pericardial Injury Syndromes, Inflammatory Bowel Disease, Loffler Syndrome, Stevens-Johnson Syndrome, Giant Cell Aortitis, Hypereosinophilic Syndromes, Acute Pancreatitis, etc.

The presence of a pericardial rub is pathognomonic for pericarditis, although its absence does not exclude the syndrome. This rasping sound has a timing consistent with the cardiac cycle and is creaking in nature, like the sound of leather on leather. It is best appreciated with the diaphragm of the stethoscope applied to the lower left sternal edge and with the patient leaning forward in end-expiration. The sound classically has a triple cadence with components related to atrial systole, ventricular systole, and ventricular diastole. The rub is triphasic in nearly 50% of the cases, biphasic in 33% of the cases, and monophasic in 10% of the cases. The intensity of the sound can be attenuated by subcutaneous tissue thickness and hyperinflated lung volume. Furthermore, the development of a pericardial effusion as part of the inflammatory syndrome can lead to waxing and waning of the rub over days, although a loud pericardial rub can still be heard occasionally in the presence of a significant effusion. The sound should be differentiated from a pleural rub (which is similar in character and timed with the respiratory cycle), subcutaneous emphysema (which may be an associate in postsurgical or traumatic cases), and loud intracardiac murmurs (such as ventricular septal defects).

Dense fibrosis and adhesion of the parietal and visceral layers of the pericardium creates a rigid case around the heart, limiting its filling and causing profound disturbances of cardiac function. This final common pathway may be the end result of one (or more) of many etiologic agents, including infection, post cardiac surgery, and radiation. The constrictive process can follow the etiology acutely, subacutely (months), or chronically (years). The clinical presentation is well recognizable, with debilitating right heart failure and a poor prognosis. A voluminous literature exists about the many methods of differentiating this constellation from that of restrictive cardiomyopathy, which presents with similar clinical signs and symptoms.

2.1. Mastering the skills of interpretation of microbiological blood tests in the field of the topic

The microbiology of infective endocarditis has evolved significantly over the last century. Previously a community-acquired disease affecting predominantly patients with rheumatic heart disease, IE is now being seen in new populations including IV drug users, patients with prosthetic valves, and patients infected through health-care-associated bacteremia. Improved blood culture technologies and non-culture laboratory methods have also resulted in a lower rate of culture-negative cases. Because of differing proportions of particular risk groups, the etiologic agents responsible for causing infective endocarditis vary significantly among continents, countries, regions within countries, and even among different years in an individual hospital. This discus-sion of the etiologic agents of infective endocarditis will begin with native valve endocarditis followed by consideration of special situations including prosthetic valve endocarditis, infective endocarditis in injection drug users, and culture-negative endocarditis.

The common causes of native valve endocarditis are members of the normal flora of the skin, oropharynx, and the gastrointestinal and genitourinary systems. The vast majority of native valve endocarditis cases are caused by Staphylococcus and Streptococcus species. Several recent publications show that Staphylococcus aureus seems to have overtaken the viridans group Streptococci as the most common cause of native valve infective endocarditis. However, a population-based study of IE cases in Olmstead County, Minnesota, from 1970 to 2000 revealed no significant trends over time with respect to either the overall incidence of infective endocarditis or the relative proportion of cases caused by Staphylococci and Streptococci. These apparently contradictory observations likely result from differences in patient risk factors (e.g., low IVDU rates in Olmstead County) and referral patterns (more S. aureus IE referred to tertiary care centers).

Prosthetic Valve Endocarditis

Overall, prosthetic valve endocarditis (PVE) accounts for 10–30% of all infective endocarditis cases. The risk of endocarditis is highest in the first few months fol-

lowing surgery, with cumulative rates of 1.0–1.4% at one year and 3.0–5.7% at five years after valve replacement. When compared to native valve IE, (CoNS) infection is much more common in PVE; Gram-negative bacilli, fungi and diphtheroids are also more likely to cause PVE, while S. aureus enterococci are less frequently causes of PVE than they are of native value infective endocarditis. The relative importance of the causative organisms in PVE depends on the timing of infection in relation to valve replacement surgery. Early PVE is most often related to intraoperative contamination of the surgical field or postoperative bacteremia. As such, the bacterial flora of the skin and hospital associated pathogens predominate.

CoNS (most frequently S.epidermidis) are responsible for about 30–50% of PVE within this group, S.aureus (with an increasing proportion of MRSA) causes 15–20%, and Gram-negative bacilli causes 10–20%. Fungi (Candida species), diphtheroids and enterococci (with rare cases of VRE) each cause at least 5% of early PVE cases, and the streptococci are very rare causes of prosthetic valve endocarditis in the early postoperative period. The distribution of etiologic agents causing late prosthetic valve endocarditis is very similar to that for native valve infective endocarditis, with the streptococci being the most frequently isolated organisms in most reported series. Patients with late prosthetic valve endocarditis tend to have more CoNS and less S. aureus when compared to those with native valve IE. The Gram-negative bacilli and fungi seen in the early period after valve replacement are recovered infrequently in late prosthetic valve endocarditis. The HACEK organisms are isolated in up to 5% of patients presenting with late onset prosthetic valve endocarditis.

Intermediate-onset prosthetic valve endocarditis includes a mixture of pa-tients who are presenting relatively late with peri-operatively acquired infections and individuals who have developed communityacquired endocarditis. As a result, the pattern of organisms causing prosthetic valve endocarditis developing at this time is essentially an average of the proportions of cases caused by each group of organisms observed in the early and late periods.

Intravenous Drug Users

The majority of infective endocarditis in the Intravenous drug use group is caused by Staphylococcus aureus, which is responsible for 50–75% of cases. The streptococci and enterococci are the next-most-common organisms (7–10%), with small percentages caused by CoNS, Gram-negatives, and Candida species. Polymicrobial infective endocarditis is relatively common in the Intravenous drug use population, occurring in up to 5% of cases. S.aureus most commonly causes right-sided (tricuspid) endocarditis in the intravenous drug use setting. It was definite that S.aureus native valve infective endocarditis cases. So, of 170 patients with right-sided S.aureus infective endocarditis, 131 (77%) provided a history of IV drug use. In the same study, MRSA was observed infrequently in the IVDU population: 6/43 (14.0%) patients with MRSA infective endocarditis used IV drugs compared to 136/248 (54.8%) of those with infection caused by susceptible strains. However, increasing rates of MRSA in intravenous drug use have been observed and outbreaks have been documented. Gram-negative infective endocarditis in drug users can be caused by organisms that are en-countered only rarely in non- Intravenous drug use patients. Pseudomonas aeruginosa endocarditis is uncommon and occurs nearly exclusively in Intravenous drug use. Pseudomonas aeruginosa infective endocarditis is usually right sided, but can involve leftsided valves, in which case the clinical course is more complicated. A cluster of 36 cases of Serratia marcescens infective endocarditis was seen among heroin users in San Francisco in the 1970s, with high associated mortality. Campylobacter fetus, Pasteurella spp., Brucella spp., Bordetella spp., Franciscella tularensis, Aeromonas hydrophila, and Yersinia enterocolitica are other Gram-negative bacilli that are occasionally encountered in the setting of IV drug use.

Blood-Culture-Negative Endocarditis

Reported blood culture-negative endocarditis (BCNE) rates have historically varied by study population, ranging from 2.5% to 31%. These rates are still consistent among recent studies conducted in Spain (13.7%), London (12.2%), and Sweden (20%). A recent review of 26 case series published between 1993 and 2003 showed BCNE rates of about 10%. These rates are likely artificially high because of preceding antibiotic therapy. This effect was quantified in a retrospective review of 107 de-

finite IE cases at a center in Spain, in which 14/20 patients with negative blood cultures had received prior antibiotics, leaving 6/107 (5.6%) with BCNE. Thus, excluding the cases confounded by antibiotic therapy prior to blood cultures, the frequency of "true" culture-negative endocarditis is much less, likely around 5%. By definition, standard culture methods are inadequate to allow detection of the causative agents of BCNE. The largest study to address the etiology of BCNE involved 348 patients with suspected BCNE in France. The authors attempted to determine the causative organism using a comprehensive serology panel, shell vial cultures and analysis of valve specimens by multiple methods, including PCR. These investigations showed that 167 cases (48%) were due to Coxiella burnetti, 99 (28%) due to Bartonella spp., 5 (1%) due to rare fastidious organisms, and 73 (21%) without an identified cause. Of the 73 undiagnosed cases, 58 had received antibiotics before the blood cultures, leaving only 15 (4.3%) unexplained cases. Coxiella burnetti is reported to cause 3–5% of all endocarditis in France, Israel, and Great Britiain. Underlying heart disease, immunocompromising conditions and animal contact are the major risk factors. Reported outcomes of C. burnetti IE were previously poor with nearly two-thirds of patients developing congestive heart failure (CHF), but in this cohort only 38% developed CHF and mortality was only 3% (4/150). This improvement likely reflects better and more rapid diagnostics and more timely treatment. Bartonella spp. are reported to cause 3% of all endocarditis. Epidemiology was distinct for the two species, with B. quintana seen in patients who were homeless or alcoholic with exposure to body lice, and B. henselae in individuals with a history of exposure to cats. Trophyrema whipplei, the Whipple disease bacterium, is an emerging cause of culturenegative endocarditis.

Microbiologic Diagnosis Blood Cultures

Blood culture remains the single most important investigation in a patient suspected of having infective endocarditis. If appropriately collected prior to antibiotic administration, blood cultures can be expected to yield growth of the causative organism in over 90% of cases of infective endocarditis. Identification of the organism may allow the treating physician to determine the original source of bacteremia, and facili-

tates the choice of the appropriate therapeutic agent(s) and treatment duration. The Modified Duke Criteria include blood culture as one of the major diagnostic criteria. In order to fulfill the major microbiologic criterion, blood culture support for the diagnosis of IE is defined as isolation of "typical" microorganisms (viridans streptococci, Streptococcus bovis, HACEK group, S.aureus, community-acquired Enterococcus spp.) from at least two separate blood cultures, blood cultures persistently positive for "microorganisms consistent with IE," or a single culture positive for Coxiella burnetti.

Intravascular infections including IE are characterized by the presence of continuous bacteremia, and in the majority of IE cases most or all of the pre-therapy blood cultures will be positive. Demonstration of continuous bacteremia by definition requires more than one blood culture result, and the yield of blood cultures is dependent on both the number of cultures obtained and the volume of blood cultured.

For the majority of patients, one blood culture set consisted of 20 mL di-vided equally between one aerobic and one anaerobic bottle. The investigators found that a second 20 mL blood draw increased blood culture yield by 17–20%, and that this additional pick-up rate was the same whether the second culture set was drawn immediately after the first, or at any other time within the next 24 hours. The addition of a third 20 mL draw within 24 hours further increased the blood culture yield by 10%. Most experts agree that three separate blood culture sets (20–30 L in two or three bottles) should be sufficient to detect over 95% of IE-associated bacteremias in the absence of preceding antibiotics. In addition to maximizing the diagnostic yield, the practice of obtaining multiple blood cultures can also be useful in determining whether a positive result represents contamination, in which case only one culture would be expected to grow the contaminating organism.

The timing of blood culture draws depends on the overall clinical status of the patient. In the setting of a septic patient with suspected acute IE, therapy should not be delayed to allow blood cultures to be drawn, and two or three separate venipunctures can be performed a few minutes apart while arrangements are made for initiation of empiric antibiotic therapy. Conversely, a clinically stable patient who has

been ill for weeks can safely remain off antibiotics for at least 24 hours while serial blood cultures are obtained. In patients who have received antibiotic therapy before being worked up for IE, blood culture media containing antibioticinactivating resin should be used, and in selected circumstances withdrawal of antibiotics in order to allow cultures to be drawn would be appropriate. Newer blood culture media and modern automated blood culture systems represent a significant improvement over older methods. The majority of non-fastidious organisms will trigger a positive signal in blood culture instruments within 72 hours.

Most clinical laboratories incubate routine blood cultures for five days, as most positive cultures appearing after longer incubation represent contaminants. However, some fastidious organisms that cause IE, including the HACEK group, Brucella species and others, may require longer periods of incubation before triggering automated blood culture systems. The majority of fastidious organisms causing infective endocarditis will grow within ten days, but others (e.g., Bartonella species) can require several weeks to grow and may not trigger blood culture instruments even when they do grow. In the setting of clinically suspected IE, therefore, blood culture specimens require special management within the laboratory. Approaches vary among institutions and in-clude extended incubation of the bottles collected from patients identified as suspect infective endocarditis cases, terminal subcultures of negative blood culture bottles to solid culture media at the end of the planned incubation period, or a combination of both. Highly specialized culture techniques can be used for isolation of specific rare causes of infective endocarditis such as Coxiella burnetti, Bartonella species, and Tropheryma whipplei when they are suspected.

Candida species cause approximately 50% of proven cases of fungal endocarditis. Although blood cultures are thought to have poor sensitivity for detec-tion of candidemia, more specialized blood culture media have no advantage over standard blood culture bottles for detection of Candida species. Special fungal blood culture media such as Bactec Myco-F-lytic bottles are superior in supporting growth of filamentous fungi such as Aspergillus species, and could be considered for use in immunocompromised patients or known IV drug users with suspected infective endocardi-

tis. The lysis-centrifugation (Isolator) method is superior to other available processes for detection of Histoplasma capsulatum from blood samples. Emboli leading to operative intervention are seen relatively commonly in cases of fungal endocarditis given the typically large vegetation size. Because blood cultures are frequently negative in fungal endocarditis, these emboli can provide crucial information about the causative organism, and they should be cultured and stained for fungal organisms when they are encountered and removed.

Methods for Diagnosis in Culture-Negative IE Serology

Serologic testing can be useful in determining the cause of IE in true cul-ture-negative cases, which are usually caused by organisms that are difficult to culture including Coxiella burnetti, Bartonella spp., Chlamydia spp., and Legionella species. The immune response to C. burnetti involves development of antibodies against phase 1 and phase 2 antigens. In acute infection, IgM and IgG antibodies develop against phase 2, and only IgM antibodies develop against phase 1. Endocarditis is a manifestation of chronic Q fever, which is characterized by high anti-phase 1 IgG titers. Positive Q fever serology, defined as a phase 1 IgG titer of >1:800, is listed as one of the major modified Duke criteria. A Bartonella antibody titer of 1:1,600 has been reported to have a positive predictive value of 88% for Bartonella infective endocarditis. However, titers may not be reproducible given lot-to-lot variability of antigen preparations used for testing. Patients with Bartonella infection also frequently develop cross-reacting antibodies that result in falsepositive Chlamydia spp. serology. Additional assays to be considered in culture-negative infective endocarditis cases include serologic studies for Brucella species and Legionella serology or urinary antigen testing.

Molecular Diagnostics

In spite of limitations including the potential presence of PCR inhibitors in clinical samples and the possibility of sample-to-sample contamination, molecular amplification methods can be useful in establishing the cause of IE. To date, PCR methods have been applied with most success to surgically excised valve tissues. Because several possible etiologic agents are normally being considered in cases of culturenega-

tive IE, the most commonly applied approach involves the use of “universal” PCR primers. These primers are directed against highly conserved sequences that are common to all bacteria, thereby allowing amplification of genetic material from virtually any species of bacteria. The segment to be amplified (most often genes encoding for 16S rRNA) is chosen based on the presence of intervening regions with sequence variability, allowing identification of organisms by sequencing of the PCR product with subsequent comparison of the result to a sequence database. PCR identification was possible in 26 of 30 cases with positive blood cultures prior to surgery, and in 5 of 6 blood culture-negative cases (four Bartonella species, one S.gallolyticus). When a particular diagnosis is suspected, species-specific PCR assays can also be employed. Protocols have been developed for many of the agents of culture-negative IE including C.burnetti, Bartonella spp., Brucella spp., Tropheryma whipplei, Chlamydia spp. and Legionella spp.

Histology

In cases of suspected infective endocarditis for which the causative organism is not known prior to surgical intervention, heart valve material should be submitted for further investigation by histology and culture. Because of preceding antibiotic therapy, bacterial cultures of valve tissue obtained at surgery are positive in only a minority (10–15%) of cases. Histologic examination of excised valve tissue can be used both to confirm the diagnosis of infective endocarditis and to determine the probable causative organism. Pathologic findings compatible with infective endocarditis are considered to be evidence of definite endocarditis within the modified Duke criteria. Routine stains, including H&E and tissue Gram stains, will show infiltrates of inflammatory cells and can allow common causative organisms to be visualized. Special stains, including Warthin-Starry (Bartonella spp.), periodic acid-Schiff (T.whipplei, fungi), Gimenez (C.burnetti, Legionella spp.), and Gomori methenamine silver (fungi) stains, are needed for detection of less common causes of infective endocarditis.

Procedure of the Bacteriologic Investigations

Three aerobic blood cultures (with a minimum of 10mL per bottle), from separate venipuncture sites, should be obtained over at least an hour before be-ginning therapy. Blood cultures inoculated with at least 5 mL of blood had a 92% detection rate for bacteremia compared to only 67% for bottles inoculated with less than 5 mL in one study The estimated yield from blood cultures increased approximately 3% per mL of blood cultured. Anaerobic cultures may be performed but only rarely will the organism be anaerobic. If a patient has not been treated with antibiotics prior to obtaining the blood cultures there is minimal benefit beyond three cultures. However, there may be additional diagnostic yield if antibiotics had been administered or if the initial blood cultures were negative. Not all bacteremias imply the presence of IE. Certain species are more commonly associated with the disease.

2.2. Mastering the skills of interpretation of blood tests in the field of the topic (acute phase reactants, total protein and proteins' fractions).

Laboratory investigations may reveal anemia, leukocytosis with a left shift, elevated erythrocyte sedimentation rate, dysproteinemia, elevated lkevel of C-reactive protein (5 mg/dL and more) and glomerulonephritis (with hematuria or active urinary sediment). Immunologic perturbation may also occur in subacute or chronic cases leading to high titers of rheumatoid factor. Although acute phase reactants (CRPm fibrinogen), total protein and proteins' fractions are essential for determining activity of inflammatory reaction, all these ests are non-specific for infective endocarditis and pericardities.

2.3. Mastering the skills of ECG and echocardiogramms' interpretation in the field of the topic

The chest x-ray may show evidence of preexisting valvular disease (valvular calcification or cardiomegaly) or a complication arising from the infection (congestive heart failure or septic pulmonary emboli). Rarely, suppurative pericardial effusion from periannular abscess formation may produce a globular heart on x-ray. A careful examination of the electrocardiogram should be made to rule out heart block (as this is one of the complications of IE as the infectious process involves the aortic valve annulus and membranous interventricular septum).

Prior to the availability of echocardiography the only way to visualize a vegetation was by surgery or autopsy. The development of echocardiography and the identification of criteria for the diagnosis of infective endocarditis have significantly improved our ability to diagnose and treat this disease. Echocardiography has become one of the major diagnostic procedures available today. The echocardiographic hallmark of infective endocarditis is an endocardial mass lesion usually referred to as a "vegetation" (as mentioned earlier). This is usually defined as an oscillating mass attached to an endocardial surface, such as a valve or supporting structure, or a structure in the path of regurgitant jets. Additionally, echolucency, suggesting the presence of abscess formation, and Doppler evidence of valvular dysfunction should be sought.

So, when appropriately used, echocardiography (TTE and TEE) is ex-tremely useful in defining both the diagnosis and prognosis of infective endocarditis. Categorization of patients into strata of clinical probability of disease and into strata of clinical risk for morbidity and mortality may help to determine the most appropriate timing of the echocardiographic examination and the choice of the initial echocardiographic modality.

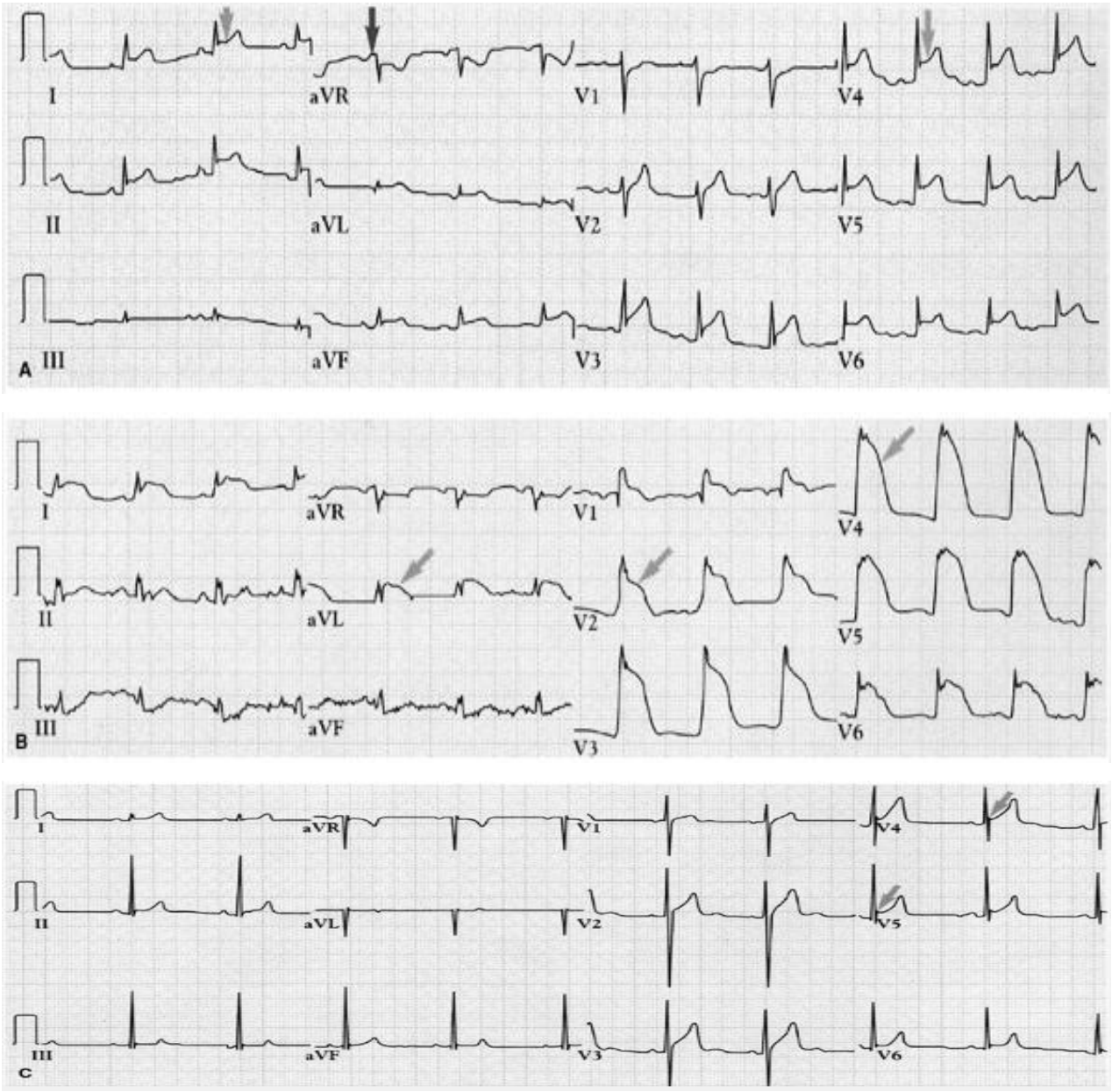
Investigations in pericardities

The electrocardiogram represents the most useful diagnostic test in acute pericarditis. Inflammation of the subepicardial myocardium is thought to be the mechanism producing ST and T-wave changes, whereas inflammation of the atrium is thought to cause the PR-segment changes. The PR-segment deviations may precede the ST changes. In contrast to the regional ST changes of myocardial ischemia, pericarditis generally produces widespread electrocardiogram (ECG) changes in limb and precordial leads. Four phases of ECG abnormalities have been recognized: ST elevation and upright T waves (stage 1) is present in 90% of cases. Over time, the ST changes resolve and the ECG may look normal (stage II). There may be further evolution to T-wave inversion (stage III) and finally to normal (stage IV).

The ECG abnormalities should be differentiated most importantly from acute myocardial ischemia (Fig.5). The ST changes are more widespread in pericarditis and have a typical saddle-shaped or upward concave appearance. Unlike myocardial in-

farction, there are no Q waves or loss of R-wave progression. The other important differential diagnosis of these ECG changes is the early-repolarization pattern. Although difficult without clinical correlation, differentiation can be made by the presence of PR-segment elevation (especially aVR) and ST elevation in V6, which is uncommon in the early-repolarization syndrome. Most patients with acute pericarditis remain in sinus rhythm.

Figure 5: ECG for acute pericarditis



Echocardiography is the diagnostic tool of choice for pericardial effusion. Initially, M-mode was the standard, with a high sensitivity for posterior pericardial fluid. The

advent of two-dimensional echocardiography has shown the various presentations of effusion, including circumferential, posterior, and loculated. The last are more common when scarring has supervened, for example, after surgery, trauma, or purulent pericarditis. The size of effusions can be graded as small (<10 mm of echo-free space in systole and diastole), moderate (>10 mm at least posteriorly), large (>20 mm), or very large (compression of the heart). Furthermore, two-dimensional echocardiography can give information about the nature of the fluid, suggesting the presence of fibrin, clot, tumor, air, and calcium. Care must be taken to differentiate pericardial fluid from pleural fluid and ascites. Left pleural effusions can be difficult to differentiate from pericardial fluid. By transthoracic echocardiography in the parasternal long-axis view, pericardial fluid can be seen to reflect at the posterior atrioventricular groove, whereas pleural fluid continues under the left atrium, posterior to the descending aorta. Spin-echo and cine MRI can also be used to assess the size and extent of simple and complex pericardial effusions similar to echocardiography. The effusions seen by MRI may tend to be larger than those detected by echocardiographyPericardial effusion is diagnosed in routine echocardiography practice in almost 1 in 10 patients. Large pericardial effusions that develop slowly can be remarkably asymptomatic, whereas rapidly accumulating smaller effusions can present with tamponade. Massive chronic pericardial effusion is a diagnosis as-cribed to a syndrome consisting of a large pericardial effusion present for at least 3 months and not attributable to any systemic cause. These effusions can be present for many years and were well tolerated in one series, with tamponade a rarity. However, in two series, cardiac tamponade occurred in near one third of patients. In the larger study, 28 patients with large idiopathic chronic pericardial effusions were followed for a median of 7 years. Unexpected tamponade occurred in 8 patients (29%), and pericardiectomy was performed in 20 patients. Chronic nonspecific pericarditis was found in all patients evaluated by histology.

Doppler echocardiography with respirometry has emerged as a useful tool in these conditions. Limited ventricular filling and enhanced ventricular interaction account for the Doppler findings in constrictive pericarditis, whereas decreased distensibility

of the ventricles accounts for the Doppler findings in restriction. The similarities with restriction examined by Doppler echocardiography include a short deceleration time indicative of the dip-and-plateau hemodynamic pattern and limited filling. The main differences include enhanced respiratory variation in mitral inflow and pulmonary venous flow (at the onset of inspiration and expiration) in constriction but not restriction (unless a concomitant pericardial effusion accounting for respiratory variation is present). In restriction, there is a markedly blunted pulmonary venous systolic flow, with greater diastolic forward flow indicative of a prominent y descent and elevated left atrial pressures; in constriction, usually both systolic and diastolic flows are present. Due to enhanced ventricular interdependence, there is a decreased transtricuspid flow in expiration and enhanced expiratory flow reversals in the hepatic vein with constriction; there is increased inspiratory flow reversal in restriction. Respiratory variation in the tricuspid regurgitation peak velocity and velocity duration has been noted in constriction but not in restriction. Superior vena cava Doppler can help to distinguish respiratory variation of mitral inflow in patients with chronic obstructive lung disease and constrictive pericarditis. The systolic forward component of superior vena cava flow varies significantly with chronic obstructive lung disease, whereas there is little change with constrictive pericarditis. Color M-mode Doppler and tissue Doppler echocardiography have provided complimentary information in the evaluation of patients with constrictive pericarditis. The velocity of propagation from color M-mode and the tissue Doppler E annular velocity are normal or supranormal in constriction, representing normal compliance but abnormal relaxation. Exceptions to the finding of a normal tissue Doppler E annular velocity include patients with extensive annular calcification, LV dysfunction, or segmental differences in velocities.

There are several pitfalls in using Doppler echocardiography with respiratory monitoring for distinguishing constriction from restriction. Factors including depth of respiration, position of the sample volume, level of left atrial pressure, presence of concomitant myocardial disease or tricuspid regurgitation, and atrial fibrillation may influence the accuracy of the diagnosis. Transesophageal echocardiography may be

used to delineate the anatomy (pericardial thickening) as well describe the physiology better than transthoracic echocardiography.

Preload reduction maneuvers may be useful in lowering the left atrial pressure to enhance the respiratory variation, and volume loading may be used if the filling pressures are decreased. Mixed restriction/constriction may occur postirradiation and may have features of localized pericardial thickening with re-strictive physiology. In addition, atrial fibrillation may make it difficult to perform a Doppler evaluation of constriction and restriction. However, a series of 31 patients with constrictive pericarditis showed a similar respiratory variation of pulmonary venous flow and mitral inflow in patients with atrial fibrillation compared to normal sinus rhythm. Occasionally, ventricular pacing can be used to regularize the RR intervals in patients with atrial fibrillation. Constrictive pericarditis can also be evaluated in the operating room during mechanical ventilation. In a study with 15 patients, it was noted that positive-pressure ventilation reversed the pattern of respiratory variation of the mitral inflow and pulmonary venous flow velocities

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3. Topic 7. Practical skills for the topic №11 «Cor pulmonale. Pulmonary thromboembolism».

Venous thromboembolism (VTE) encompasses both deep vein thrombosis (DVT) and pulmonary embolism (PE). Diagnosis, management, and prevention of VTE can be standardized and adapted to critical pathways. Cardiologists need to be adept in detecting PE and in managing complicated cases that require catheter-directed thrombolysis, mechanical thrombectomy, or placement of an inferior vena caval filter. Furthermore, cardiologists should set the standard for recommending and implementing prophylaxis among their hospitalized patients and among patients on whom they consult preoperatively.

Cardiologists are often summoned to help diagnose suspected PE be-cause of their familiarity with the differential diagnosis of chest pain and dyspnea, their ability to recognize clinical manifestations of acute pulmonary hypertension, and their facility with echocardiography for risk stratification. The cardiologist is often the specialist asked to manage high-risk patients with thrombolysis and, if necessary, suction catheter embolectomy. The cardiologist may also serve as the liaison with the cardiac surgeon who is summoned to perform urgent open surgical embolectomy

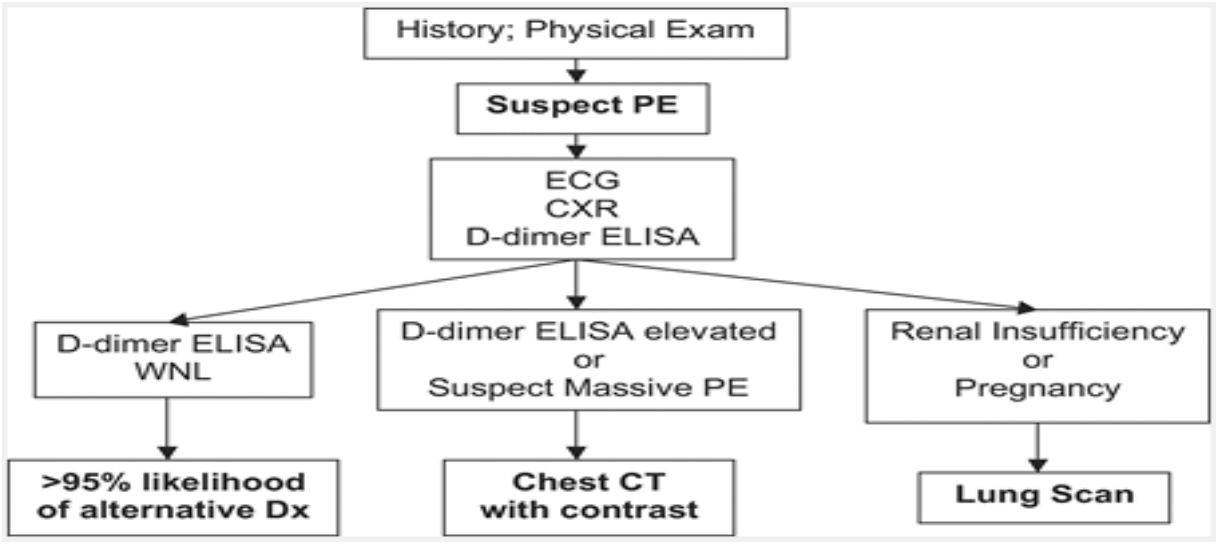
Figure 6 summarizes a critical pathway for PE diagnosis. Unexplained dyspnea and chest pain, often pleuritic, are the most common symptoms of PE. The Wells Scoring System for PE enjoys more popularity than the DVT Scoring System. However, I have never had a patient presented to me with incorporation of the Wells Scoring System unless I asked for it to be included. This Canadian system is used for clinical research purposes, so it is worth knowing. Nevertheless, gestalt is by far the most common way that clinical probability of PE is estimated. The Wells Scoring System is a point system where low probability for PE is less than 2 points, moderate probability is 2 to 6 points, and high probability is greater than 6 points. Seven variables comprised the point score: (a) clinical symptoms of DVT (3 points), (b) no alternative diagnosis (3 points), (c) heart rate greater than 100 beats per minute (1.5 points), (d) immobilization or surgery within the prior 4 weeks (1.5 points), (e) pre-

vious DVT or PE (1.5 points), (f) hemoptysis (1 point), and (g) cancer (1 point). The variable no alternative diagnosis is controversial because it is subjective, not objective, and is the driving forcев that makes the Wells Score an accurate predictor of the presence of absence of PE.

In a prospective observational study at BWH's Emergency Department, there was a trend toward increasing accuracy of PE diagnosis with increasing clinical experience. However, the difference was not as great between an intern and an attending physician as one might have expected. Physicians were asked whether they thought PE was the most likely diagnosis. The frequency of true-positive assessments was 17% for interns and 25% for attending physicians. Keep in mind that only about 10% of patients who undergo emergency imaging for PE actually have PE. Therefore, the astute clinician will formulate a differential diagnosis, even when the manifestations of PE seem obvious.

The classic findings such as tachycardia, tachypnea, or hypotension actually represent unusual patients with extensive PE and impaired compensatory mechanisms. With improved imaging modalities, PE is with increasing frequency identified in normotensive patients who may appear anxious, but whose heart rate is less than 100 beats per minute and whose respiratory rate, if actually counted inconspicuously, is less than 16 breaths per minute.

Figure 6: Diagnosis algorithm for pulmonary thromboembolism



3.1. Mastering the skills of interpretation of coagulation blood test and D-dimer measure in the field of the topic**.**

The hemostasis depends on an interaction between the plasma–based coagulation cascade, platelets, and the endothelium of blood vessels. In the clinical laboratory, in vitro analytical assays are capable of measuring only the first two components of this system. Consequently, laboratory measurements of blood coagulation represent only a close approximation of the body's hemostatic system.

Clinicians frequently order coagulation tests, such as the prothrombin time (PT), activated partial thromboplastin time (aPTT), and thrombin time (TT), to assess blood clotting function in patients. While these laboratory tests may be helpful in elucidating the cause of unexplained bleeding, they are not helpful in predicting if bleeding will occur. In fact, no single test can predict bleeding in the perioperative or postoperative period. Furthermore, these common laboratory tests are of little help in predicting blood clotting or thrombosis in the absence of vessel injury. Well-described assays are available to test for hereditary predisposition to thrombosis, but the majority of thrombophilic states cannot be quantified by any current laboratory tests.Clearly, laboratory assessment of hemostasis presents many challenges for laboratorians and the clinicians who interpret the results. This review briefly explains the common tests used to assess hemostasis, as well as their clinical context, and provides a guide for clinical chemists to assess unexplained bleeding.

Clearly, laboratory assessment of hemostasis presents many challenges for laboratorians and the clinicians who interpret the results. This review briefly explains the common tests used to assess hemostasis, as well as their clinical context, and provides a guide for clinical chemists to assess unexplained bleeding.

The ABCs of Coagulation Tests

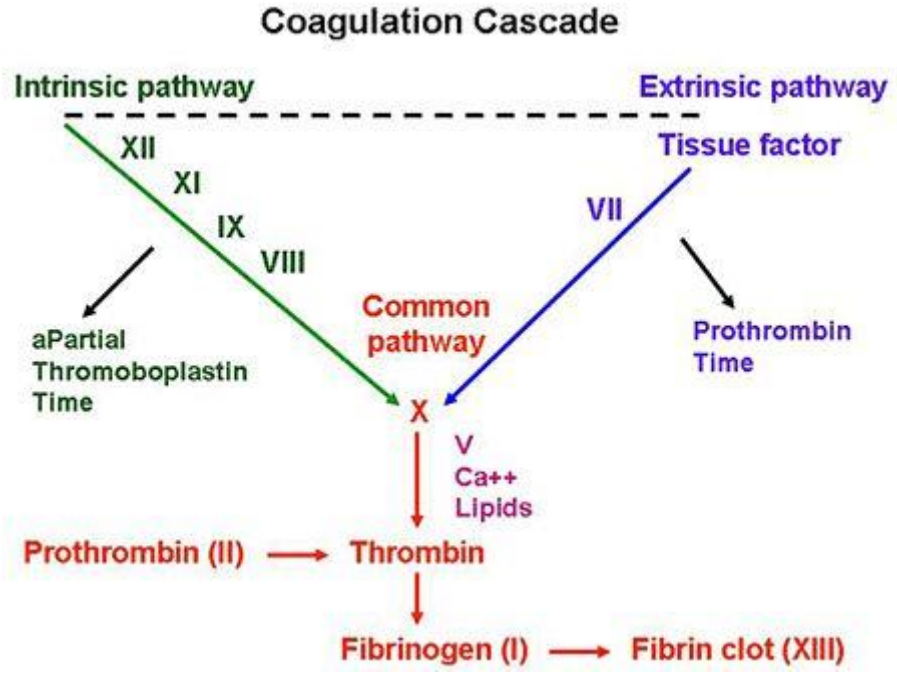
Laboratory tests for hemostasis typically require citrated plasma derived from whole blood. Specimens should be collected into tubes containing 3.2% sodium citrate (109 mM) at a ratio of 9 parts blood and 1 part anticoagulant. The purpose of the citrate is to remove calcium ions that are essential for blood coagulation; however,

failure to fill the draw tube adequately causes the final citrate concentration of the patient sample to be too high. This is important because PT and aPTT tests require the addition of calcium. If the specimen contains excess citrate, addition of calcium may be inadequate, and the low plasma calcium will lead to an artificial prolongation of PT or aPTT.

A similar but more subtle problem might arise if the patient's hematocrit is unusually high, typically ≥55%. Normally, 10 mL of blood with a hematocrit of 40% contains 6 mL of plasma. If the hematocrit is abnormally elevated, for example 65%, the specimen will contain only 3.5 mL of plasma, effectively under-filling the draw tube with plasma, leading to overcitration of the plasma.

For the PT test, adding a thromboplastin reagent containing a tissue factor, calcium, and phospholipids initiates coagulation of the pre-warmed specimen via the extrinsic coagulation pathway (Figure 7). Similarly, the aPTT test is initiated by adding a negatively charged surface such as silica to the plasma, as well as a phospholipid extract that is free of tissue factor. The coagulation pathway that occurs in the aPTT test represents the intrinsic coagulation pathway (Figure 7).

Figure 7: Coagulation cascade



The coagulation cascade is a series of enzymatic reactions that turn inactive precursors into active factors. The end result of the cascade is the production of fibrin, a protein that binds platelets and other materials in a stable clot. The cascade has two initial pathways: the extrinsic (tissue factor-mediated) and the intrinsic (contact system-initiated). These two pathways converge to become the common pathway with the activation of factor X. The steps in the cascade that are measured by the three common coagulation assays, PT, aPTT, and TT, are indicated.

When a patient has an abnormally prolonged PT or aPTT, laboratories should perform a mixing study of the specimen. To perform the test, the technologist mixes an equal volume of the patient's citrated plasma with normal pooled plasma (NPP) and repeats the PT and/or aPTT. If the clotting assay time now falls within the PT and/or aPTT reference intervals, the initial abnormal result was due to one or more clotting factor deficiencies. In contrast, the presence of inhibitors in patient plasma interferes with the clotting factors in the NPP, but the mixing study results will not produce normal clotting times. Another common assay used to assess hemostasis is TT. This test measures the ability of fibrinogen to form fibrin strands in vitro. To perform the test, the technologist adds exogenous thrombin to pre-warmed plasma. This step ensures that the result is independent of endogenous thrombin or any of the other clotting factors. TT is particularly sensitive to heparin.

Biomarkers for monitoring safety and tolerability of anticoagulant therapy inprofilaxis of PTE

Warfarin is one of the most difficult drugs to dose and monitor because of marked patient-to-patient variability, drug drug interactions, and drug food interactions. Warfarin is not given in a fixed dose. Instead, it is administered in an adjusted dose to achieve a target prothrombin time expressed as an INR. For most patients, the target INR is between 2.0 and 3.0.

Beware that 1% to 3% of patients have a genetic mutation that delays metabolism of the S-racemer of warfarin. These patients become fully anticoagulated with tiny doses of warfarin, in the range of 1.0 to 1.5 mg daily.

Centralized anticoagulation services help patients receiving warfarin therapy to achieve better outcomes compared to the usual care provided by their personal physicians. This approach to anticoagulation management is rapidly gaining acceptance throughout North America and Europe as a strategy that maximizes patient safety. A centralized approach allows expert nurses, pharmacists, and physicians' assistants to develop expertise and coordinate efforts that minimize bleeding and clotting complications. The core philosophy is to achieve a coordinated and systematic approach.

There is enormous interest in developing safer and more effective oral antithrombotic agents. Oral inhibitors of thrombin or factor Xa will have to be at least as effective, at least as safe, and yet require less laboratory monitoring. To achieve these goals, the compounds will need to have high and consistent oral bioavailability. One promising approach is administration of oral heparin using a novel carrier that mediates passive gastrointestinal absorption of a noncovalent complex with heparin in a dose-dependent manner. Another strategy is use of a new oral direct thrombin inhibitor, such as dabigatran, that can be administered in a fixed dose without coagulation laboratory monitoring.

D-dimer

Arterial blood gases are unreliable and can be misleading. Specifically, patients who are otherwise healthy can present with large PE and yet maintain a high arterial PO2 and a normal arterial-alveolar oxygen gradient. The only useful blood screening test is the plasma D-dimer ELISA. D-dimers are released in the presence of PE because of endogenous fibrinolysis. Plasmin dissolves some of the fibrin clot from PE, and subsequently, D-dimers are released into the plasma. The D-dimers can be recognized by commercially available monoclonal antibodies. The D-dimer has a high negative predictive value for PE. This means that if the D-dimer is normal, it is extremely unlikely that PE is present.

D-dimers are highly sensitive for the diagnosis of PE. This high sensitivity is crucially important in a screening test. However, D-dimers are nonspecific and will often be elevated in conditions that mimic PE such as acute myocardial infarction or pneumonia. They are also elevated in patients with cancer, in second or third trimes-

ter pregnancy, and in the postoperative state. Plasma D-dimer levels are usually elevated in hospitalized patients. Therefore, their contribution to diagnosis is greatest in outpatients suspected of PE; their use among hospitalized patients is minimal because the test results are rarely normal.

Cardiac Biomarkers

Imaging the right ventricle is probably not necessary if the patient appears clinically stable and has normal levels of cardiac biomarkers. Cardiac troponins are sensitive and specific biomarkers of myocardial cell damage. Elevations of tro-ponin in PE patients are mild and of short duration compared with acute coro-nary syndromes. In acute PE, troponin levels correlate well with the extent of RV dysfunction

Natriuretic peptides represent another class of cardiac biomarkers. The principal stimulus for synthesis and secretion of brain natriuretic peptide (BNP) is ventricular cardiomyocyte stretch. The prohormone, proBNP, has 108 amino acids.

The biologically active BNP is a 32-amino acid peptide, with a plasma half life of 20 minutes. The remaining part of the prohormone, N-terminal (NT)-proBNP, has 76 amino acids and a half life of 60 to 120 minutes. The major role of cardiac biomarkers in risk stratification is to identify low-risk patients who do not require imaging of the right ventricle. Patients with normal levels of troponin and BNP are low risk. A simple risk stratification algorithm for PE patients is to employ either troponin or NT-proBNP testing as an initial step. Echocardiography should then be obtained if elevated biomarker levels are found. Echocardiography is not needed if both troponin and BNP (or pro-BNP) are normal

3.2. Mastering the skills of ECG and echocardiogramms' interpretation in the field of the topic**.**

All patients suspected of PE undergo electrocardiography. Although new-onset atrial fibrillation/flutter and a new S1Q3T3 sign are often cited as helpful clues, these findings are rare. The most common manifestation of right heart strain is T wave inversion in leads V1 to V4.

Classic risk stratification used to rely primarily on frequent assessment of systemic arterial pressure and heart rate. When patients became dependent on pressors to maintain a systolic blood pressure greater than 90 mm Hg, they were labeled as high risk. This strategy delayed intervention with thrombolysis or embolectomy until patients were developing multisystem organ failure due to evolving cardiogenic shock. By that point, the response to aggressive intervention with thrombolysis or embolectomy was often disappointing. Our approach to risk stratification has changed markedly.

We now believe that among normotensive patients, assessment of RV function is pivotal to prognosticate accurately after PE is diagnosed. This assessment can at times be accomplished by finding normal cardiac biomarkers. However, patients who develop worsening RV function despite adequate anticoagulation have an ominous prognosis and are at high risk of in-hospital complications, including recurrent PE, respiratory failure, and death.

The International Cooperative Pulmonary Embolism Registry (ICOPER) enrolled 2,454 patients from 52 hospitals in 7 countries and is the largest PE registry that has ever been published. In ICOPER, age greater than 70 years increased the likelihood of death by 60%. Six other risk factors independently increased the likelihood of mortality by a factor of twofold to threefold: cancer, clinical congestive heart failure, chronic obstructive pulmonary disease, systemic arterial hypotension with a systolic blood pressure of <90 mm Hg, tachypnea (defined as >20 breaths per minute), and RV hypokinesis on echocardiogram, an especially useful sign to identify high-risk patients who might be suitable for aggressive interventions such as thrombolysis or embolectomy.

It is important to emphasize that RV dysfunction on echocardiogram is an important predictor of prognosis, even in patients with a systolic blood pressure greater than 90 mm Hg. Among this population in ICOPER, the 30-day survival rate was 91% in patients without RV hypokinesis compared with 84% in those with RV hypokinesis on baseline echocar-diography.

Combined Biomarkers and Echocardiography

The combination of elevated biomarkers and moderate or severe RV dysfunction can portend a lethal outcome. At BWH, the combination of echocardiographic RV enlargement and elevated troponin significantly increased the 30-day mortality (38%) compared with patients with elevated troponin alone (23%), RV dilation alone (9%), and neither (5%).

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4. Тема 8. Practical skills for the topic №№ 12-13 «Cardiac rhythm disorders. Cardiac conductivity disorders ».

Because of the increasing availability of sophisticated electrophysiologic techniques for the study of cardiac tissues both in vivo and in vitro and the ability to study arrhythmias and conduction disturbances both in experimental models and in patients, knowledge about the mechanisms of arrhythmias and conduction disturbances has increased greatly. Although much is now known, much remains to be understood. Arrhythmias are due to normal or abnormal impulse generation, abnormal impulse conduction, or a combination of simultaneous abnormalities of impulse generation and conduction. This guideline provides an overview of these mechanisms and identifies the clinical arrhythmias with which they are thought to be associated. This is followed by a much more detailed discussion of these mechanisms as they are currently understood. The detailed discussion requires that the reader have a rudimentary knowledge of the basic cellular electrophysiology of the heart, including the ionic channels and membrane currents causing the resting potential and the cardiac action potential, as well as the mechanisms for automaticity and conduction. However, much of this material is included in a detailed discussion of the mechanisms of arrhythmias, since the chapter considers how alterations in normal electrophysiology lead to abnormal cardiac rhythms.

The diagnosis and management of cardiac arrhythmias and conduction disturbances require the coordination of electrocardiographic (ECG) analysis of the rhythm disturbance, assessment of the clinical setting, and identification of an end point and method of therapy. ECG recognition of arrhythmias requires an organized system of analysis of atrial and ventricular myocardial activation and deduction of atrioventricular (AV) conduction patterns. Forms of arrhythmias are separated into those that cause limited symptoms but may trigger symptomatic sustained arrhythmias under appropriate conditions (e.g., premature atrial or ventricular impulses) and those that are sustained symptomatic and/or potentially fatal arrhythmias [e.g., supraventricular

tachycardias (SVTs), ventricular tachycardias (VTs), ventricular fibrillation (VF), or bradycardias].

Clinical settings are broadly divided into those that are acute or transient, such as acute ischemia, the acute phase of myocardial infarction, electrolyte dis-turbances, or proarrhythmic effects of antiarrhythmic drugs, and those that provide a persistent substrate for arrhythmias, such as chronic ischemic heart disease, cardiomyopathies, and anatomic and physiologic substrates for the various paroxysmal supraventricular tachyarrhythmias. Analogous to the concept of "triggering" and "sustained" arrhyth-mias, transient ischemia and hemodynamic disturbances may be viewed as triggering events and chronic ischemic heart disease and the hypertrophied or myopathic heart as sustaining substrates. The goals, or end points, of therapy of cardiac arrhythmias are dependent on the forms, clinical settings, and mechanisms of arrhythmia. Broad-ly, goals of treatment may be antiarrhythmic (targeted to the suppression of ambient or triggering arrhythmias or events) or antitachycardiac, antifibrillatory, or heart rate supporting (in which the goal is prevention or reversion of sustained arrhythmias), whether the arrhythmias are well tolerated, symptomatic, or life-threatening

The Standard Electrocardiogram

The standard 12-lead ECG and rhythm strips provide a direct and easily accessi-ble method for diagnosing disturbances of cardiac rhythm. The simultaneous-lead rhythm strip accompanying the 12-lead ECG on many current ECG machines, plus the option of recording longer multilead rhythm strips, will yield sufficient informa-tion for a prompt and accurate diagnosis of most cardiac rhythm disturbances. For many arrhythmias, analysis requires only the recognition of P-wave and QRS mor-phology, their relative timing, and their vectors. Simple inspection of the tracing, with caliper-assisted measurements, may be sufficient; but the analysis of more com-plex arrhythmias is facilitated by the use of ladder diagrams. First used extensively by Sir Thomas Lewis, they are also referred to as Lewis lines. The ladders are usually constructed with three tiers-A, AV, and V-but additional tiers may be helpful in de-picting events related to sinoatrial (SA) conduction or ventricular ectopic rhythms. The A and V tiers are used to depict activation of atrial and ventricular muscle, re-

spectively. The middle tier (AV) is used to infer conduction characteristics in the AV junction. Since atrial and ventricular activation are the only direct registrations of cardiac electrical activity on the standard ECG, they are diagrammed first. The A line is drawn from the beginning of the P wave and the V line from the beginning of the QRS. Time is indicated by the slope of the line, and the site within a tier in which impulse propagation begins (upper, middle, or lower) shows the direction the impulse is traveling. The site of origin may be represented by a black dot. A blocked impulse is indicated by a short bar at a right angle to the line indicating direction of conduction, and aberrant intraventricular conduction is shown as a pair of slightly divergent lines.

Special Leads

When the standard ECG does not provide sufficient information to establish a diagnosis, usually due to inability to identify P waves, special lead systems may be used. The simplest is the Lewis lead configuration, in which the right and left arm electrodes are deployed as a bipolar lead to the right of the sternum in a superior-inferior orientation. A bipolar esophageal lead can record left atrial activity, and an intraatrial electrode catheter can record atrial activity from within the right atrium. For both techniques, it is necessary to have at least one standard surface ECG lead recorded simultaneously with the special lead. Continuous Monitor Recordings Continuous monitoring of cardiac rhythm may be performed in hospital in special care units or in the ambulatory patient using various types of portable recording devices. Some systems provide the capability for simultaneous multilead recordings that improve diagnostic yield considerably. Long-term storage capabilities for inpatient monitoring permit off-line analysis of complex rhythm disturbances if the physician is not available at the time the arrhythmia occurs. The two most popular leads for use in bedside monitoring are lead II and MCL-I, the latter providing a pattern similar to V1.

For infrequently occurring arrhythmias, a number of event recorders are now available. They allow the patient to activate the device when an event occurs, providing internal storage that can be transmitted by telephone to a central station for later

review. Transtelephonic transmitters also can be used in real time for more persistent or frequent events. Finally, a small subcutaneous implantable recorder is available for patients with infrequent arrhythmias that warrant an aggressive documentation attempt. The device may be explanted after a diagnosis is established.

Exercise Testing for Cardiac Arrhythmias

Treadmill stress testing may be used to initiate an evanescent arrhythmia, document an exercise relationship to its onset, and evaluate both efficacy and adverse responses to therapy. The standard treadmill is used, and thallium or echocardiographic imaging is not necessary unless an ischemic basis correlating with the onset of arrhythmia is suspected. The procedure is especially useful for eliciting and evaluating therapy of exercise-induced ventricular arrhythmias, for distinguishing autonomic from structural disease mechanisms of sinus or AV node dysfunction, and for evaluating adverse effects of drug therapy, such as rate-dependent proarrhythmic effects, as may occur with strong Na+-channel blockers, such as flecainide. Exercise testing may also provide some general insights into the refractory period of an accessory pathway in Wolff-Parkinson-White (WPW) syndrome. Abrupt disappearance of the delta wave during exercise induced increase in heart rate suggests encroachment on the refractory period, while gradual disappearance may simply be due to enhanced AV nodal conduction.

Signal-Averaged Electrocardiography, Heart Rate Variability, and Baroreceptor Sensi-tivity

Signal-averaged electrocardiography, heart rate variability, and baroreceptor sensitivity provide information on mortality risk and the probability of life-threatening arrhythmias, whether used separately or combined with other estimates of risk [e.g., premature ventricular contractions (PVCs) and nonsustained VT on 24-h ambulatory monitoring and ejection fraction (EF) measurements]. They have been applied most intensively after myocardial infarction.

Signal-averaged electrocardiography employs amplification of low-amplitude signals occurring after the termination of the standard electrocardio-graphic QRS complex, as recorded by high-amplification techniques. The low-amplitude signals

are repetitive electrical events caused by a delayed activation sequence of part or parts of the ventricular muscle mass. Their repetitive timing allows them to be amplified during signal averaging, while random noise is being canceled out. The resultant signal is a high-gain, high frequency QRS complex, followed by low-amplitude signals representing the late potentials. The terminal delayed activation pattern represents a pathophysiologic marker for susceptibility to ventricular arrhythmias. It results from fragmented activation in an area of delayed conduction, which is a well established substrate for reentrant arrhythmias.

The characteristics of an abnormal signal-averaged ECG include

• a prolonged filtered QRS complex (115 ms) with a normal duration of the standard QRS complex,

• the terminal portion of the filtered QRS complex less than 40 V for 39 ms,

• less than 20 V of amplitude during the last 40 ms of the filtered QRS complex.

At least two of the three criteria must be abnormal to consider the tracing abnormal, and many would require all three to be abnormal. Residual high-frequency noise content must be less than 1 V with a 25-Hz high-pass cutoff Signal-averaged electrocardiography is most useful for demonstrating presence and absence of risk for ventricular arrhythmias and sudden death after myocardial infarction. It is most powerful as a negative predictor of risk, in that a normal signal-averaged ECG after healing of myocardial infarction identifies a greater than 97 percent probability of remaining free of ventricular arrhythmias. The positive predictive accuracy is less powerful and is heavily influenced by other variables, such as EF and ambient ventricular arrhythmias. Signal-averaged electrocardiography alone has a positive predictive value in the range of 20 percent, and combined with a low EF and ambient arrhythmias, the risk may be as high as 50 percent in some subgroups.

Heart rate variability studies provide estimates of sympathetic and parasympathetic balance. Blunting of the normal patterns of variability of sinus rate over time in subgroups of myocardial infarction and cardiac arrest survivors ap-pears to increase the risk of life-threatening events. As is the case for signal-averaged electrocardiography, the test is used primarily for prognostic information rather than as a

therapeutic guide. Baroreceptor sensitivity estimates the relationship between phenylephrine-induced blood pressure increase and concomitant fall in heart rate as an indication of parasympathetic responsiveness to the pure adrenergic stimulus. Following a myocardial infarction, a blunted baroreceptor sensitivity predicts an increased risk of VT and death. A recent large study also demonstrated its power for predicting adverse outcome following a myocardial infarction, which was further enhanced when combined with other risk variables, such as low EF and ambient arrhythmias.

4.1. Mastering the skills of ECG interpretation in the field of the topic**.**

The heart is capable of only five basic types of rhythm disturbances:

1. The electrical activity follows the usual conduction pathways we have already outlined, but it is either too fast, too slow, or irregular. These are arrhythmias of sinus origin.
2. The electrical activity originates from a focus other than the sinus node. These are called ectopic rhythms.
3. The electrical activity is trapped within an electrical racetrack whose shape and boundaries are determined by various anatomic or electrical myocardial features. These are called reentrant arrhythmias. They can occur anywhere in the heart.
4. The electrical activity originates in the sinus node and follows the usual pathways but encounters unexpected blocks and delays.
5. The electrical activity follows accessory conduction pathways that bypass the normal ones, providing an electrical shortcut, or short circuit. These arrhythmias are termed preexcitation syndromes.

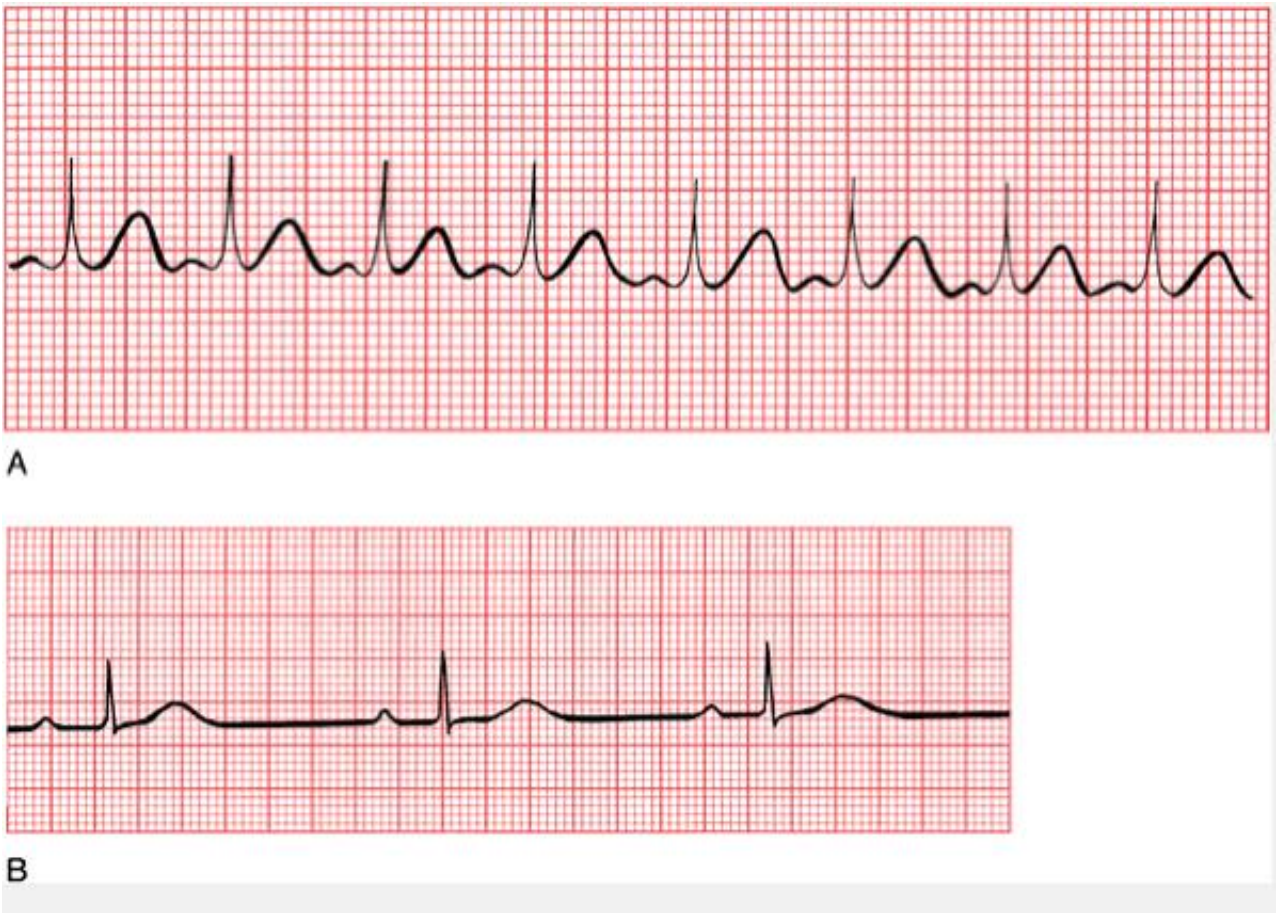
Sinus Tachycardia and Sinus Bradycardia

Normal sinus rhythm is the normal rhythm of the heart. Depolarization originates spontaneously within the sinus node. The rate is regular and between 60 and 100 beats per minute. If the rhythm speeds up beyond 100, it is called sinus tachycardia; if it slows down below 60, it is called sinus bradycardia (Figure 7).

Sinus tachycardia and sinus bradycardia can be normal or pathologic. Strenuous exercise, for example, will speed the heart rate over 100 beats per minute, whe-

reas resting heart rates below 60 beats per minute are typical in well-conditioned athletes.

Figure 7: Sinus tachycardia and bradicardia



Notes: (A) Sinus tachycardia. Each beat is separated by two and one half large squares for a rate of 120 beats per minute. (B) Sinus bradycardia. More than seven large squares separate each beat, and the rate is 40 to 45 beats per minute.

On the other hand, alterations in the rate at which the sinus node fires can accompany significant heart disease. Sinus tachycardia can occur in patients with congestive heart failure or severe lung disease, or it can be the only presenting sign of hyperthyroidism. Sinus bradycardia is the most common rhythm disturbance seen in the early stages of an acute myocardial infarction; in otherwise healthy individuals, it can result from enhanced vagal tone and can cause fainting.

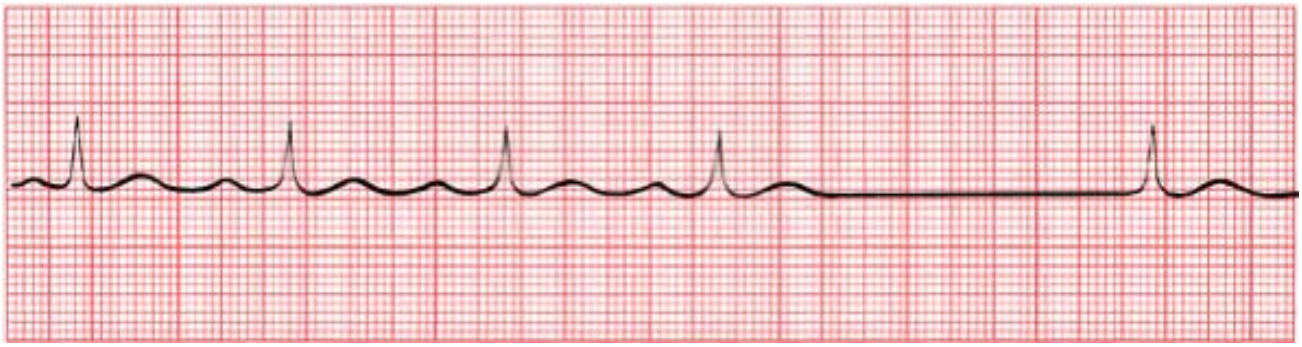
Sinus Arrhythmia

Often, the ECG will reveal a rhythm that appears in all respects to be normal sinus rhythm except that it is slightly irregular. This is called sinus arrhythmia. Most often, it is a normal phenomenon, reflecting the variation in heart rate with inspiration and expiration.Inspiration accelerates the heart rate, and expiration slows it down

Sinus Arrest, Asystole, and Escape Beats

Sinus arrest occurs when the sinus node stops firing (Figure 8). If nothing else were to happen, the EKG would show a flat line without any electrical activity, and the patient would die. Prolonged electrical inactivity is called asystole.

Figure 8: Sinus arrest occurs after the fourth beat. The fifth beat, restoring electrical activity to the heart, is a junctional escape beat. Note the absence of P waves.



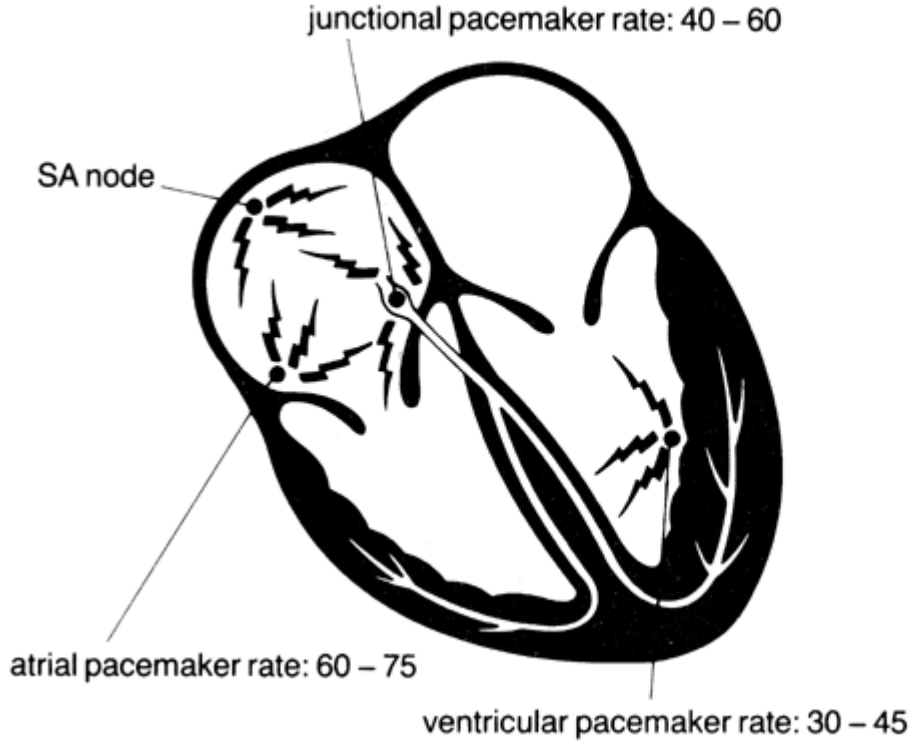
Fortunately, virtually all myocardial cells have the ability to behave as pacemakers. Ordinarily, the fastest pacemaker drives the heart, and under normal circumstances, the fastest pacemaker is the sinus node. The sinus node overdrives the other pacemaker cells by delivering its wave of depolarization throughout the myocardium before its potential competitors can complete their own, more leisurely, spontaneous depolarization. With sinus arrest, however, these other pacemakers can spring into action in a kind of rescue mission. These rescuing beats, originating outside the sinus node, are called escape beats.

Nonsinus Pacemakers

Like the sinus node, which typically fires between 60 and 100 times each minute, these other pacemaker cells have their own intrinsic rhythm. Atrial pacemakers usually discharge at a rate of 60 to 75 beats per minute. Pacemaker cells located near the AV node, called junctional pacemakers, typically discharge at 40 to 60 beats per

minute. Ventricular pacemaker cells usually discharge at 30 to 45 beats per minute (Figure 9).

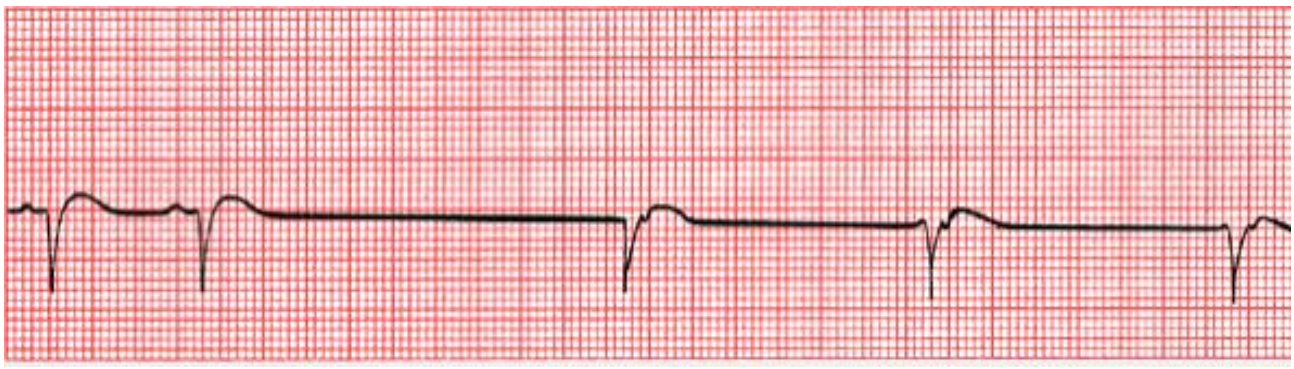
Figure 9: Location of source of non-sinus rhythms



Each of these nonsinus pacemakers can rescue an inadequate sinus node by providing just one or a continual series of escape beats. Of all of the available escape mechanisms, junctional escape is by far the most common.

With junctional escape, depolarization originates near the AV node, and the usual pattern of atrial depolarization does not occur (Figure 10). As a result, a normal P wave is not seen. Most often, there is no P wave at all. Occasionally, however, a retrograde P wave may be seen, representing atrial depolarization moving backward from the AV node into the atria. The mean electrical axis of this retrograde P wave is reversed 180B° from that of the normal P wave. Thus, whereas the normal P wave is upright in lead II and inverted in lead AVR, the retrograde P wave is inverted in lead II and upright in lead AVR.

Figure 10: Junctional escape.



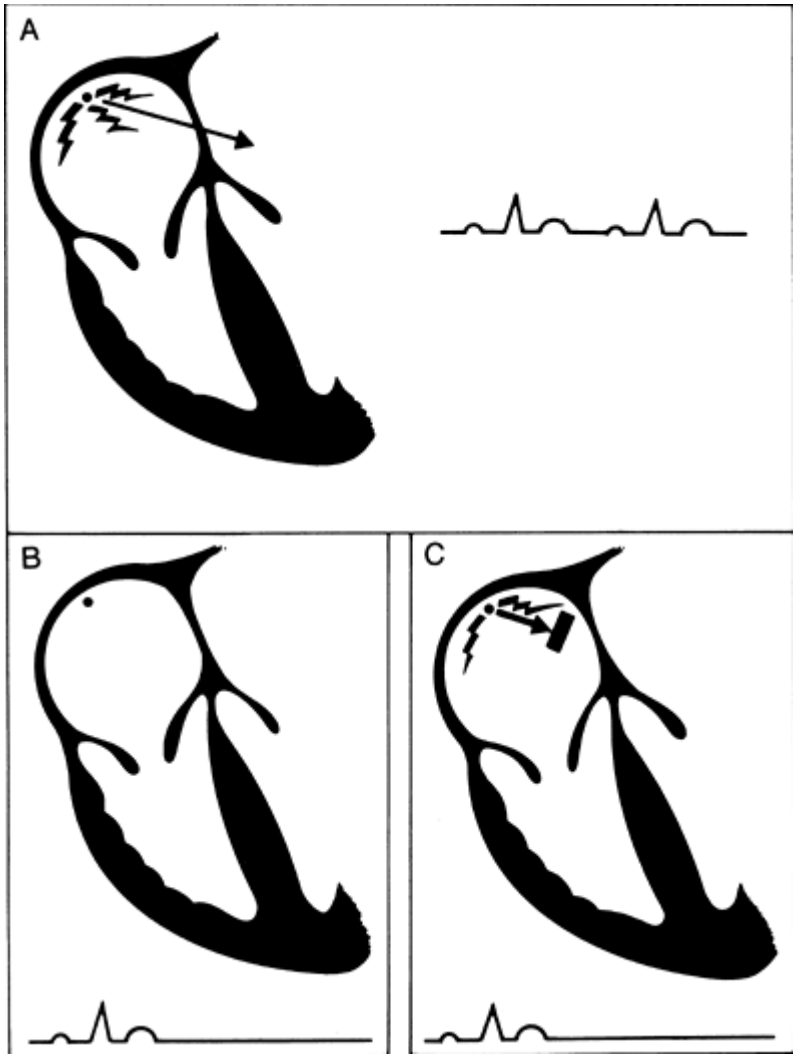
Notes: The first two beats are normal sinus beats with a normal P wave preceding each QRS complex. There is then a long pause followed by a series of three junctional escape beats occurring at a rate of 40 to 45 beats per minute. Retrograde P waves can be seen buried in the early portion of the T waves. Retrograde P waves can occur before, after, or during the QRS complex, depending on the relative timing of atrial and ventricular depolarization. If atrial and ventricular depolarization occur simultaneously, the much larger QRS complexes will mask the retrograde P waves

Sinus Arrest Versus Sinus Exit Block

Because sinus node depolarization is not recorded on the ECG, it is impossible to determine whether a prolonged sinus pause is due to sinus arrest or to failure of the sinus depolarization to be transmitted out of the node and into the atria, a situation called sinus exit block (Figure 11). You may hear these different terms bandied about from time to time, but for all intents and purposes, sinus arrest and sinus exit block mean the same thing: there is a failure of the sinus mechanism to deliver its current into the surrounding tissue (Fugure 12).

Special note for the electrically infatuated: transient sinus arrest and sinus exit block can sometimes be distinguished on the ECG. With sinus arrest, resumption of sinus electrical activity occurs at any random time (the sinus node simply resumes firing). However, with sinus exit block, the sinus node has continued to fire silently, and termination of the block allows the sinus node to resume depolarizing the atria after a pause that is some multiple of the normal cycle (exactly one missed P wave, or exactly two missed P waves, or more).

Figure 10: Illustration of turning normal sinus rhythm into sinus arrest / block

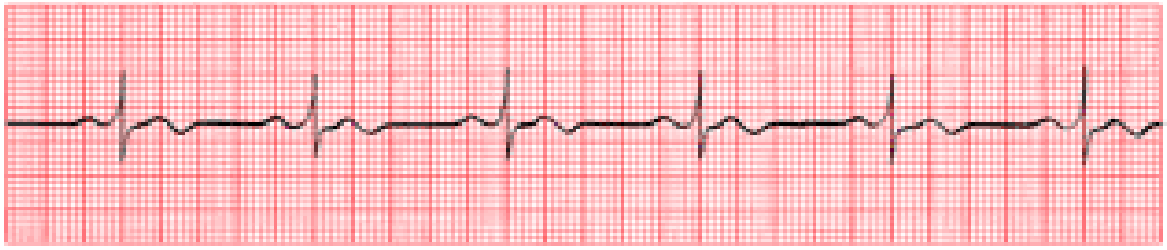


Notes: (A) Normal sinus rhythm. The sinus node fires repeatedly, and waves of depolarization spread out into the atria. (B) Sinus arrest. The sinus node falls silent. No current is generated, and the EKG shows no electrical activity. (C) Sinus exit block. The sinus node continues to fire, but the wave of depolarization fails to exit the sinus node into the atrial myocardium. Again, the EKG shows no electrical activity.

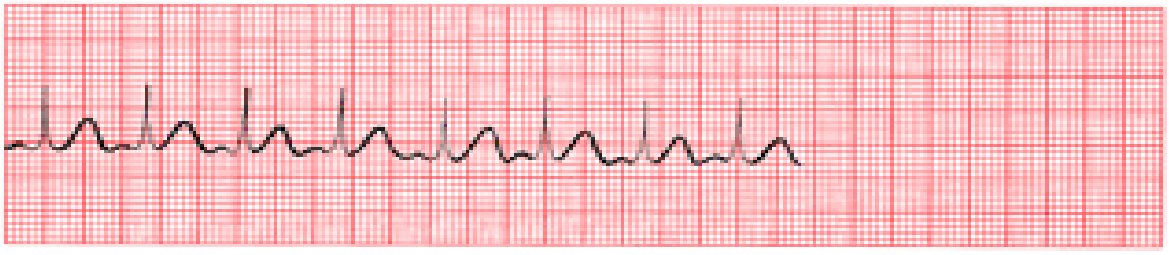
Ectopic Rhythms

Ectopic rhythms are abnormal rhythms that arise from elsewhere than the sinus node. In this way, they resemble escape beats, but here we are talking about sustained rhythms, not just one or a few beats. Ectopic rhythms can be caused by any of the precipitating factors described previously

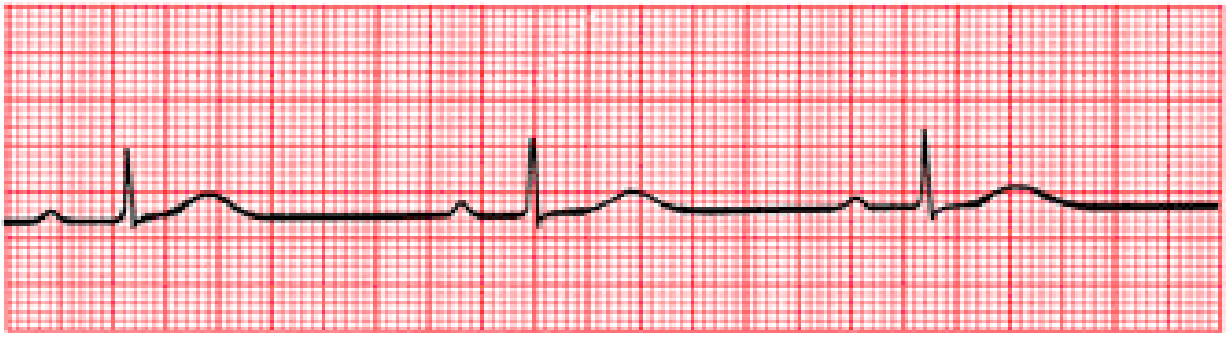
Figure 12: Several types of supraventricular arrhythmias



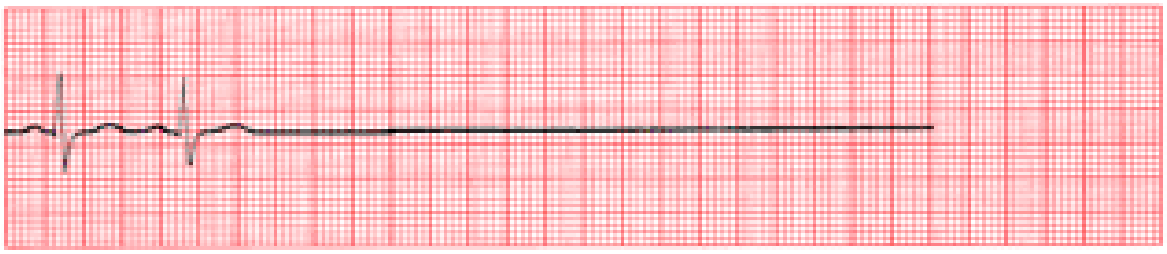
Normal sinus rhythm



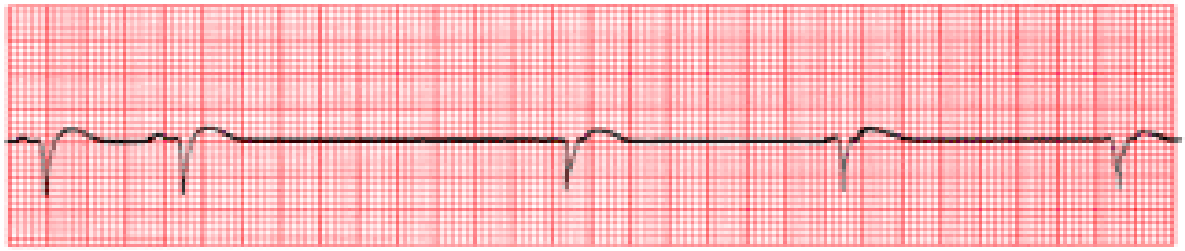
Sinus tachycardia



Sinus bradycardia



Sinus arrest or exit block



Sinus arrest or exit block with junctional escape

If we look at the cellular level, they arise from enhanced automaticity of a nonsinus node site, either a single focus or a roving one. The fastest pacemaker usually drives the heart, and under normal circumstances, the fastest pacemaker is the sinus node. Under abnormal circumstances, any of the other pacemakers scattered throughout the heart can be accelerated, that is, stimulated to depolarize faster and faster until they can overdrive the normal sinus mechanism and establish their own transient or sustained ectopic rhythm. One of the most common causes of enhanced automaticity is digitalis toxicity.

Re-entrant Rhythms

Whereas enhanced automaticity represents a disorder of impulse formation (i.e., new impulses formed elsewhere than the sinus node take over the heart), reentry represents a disorder of impulse transmission. The results, however, are similar: creation of a focus of abnormal electrical activity. Here is how reentry works:

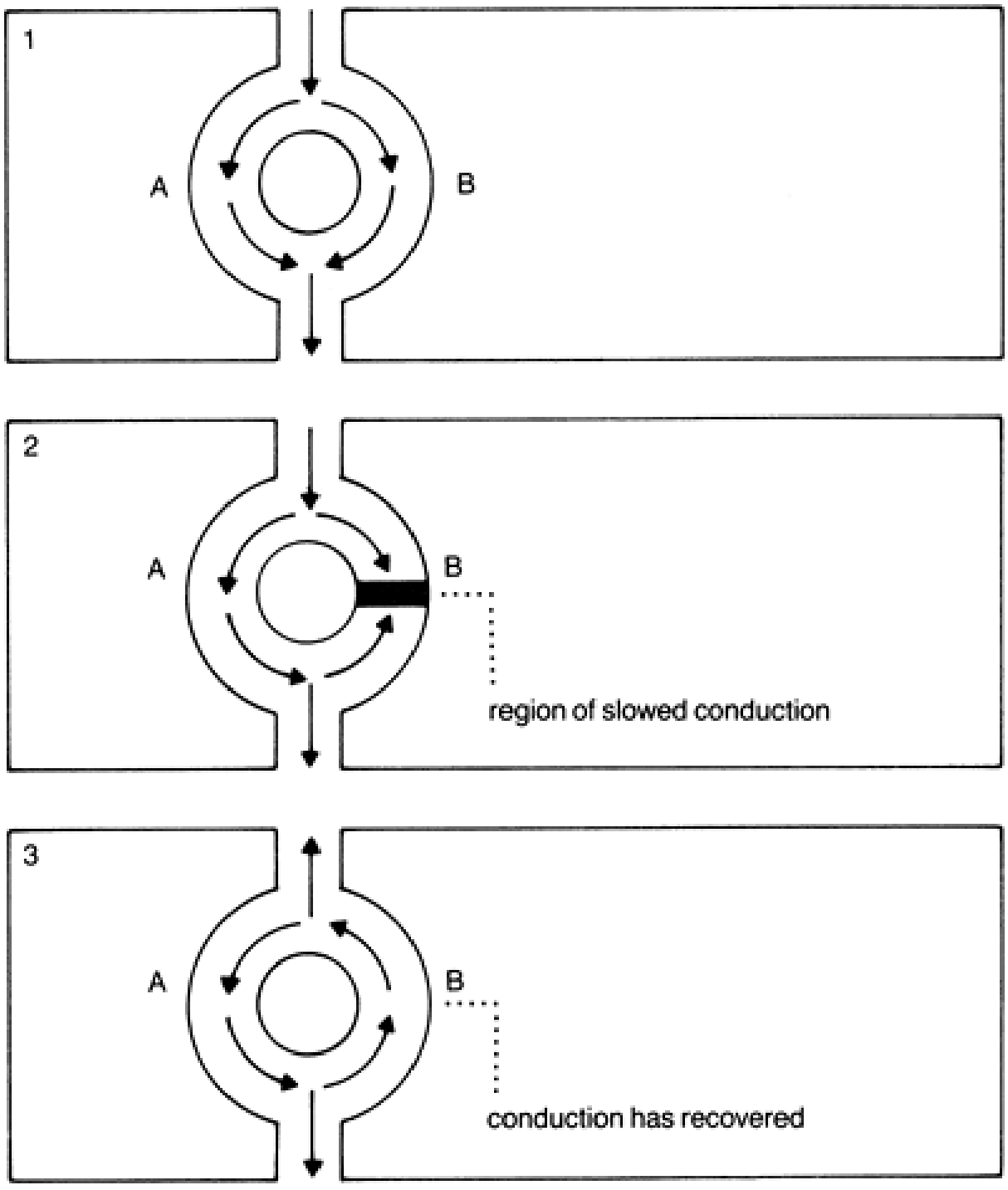
Picture a wave of depolarization arriving at two adjacent regions of myocardium, A and B, as shown in part 1 of the figure on the next page. A and B conduct the current at the same rate, and the wave of depolarization rushes past, unperturbed, on its way to new destinations. This is the way things usually operate.

Suppose, however, that pathway B transmits the wave of depolarization more slowly than pathway A. This can result, for example, if pathway B has been damaged by ischemic disease or fibrosis, or if the two pathways are receiving different degrees of input from the autonomic nervous system. This situation is depicted in part 2 of the figure. The wave of depolarization now rushes through pathway A but is held up in pathway B. The impulse emerging from pathway A can now return back through pathway B, setting up an uninterrupted revolving circuit along the two pathways (Fig. 14). As the electrical impulse spins in this loop, waves of depolarization are sent out in all directions. This is called a reentry loop, and it behaves like an electrical racetrack, providing a source of electrical activation that can overdrive the sinus mechanism and run the heart.

A reentry loop can vary greatly in size. It can be limited to a small loop within a single anatomic site (e.g., the AV node), it can loop through an entire chamber

(either an atrium or ventricle), or it can even involve both an atrium and ventricle if there is an accessory pathway of conduction connecting the two chambers.

Figure 14: A model showing how a reentrant circuit becomes established.



Notes: (1) Normally pathways A and B (any two adjacent regions of cardiac function) conduct current equally well. (2) Here, however, conduction through pathway B is temporarily slowed. Current passing down A can then turn back and conduct in a retrograde fashion through B. (3) The reentry loop is established.

Finally, if there are normal-appearing P waves with a normal P wave axis, then the origin of the arrhythmia is almost certainly within the atria. If no P waves are present, then the rhythm must have originated below the atria, in the AV node or the ventricles. The presence of P waves with an abnormal axis may reflect retrograde activation of the atria from impulses originating below the atria, in the AV node or in the ventricles, that is, from current flowing backward to the atria through the AV node or through an accessory pathway (more on all of this later).

Therefore, a narrow normal QRS complex implies that ventricular depolarization is proceeding along the usual pathways (AV node to His bundle to bundle branches to Purkinje cells). This is the most efficient means of conduction, requiring the least amount of time, so the resulting QRS complex is of short duration (narrow). A narrow QRS complex, therefore, indicates that the origin of the rhythm must be at or above the AV node. A wide QRS complex usually implies that the origin of ventricular depolarization is within the ventricles themselves. Depolarization is initiated within the ventricular myocardium, not the conduction system, and therefore spreads much more slowly. Conduction does not follow the most efficient pathway, and the QRS complex is of long duration (wide).

Noted, if the P wave and QRS complexes correlate in the usual one-to-one fashion, with a single P wave preceding each QRS complex, then the rhythm almost certainly has an atrial origin. Sometimes, however, the atria and ventricles depolarize and contract independently of each other. This will be manifested on the ECG by a lack of correlation between the P waves and QRS complexes, a situation termed AV dissociation.

Supraventricular Arrhythmias

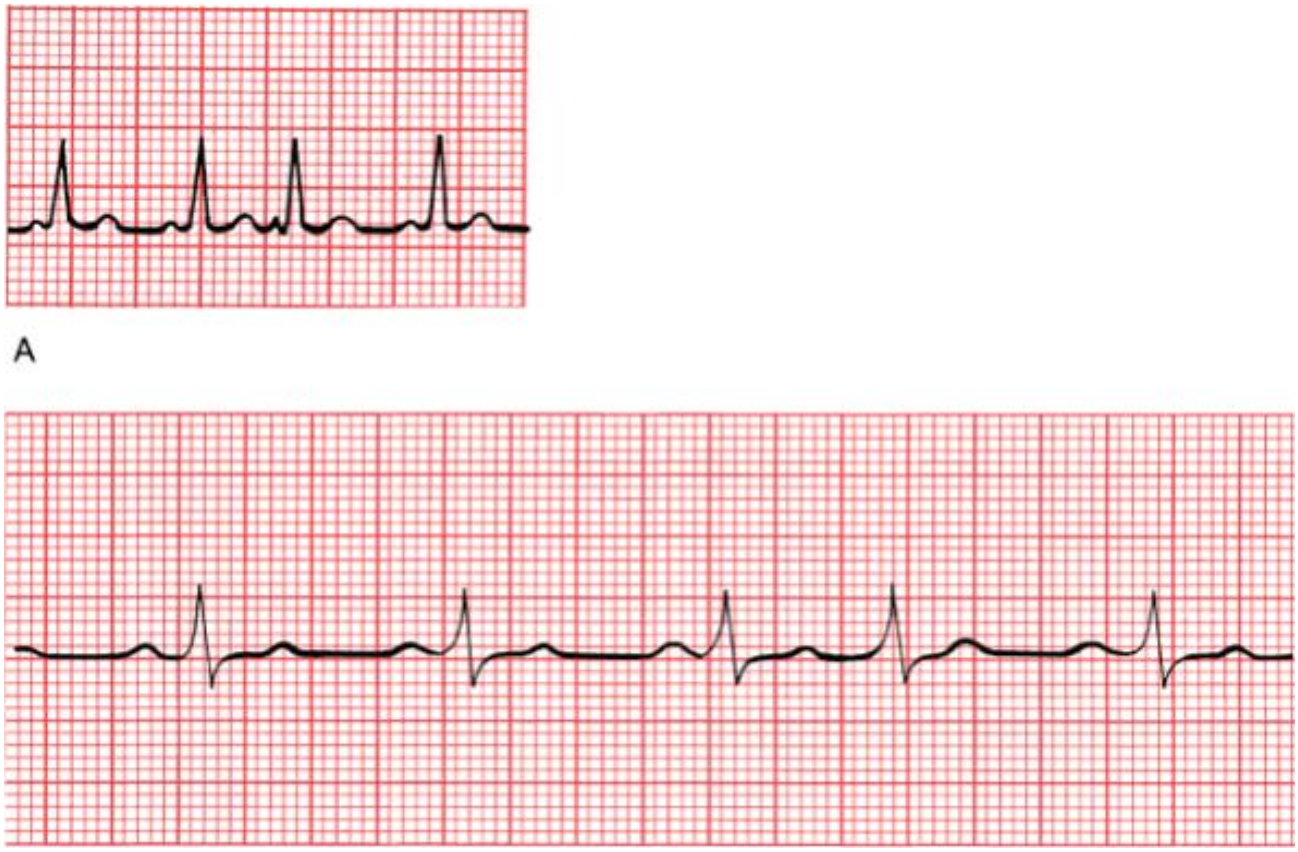
Let us look first at the arrhythmias that originate in the atria or the AV node, the supraventricular arrhythmias. Atrial arrhythmias can consist of a single beat or a sustained rhythm disturbance lasting for a few seconds or many years.

Atrial and Junctional Premature Beats

Single ectopic supraventricular beats can originate in the atria or in the vicinity of the AV node. The former are called atrial premature beats (or premature atrial con-

tractions); the latter, junctional premature beats. These are common phenomena, neither indicating underlying cardiac disease nor requiring treatment. They can, however, initiate more sustained arrhythmias

Figure 15: Atrial and Junctional Premature Beats



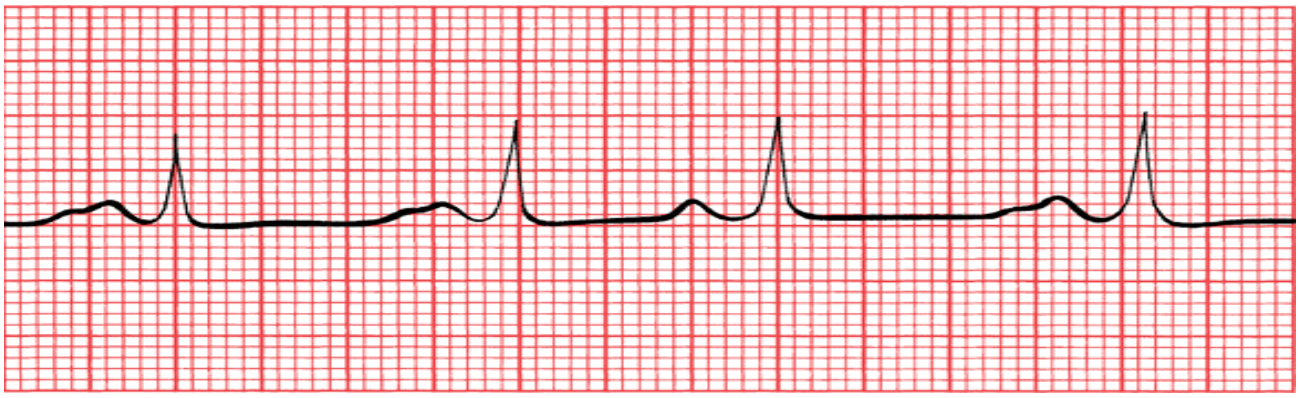
Notes: (A) The third beat is an atrial premature beat. Note how the P wave contour of the premature beat differs from that of the normal sinus beat. (B) The fourth beat is a junctional premature beat. There is no P wave preceding the premature QRS complex.

An atrial premature beat can be distinguished from a normal sinus beat by the contour of the P wave and by the timing of the beat.

Contour. Because an atrial premature beat originates at an atrial site distant from the sinus node, atrial depolarization does not occur in the usual manner, and the configuration of the resultant P wave differs from that of the sinus P waves. If the site of origin of the atrial premature beat is far from the sinus node, the axis of the atrial premature beat will also differ from that of the normal P waves (Fig. 16).

Timing. An atrial premature beat comes too early; that is, it intrudes itself before the next anticipated sinus wave.

Figure 16: Allorhythmic atrial premature beat



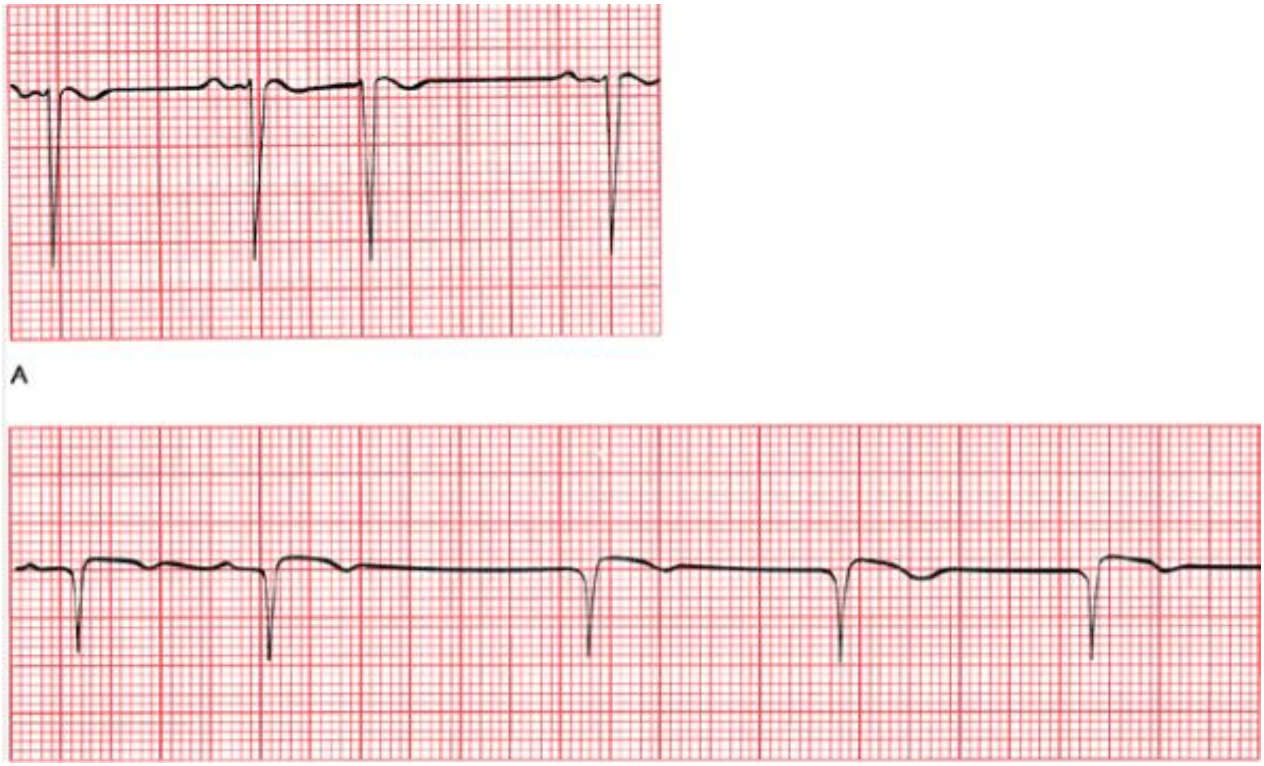
Notes: The third beat is an atrial premature beat. The P wave is shaped differently from the other, somewhat unusual-looking P waves, and the beat is clearly premature.

With junctional premature beats, there is usually no visible P wave, but sometimes a retrograde P wave may be seen (Fig.17). This is just like the case with the junctional escape beats seen with sinus arrest. What is the difference between a junctional premature beat and a junctional escape beat? They look exactly alike, but the junctional premature beat occurs early, prematurely, interposing itself into the normal sinus rhythm. An escape beat occurs late, following a long pause when the sinus node has failed to fire. Both atrial and junctional premature beats are usually conducted normally to the ventricles, and the resultant QRS complex is therefore narrow.

There are five types of sustained supraventricular arrhythmias that you must learn to recognize:

- Paroxysmal supraventricular tachycardia (PSVT), sometimes also called AV nodal reentrant tachycardia
- Atrial flutter
- Atrial fibrillation
- Multifocal atrial tachycardia (MAT)
- Paroxysmal atrial tachycardia (PAT), sometimes also called ectopic atrial tachycardia.

Figure 17: (A) A junctional premature beat.



Notes: The third beat is obviously premature, and there is no P wave preceding the QRS complex. (B) The third beat is a junctional escape beat, establishing a sustained junctional rhythm. It looks just like a junctional premature beat, but it occurs late, following a prolonged pause, rather than prematurely.

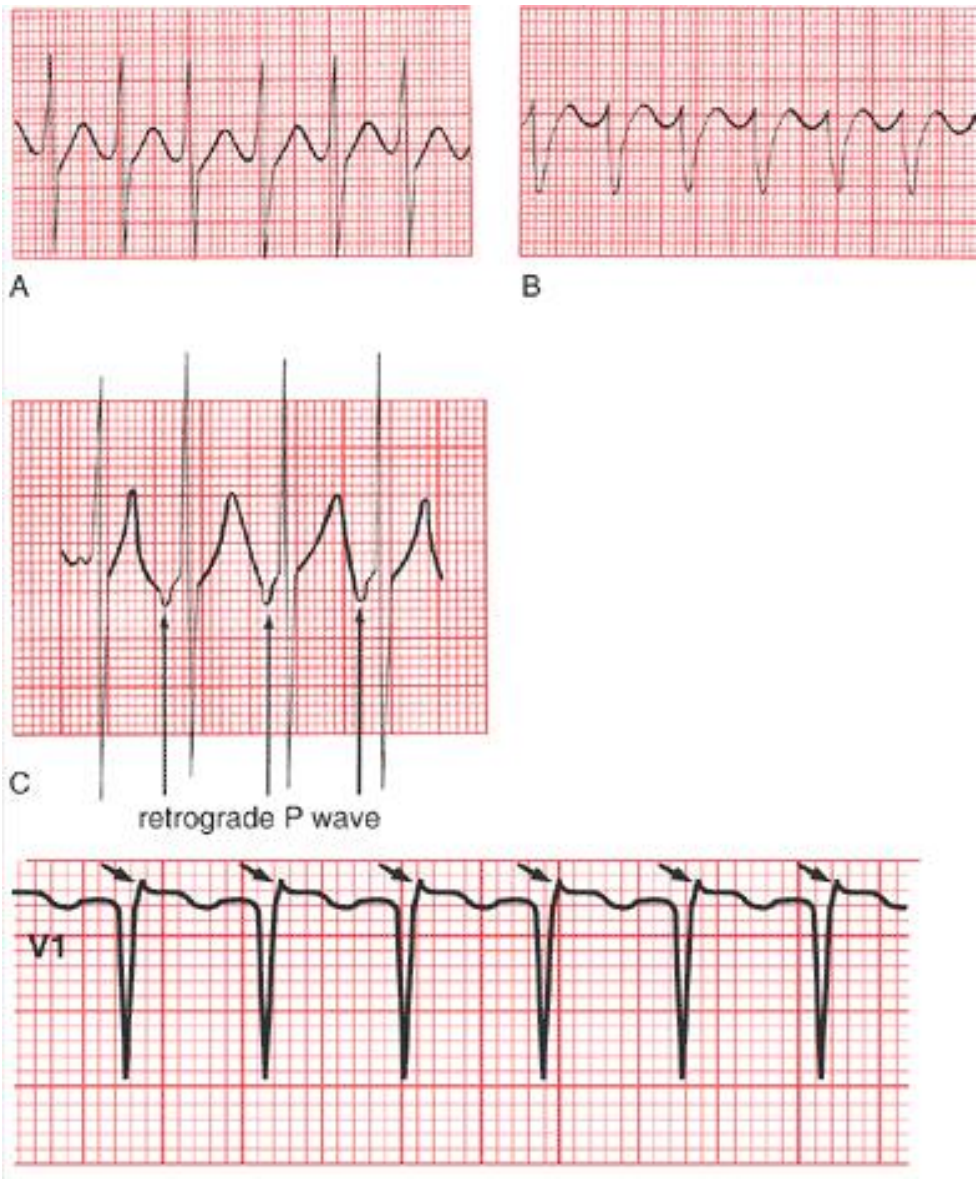
Paroxysmal Supraventricular Tachycardia

Paroxysmal supraventricular tachycardia (PSVT) is a very common arrhythmia. Its onset is sudden, usually initiated by a premature supraventricular beat (atrial or junctional), and its termination is just as abrupt. It can occur in perfectly normal hearts; there may be no underlying cardiac disease at all. Not uncommonly, alcohol, coffee, or just sheer excitement can elicit this rhythm disturbance.

PSVT is an absolutely regular rhythm, with a rate usually between 150 and 250 beats per minute. There are several types of PSVT. The most common type is driven by a reentrant circuit looping within the AV node. Retrograde P waves may sometimes be seen in leads II or III, but your best chance would be to look in lead V1 for what is called a pseudo-R', a little blip in the QRS complex that represents the superimposed P wave. More often than not, however, the P waves are so buried in the

QRS complexes that they cannot be identified with any confidence. As with most supraventricular arrhythmias, the QRS complex is usually narrow (Fig. 18).

Figure 18: Paroxysmal supraventricular tachycardia



Notes: Paroxysmal supraventricular tachycardia in three different patients. A shows simultaneous activation of the atria and ventricles; therefore, the retrograde P waves are lost in the QRS complexes. B shows a supraventricular tachycardia mimicking a more serious rhythm called ventricular tachycardia. In C, retrograde P waves can be seen. (D) A good example of the pseudo-R' configuration in lead V1 representing the retrograde P waves (arrows) of PSVT.

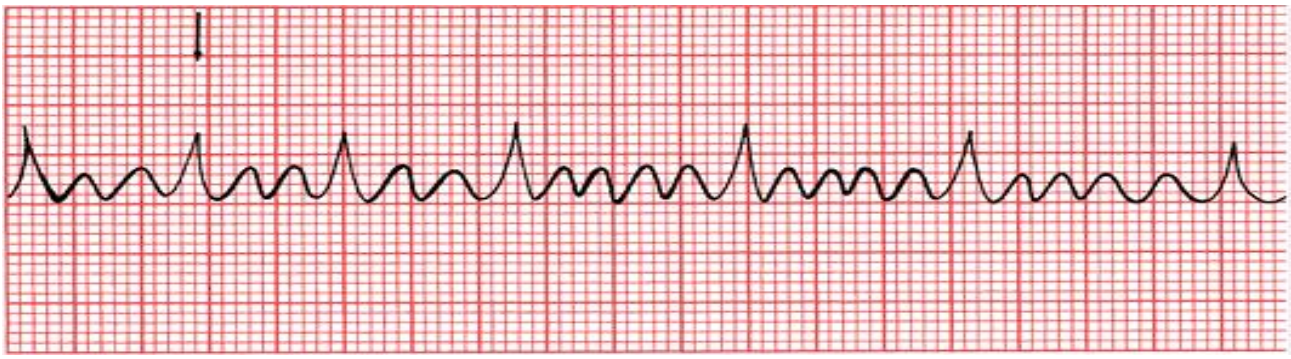
Atrial Flutter

Atrial flutter is less common than PSVT. It can occur in normal hearts or, more often, in patients with underlying cardiac pathology. It, too, is absolutely regular. P waves appear at a rate of 250 to 350 beats per minute. In its most common form, it is generated by a reentrant circuit that runs largely around the annulus of the tricuspid valve.

In atrial flutter, atrial depolarization occurs at such a rapid rate that discrete P waves separated by a flat baseline are not seen. Instead, the baseline continually rises and falls, producing so-called flutter waves. In some leads, usually leads II and III, these may be quite prominent and may create what has been termed a saw-toothed pattern.

Some just bump into a refractory node, and that is as far as they get. This phenomenon is called AV block. A 2:1 block is most common. This means that for every two visible flutter waves, one passes through the AV node to generate a QRS complex, and one does not. Blocks of 3:1 and 4:1 are also frequently seen. Carotid massage may increase the degree of block (e.g., changing a 2:1 block to a 4:1 block), making it easier to identify the saw-toothed pattern. Because atrial flutter originates above the AV node, carotid massage will not result in termination of the rhythm (Fig. 18).

Figure 18: Atrial flutter

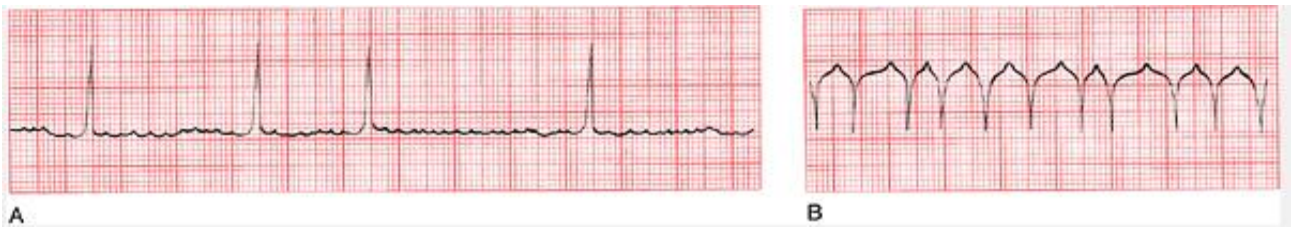


Atrial Fibrillation

In atrial fibrillation, atrial activity is completely chaotic, and the AV node may be bombarded with more than 500 impulses per minute! Whereas in atrial flutter a single constant reentrant circuit is responsible for the regular saw-toothed pattern on

the EKG, in atrial fibrillation multiple reentrant circuits are occurring in totally unpredictable fashion. No true P waves can be seen. Instead, the baseline appears flat or undulates slightly. The AV node, faced with this extraordinary blitz of atrial impulses, allows only occasional impulses to pass through at variable intervals, generating an irregularly irregular ventricular rate, usually between 120 and 180 beats per minute. However, slower or faster ventricular responses (Fig.19) can often be seen. This irregularly irregular appearance of QRS complexes in the absence of discrete P waves is the key to identifying atrial fibrillation. The wavelike forms that may often be seen on close inspection of the undulating baseline are called fibrillation waves.

Figure 19: Atrial fibrillation



Notes: (A) Atrial fibrillation with a slow, irregular ventricular rate. (B) Another example of atrial fibrillation. In the absence of a clearly fibrillating baseline, the only clue that this rhythm is atrial fibrillation is the irregularly irregular appearance of the QRS complexes

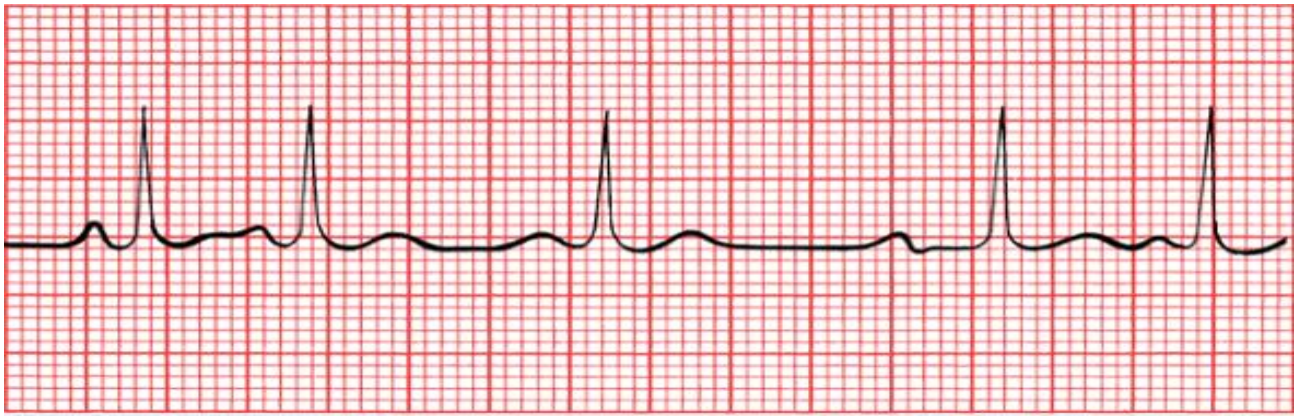
Atrial fibrillation is much more common than atrial flutter. Underlying cardiac pathology is often present, especially mitral valve disease or coronary artery disease, but hyperthyroidism, pulmonary emboli, and pericarditis must always be considered in the differential diagnosis. Longstanding hypertension is still the most common identifiable cause. In many individuals, no obvious precipitant is identified.

Multifocal Atrial Tachycardia

Multifocal atrial tachycardia (MAT) is an irregular rhythm occurring at a rate of 100 to 200 beats per minute. It probably results from the random firing of several different ectopic atrial foci. Sometimes, the rate is less than 100 beats per minute, in which case the arrhythmia is often called a wandering atrial pacemaker. MAT is very common in patients with severe lung disease. It rarely requires treatment. Carotid

massage has no effect on MAT. A wandering atrial pacemaker can be seen in normal, healthy hearts. Like atrial fibrillation, MAT is an irregular rhythm. It can be distinguished from atrial fibrillation by the easily identifiable P waves occurring before each QRS complex. The P waves, originating from multiple sites in the atria, will vary in shape, and the interval between the different P waves and the QRS complexes will vary as well. In order to make the diagnosis of MAT, you need to identify at least three different P wave morphologies (Fig. 20).

Figure 20: Multifocal atrial tachycardia.



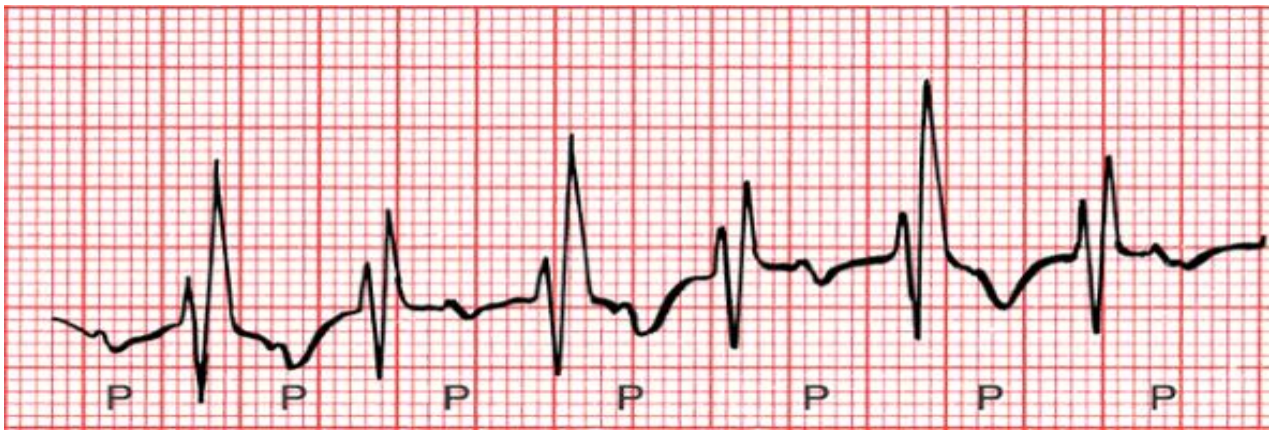
Note that (1) the P waves vary dramatically in shape; (2) the PR intervals also vary; and (3) the ventricular rate is irregular.

Paroxysmal Atrial Tachycardia

The last of our five supraventricular arrhythmias, paroxysmal atrial tachycardia (PAT), is a regular rhythm with a rate of 100 to 200 beats per minute. It can result either from the enhanced automaticity of an ectopic atrial focus or from a reentrant circuit within the atria. The automatic type typically displays a warm-up period when it starts, during which the rhythm appears somewhat irregular, and a similar cool-down period when it terminates. The less common reentrant form starts abruptly with an atrial premature beat; this form of PAT has also been termed atypical atrial flutter.

PAT is most commonly seen in otherwise normal hearts. The most common underlying cause is digitalis toxicity (Fig. 21).

Figure 21: Paroxysmal Atrial Tachycardia



Notes: P waves are not always visible, but here they can be seen fairly easily. You may also notice the varying distance between the P waves and the ensuing QRS complexes; this reflects a varying conduction delay between the atria and ventricles that often accompanies PAT

How can you tell PAT from PSVT? Many times you can't. However, if you see a warm-up or cool-down period on the ECG, the rhythm is likely to be PAT. In addition, carotid massage can be very helpful: Carotid massage will slow or terminate PSVT, whereas it has virtually no effect on PAT (although there may be some mild slowing).

Ventricular Arrhythmias

Ventricular arrhythmias are rhythm disturbances arising below the AV node.

Premature Ventricular Contractions

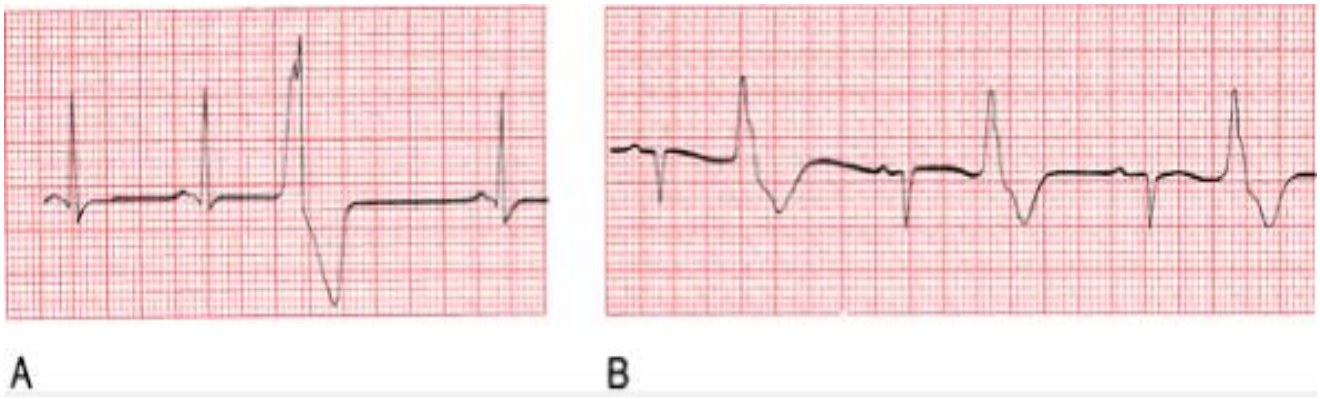
Premature ventricular contractions, or PVCs, are certainly the most common of the ventricular arrhythmias. The QRS complex of a PVC appears wide and bizarre because ventricular depolarization does not follow the normal conduction pathways. However, the QRS complex may not appear wide in all leads, so scan the entire 12-lead ECG before making your diagnosis. A retrograde P wave may sometimes be seen, but it is more common to see no P wave at all. A PVC is usually followed by a prolonged compensatory pause before the next beat appears.

Isolated PVCs are common in normal hearts and rarely require treatment. An isolated PVC in the setting of an acute myocardial infarction, however, is more ominous be-

cause it can trigger ventricular tachycardia or ventricular fibrillation, both of which are life-threatening arrhythmias.

PVCs may occur randomly or may alternate with normal sinus beats in a regular pattern. If the ratio is one normal sinus beat to one PVC, the rhythm is called bigeminy. Trigeminy refers to two normal sinus beats for every one PVC, and so on (Fig. 22).

Figure 22: premature ventricular contraction



Notes: (A) A premature ventricular contraction. (B) Bigeminy. PVCs and sinus beats alternate in a 1:1 fashion

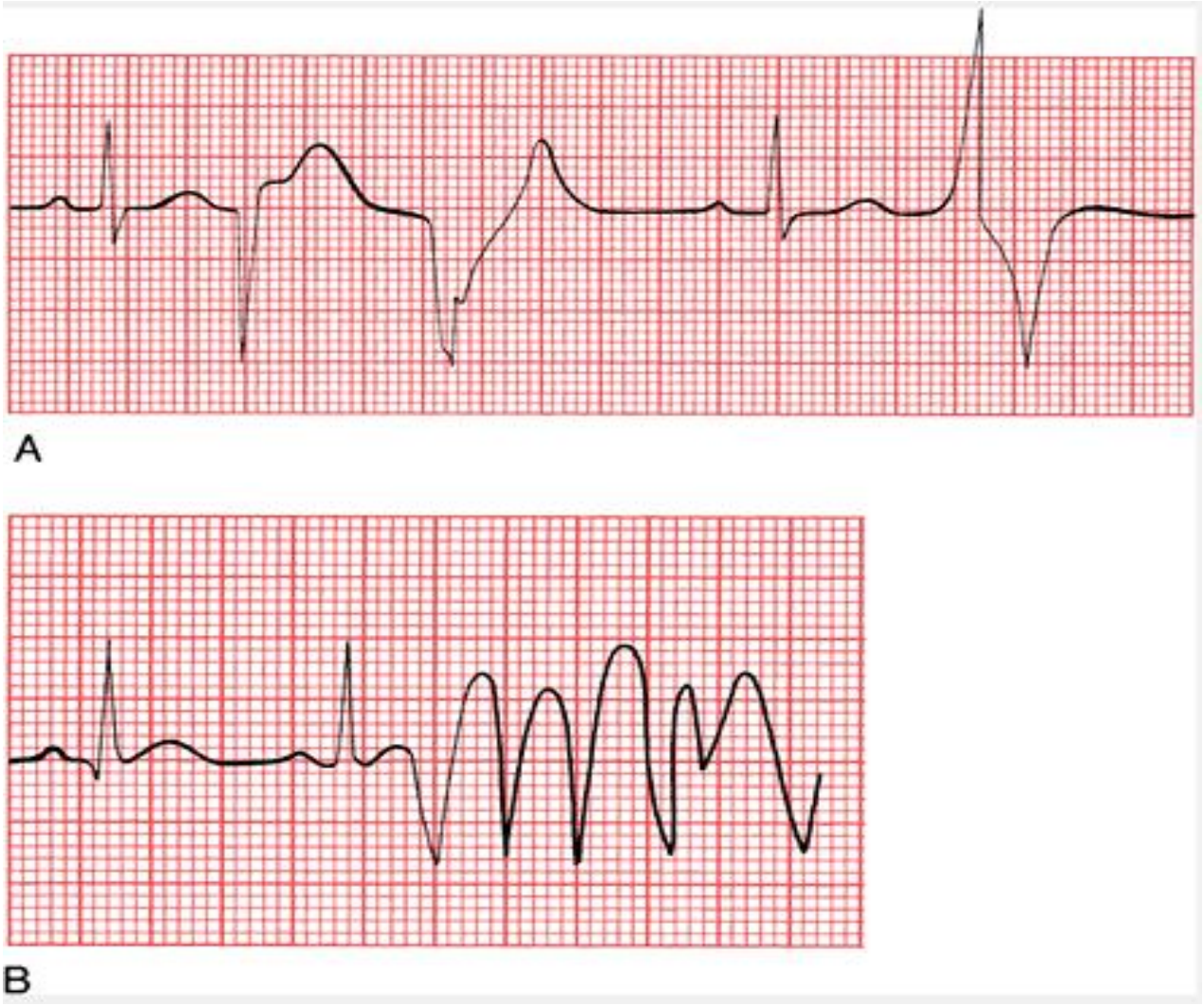
When should you worry about PVCs? Certain situations have been identified in which PVCs appear to pose an increased risk for triggering ventricular tachycardia, ventricular fibrillation, and death. These situations are summarized in the rules of malignancy:

- Frequent PVCs
- Runs of consecutive PVCs, especially three or more in a row
- Multiform PVCs, in which the PVCs vary in their site of origin and hence in their appearance
- PVCs falling on the T wave of the previous beat, called the вЂњR-on-TвЂќ phenomenon. The T wave is a vulnerable period in the cardiac cycle, and a PVC falling there appears to be more likely to set off ventricular tachycardia.
- Any PVC occurring in the setting of an acute myocardial infarction.

Although PVCs meeting one or several of these criteria are associated with an increased risk for developing a life-threatening arrhythmia, there is no evidence that

suppressing these PVCs with antiarrhythmic medication reduces mortality in any setting.

Figure 23: Salvo complexes: premature ventricular contraction

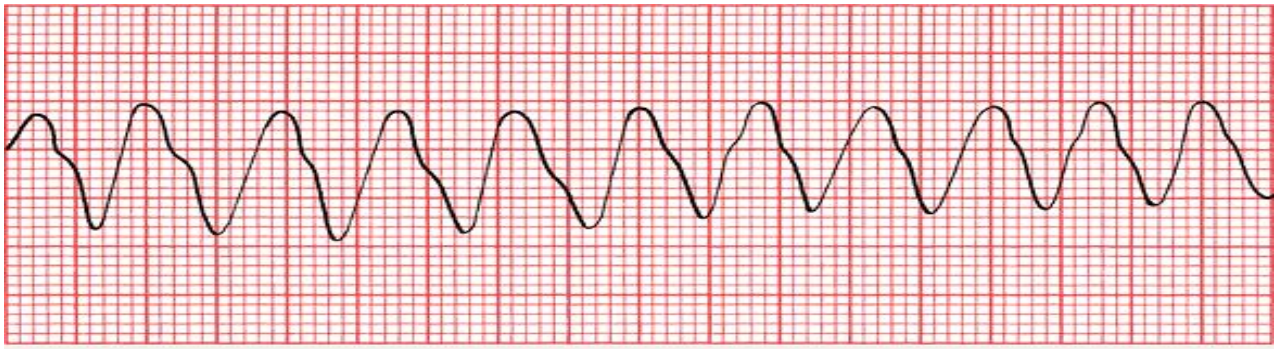


Notes: (A) Beats 1 and 4 are sinus in origin. The other three beats are PVCs. The PVCs differ from each other in shape (multiform), and two occur in a row. (B) A PVC falls on the T wave of the second sinus beat, initiating a run of ventricular tachycardia.

Ventricular Tachycardia

A run of three or more consecutive PVCs is called ventricular tachycardia (VT). The rate is usually between 120 and 200 beats per minute and, unlike PSVT, may be slightly irregular (although it may take a very fine eye to see this) (Fig. 24). Sustained VT is an emergency, presaging cardiac arrest and requiring immediate treatment.

Figure 24: Sustained ventricular tachicardia



Note: the rate is aboput 200 beat per minute

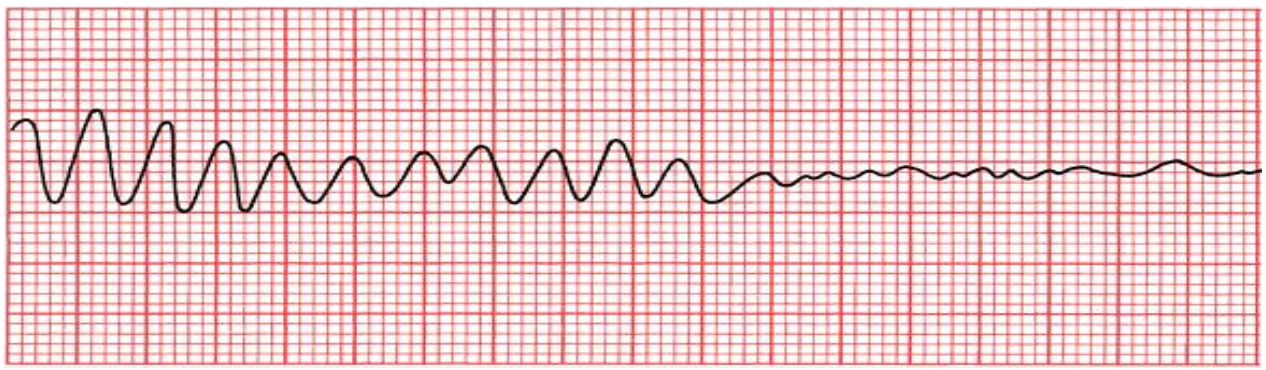
Ventricular tachycardia may be uniform, with each complex appearing similar to the one before it, as in the picture above, or it may be polymorphic, changing appearance from beat to beat. Polymorphic ventricular tachycardia is more commonly associated with acute coronary ischemia or infarction. Uniform ventricular tachycardia is more often seen with healed infarctions; the scarred myocardium provides the substrate for the reentrant ventricular tachycardia.

Ventricular Fibrillation

Ventricular fibrillation is a preterminal event. It is seen almost solely in dying hearts. It is the most frequently encountered arrhythmia in adults who experience sudden death. The ECG tracing jerks about spasmodically (coarse ventricular fibrillation) or undulates gently (fine ventricular fibrillation) (Fig. 25). There are no true QRS complexes.

In ventricular fibrillation, the heart generates no cardiac output, and cardiopulmonary resuscitation and electrical defibrillation must be performed at once.

Figure 25:

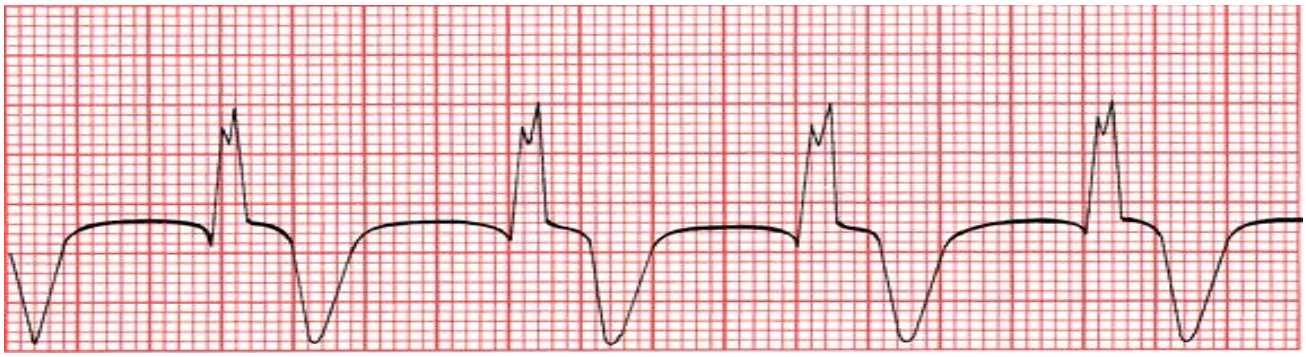


Note: Ventricular tachycardia degenerates into ventricular fibrillation

Accelerated Idioventricular Rhythm

Accelerated idioventricular rhythm is a benign rhythm that is sometimes seen during an acute infarction. It is a regular rhythm occurring at 50 to 100 beats per minute and probably represents a ventricular escape focus that has accelerated sufficiently to drive the heart. It is rarely sustained, does not progress to ventricular fibrillation, and rarely requires treatment. When the rate falls below 50 beats per minute, it is then simply called an idioventricular rhythm (i.e., the term accelerated is dropped), and in these instances look closely for P waves to exclude a sinus bradycardia (Fig. 26).

Figure 26: Accelerated idioventricular rhythm.



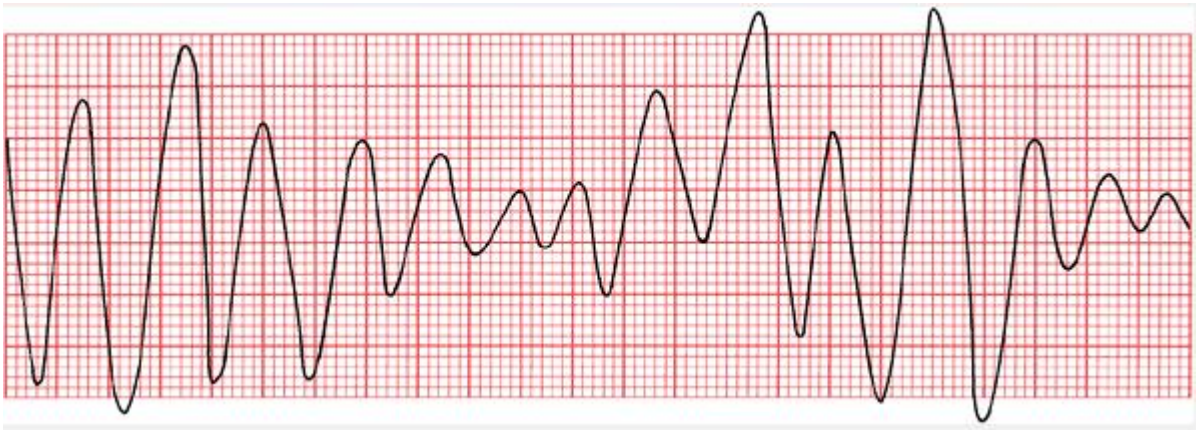
Note: There are no P waves, the QRS complexes are wide, and the rate is about 75 beats per minute.

Torsades De Pointes

Torsades de pointes is more than just the most lyrical name in cardiology. It is a unique form of ventricular tachycardia that is usually seen in patients with prolonged QT intervals. The QT interval, you will recall, encompasses the time from the beginning of ventricular depolarization to the end of ventricular repolarization. It normally constitutes about 40% of the complete cardiac cycle. A prolonged QT interval can be congenital in origin, can result from various electrolyte disturbances (notably hypocalcemia, hypomagnesemia, and hypokalemia), or can develop during an acute myocardial infarction. Numerous pharmacologic agents can also prolong the QT interval. These include antiarrhythmic drugs, tricyclic antidepressants, the phenothiazines, and some antifungal medications and antihistamines when taken concurrently with certain antibiotics, particularly erythromycin and the quinolones. A pro-

longed QT interval is generally the result of prolonged ventricular repolarization (i.e., the T wave is lengthened). A PVC falling during the elongated T wave can initiate torsades de pointes. Torsades de pointes looks just like ordinary, run-of-the-mill VT, except that the QRS complexes spiral around the baseline, changing their axis and amplitude. It is important to distinguish torsades de pointes from standard VT because they are treated very differently (Fig. 27).

Figure 27: Torsades de pointes.



Note: The QRS complexes seem to spin around the baseline, changing their axis and amplitude

Conduction Block

Any obstruction or delay of the normal pathways of electrical conduction is called a conduction block.

Sinus node block.

This is the sinus exit block that we discussed in the last chapter. In this situation, the sinus node fires normally, but the wave of depolarization is immediately blocked and is not transmitted into the atrial tissue. On the ECG, it looks just like a pause in the normal cardiac cycle

AV Blocks

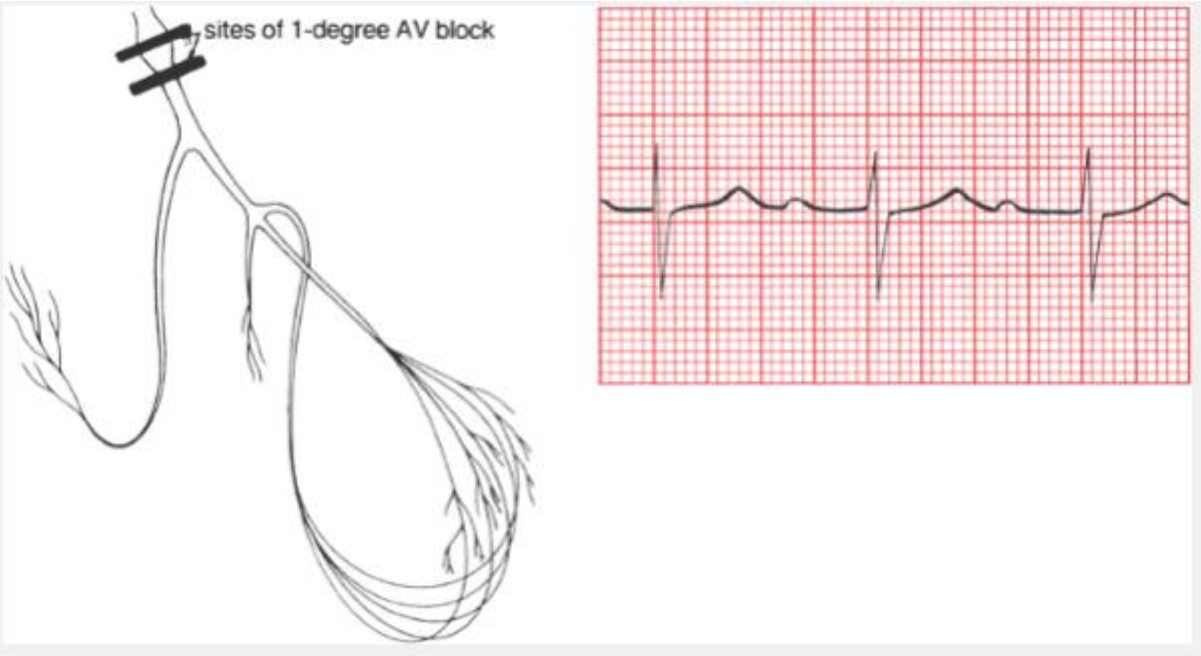
AV blocks come in three varieties, termed (with a complete lack of whimsy) first degree, second degree, and third degree. They are diagnosed by carefully examining the relationship of the P waves to the QRS complexes.

First-Degree AV Block

First-degree AV block is characterized by a prolonged delay in conduction at the AV node or His bundle (recall that the His bundle or bundle of His, depending on your grammatical preference is the part of the conducting system located just below the AV node. A routine 12-lead ECG cannot distinguish between a block in the AV node and one in the His bundle). The wave of depolarization spreads normally from the sinus node through the atria, but upon reaching the AV node, it is held up for longer than the usual one tenth of a second.Asa result, the PR interval the time between the start of atrial depolarization and the start of ventricular depolarization, a time period that encompasses the delay at the AV node is prolonged. The diagnosis of first-degree AV block requires only that the PR interval be longer than 0.2 seconds.

In first-degree AV block, despite the delay at the AV node or His bundle, every atrial impulse does eventually make it through the AV node to activate the ventricles. Therefore, to be precise, first-degree AV block is not really a block at all, but rather a delay in conduction. Every QRS complex is preceded by a single P wave (Fig. 28). First-degree AV block is a common finding in normal hearts, but it can also be an early sign of degenerative disease of the conduction system or a transient manifestation of myocarditis or drug toxicity. By itself, it does not require treatment.

Figure 28: First-degree AV block.



Note the prolonged PR interval.

Second-Degree AV Block

In second-degree AV block, not every atrial impulse is able to pass through the AV node into the ventricles. Because some P waves fail to conduct through to the ventricles, the ratio of P waves to QRS complexes is greater than 1:1.

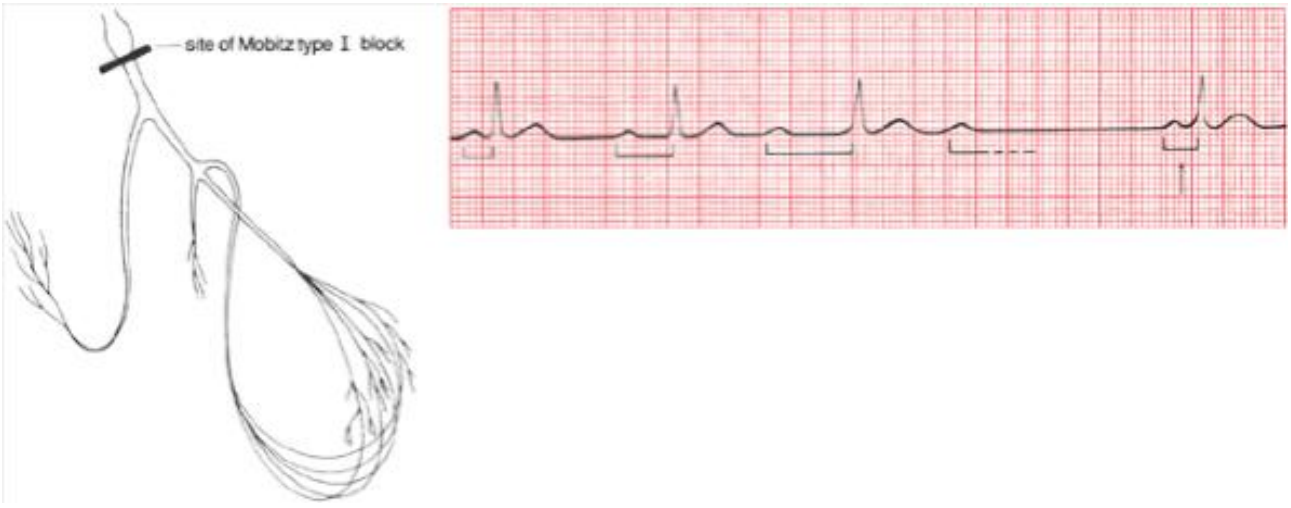
Just to make things a little more interesting, there are two types of second-degree AV block: Mobitz type I second-degree AV block, more commonly called Wenckebach block, and Mobitz type II second-degree AV block.

Wenckebach Block

Wenckebach block is almost always due to a block within the AV node. However, the electrical effects of Wenckebach block are unique. The block, or delay, is variable, increasing with each ensuing impulse. Each successive atrial impulse encounters a longer and longer delay in the AV node until one impulse (usually every third or fourth) fails to make it through. What you see on the EKG is a progressive lengthening of the PR interval with each beat and then suddenly a P wave that is not followed by a QRS complex (a dropped beat). After this dropped beat, during which no QRS complex appears, the sequence repeats itself, over and over, and often with impressive regularity.

The following tracing shows a 4:3 Wenckebach block, in which every fourth atrial impulse fails to stimulate the ventricles, producing a ratio of four P waves to every three QRS complexes (Fig. 29).

Fihure 29: Mobitz type I second-degree AV block (Wenckebach block).



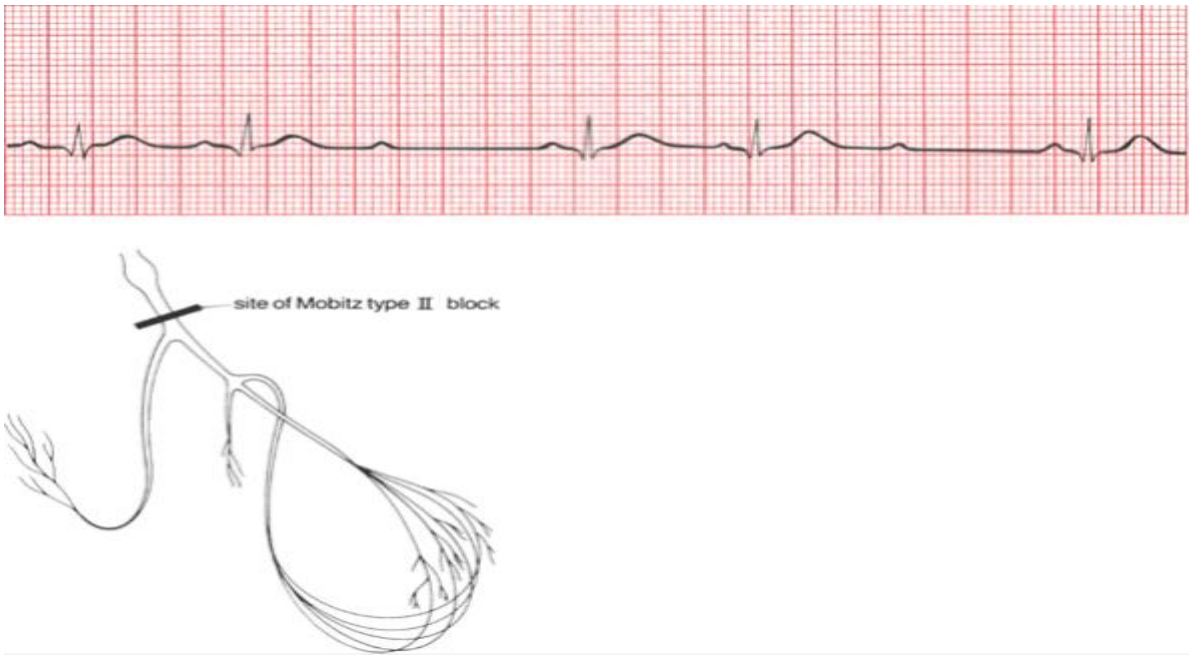
Note: The PR intervals become progressively longer until one QRS complex is dropped.

The diagnosis of Wenckebach block requires the progressive lengthening of each successive PR interval until one P wave fails to conduct through the AV node and is therefore not followed by a QRS complex.

Mobitz Type II Block

Mobitz type II block usually is due to a block below the AV node in the His bundle. It resembles Wenckebach block in that some, but not all, of the atrial impulses are transmitted to the ventricles. However, progressive lengthening of the PR interval does not occur. Instead, conduction is an all-or-nothing phenomenon. The ECG shows two or more normal beats with normal PR intervals and then a P wave that is not followed by a QRS complex (a dropped beat). The cycle is then repeated. The ratio of conducted beats to nonconducted beats is rarely constant, with the ratio of P waves to QRS complexes constantly varying, from 2:1 to 3:2 and so on (Fig. 30). The diagnosis of Mobitz type II block requires the presence of a dropped beat without progressive lengthening of the PR interval.

Figure 30: Mobitz type II second-degree AV block.



Note: On the ECG, every third P wave is not followed by a QRS complex (dropped beat).

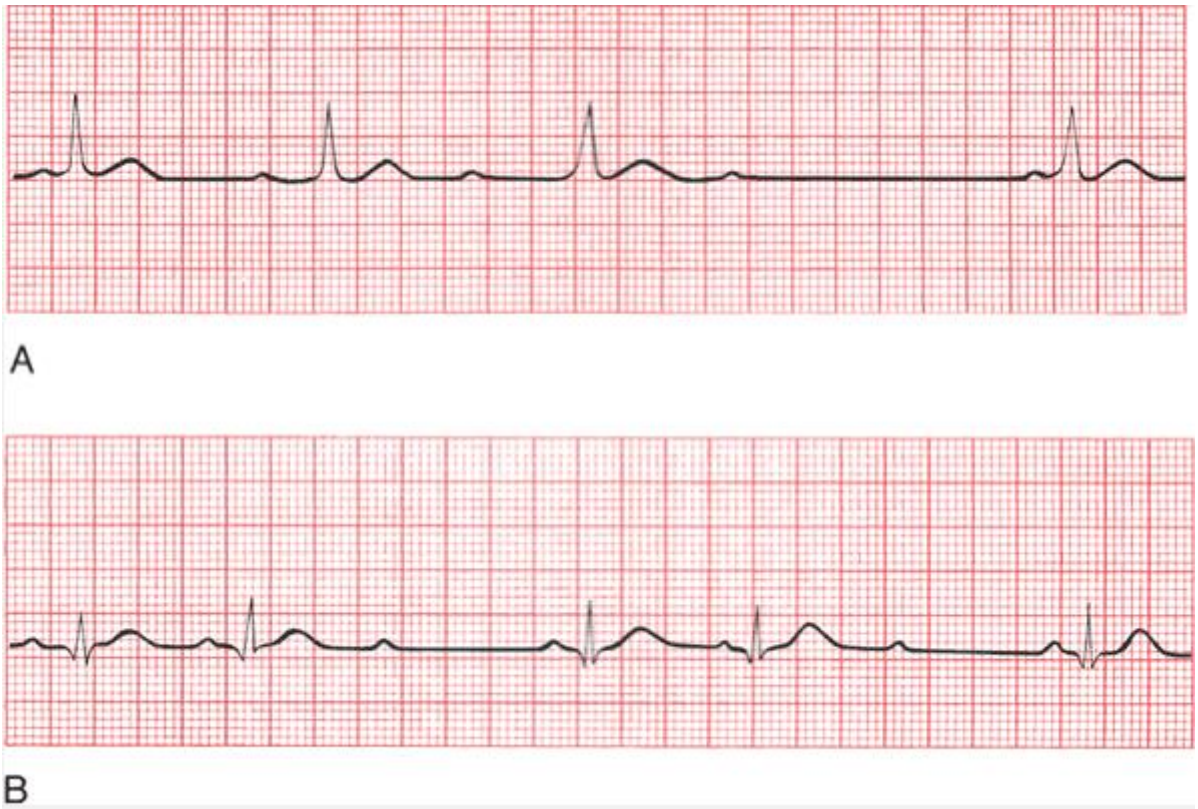
Is it a Wenckebach Block or a Mobitz Type II Block?

Compare the electrocardiographic manifestations of Wenckebach block and Mobitz type II block on the ECGs below (Fig. 31). Wenckebach block is usually due to a conduction block high up in the AV node. It is typically transient and benign and rarely progresses to third-degree heart block (see next page), which can be dangerous and even life threatening.

Mobitz type II block is usually due to a conduction block below the AV node, somewhere in the His bundle. Although less common than Wenckebach block, it is far more serious, often signifying serious heart disease and capable of progressing suddenly to third-degree heart block.

Whereas treatment is often not needed for Wenckebach block, Mobitz type II heart block often mandates insertion of a pacemaker.

Figure 30: Wenckebach block and Mobitz type II block

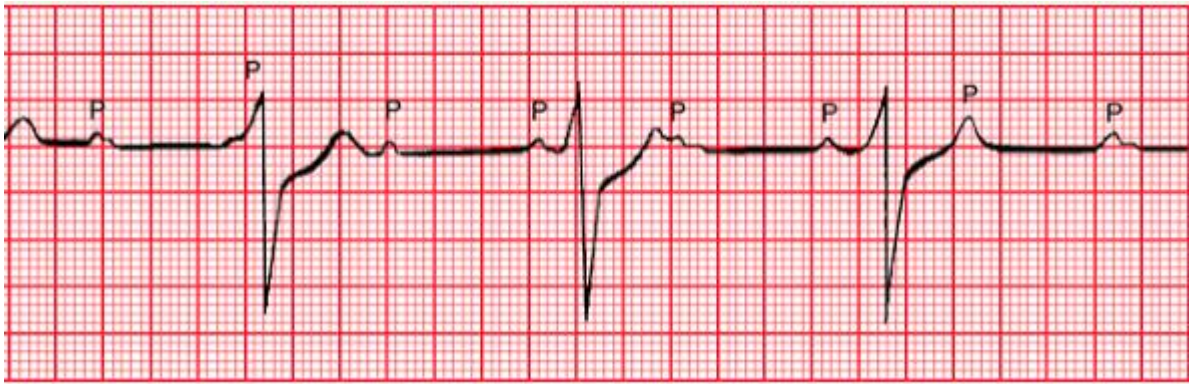


Notes: (A) Wenckebach block, with progressive lengthening of the PR interval. (B) Mobitz type II block, in which the PR interval is constant.

Third-Degree AV Block

Third-degree heart block is the ultimate in heart blocks. No atrial impulses make it through to activate the ventricles. For this reason, it is often called complete heart block. The site of the block can be either at the AV node or lower. The ventricles respond to this dire situation by generating an escape rhythm, usually an inadequate 30 to 45 beats per minute (idioventricular escape). The atria and ventricles continue to contract, but they now do so at their own intrinsic rates, about 60 to100 beats per minute for the atria, and 30 to 45 beats per minute for the ventricles. In complete heart block, the atria and ventricles have virtually nothing to do with each other, separated by the absolute barrier of the complete conduction block. We have already described this type of situation in our discussion of ventricular tachycardia: it is called AV dissociation and refers to any circumstance in which the atria and ventricles are being driven by independent pacemakers (Figure 32). The ECG in third-degree heart block shows P waves marching across the rhythm strip at their usual rate (60 to 100 waves per minute) but bearing no relationship to the QRS complexes that appear at a much slower escape rate. The QRS complexes appear wide and bizarre, just like PVCs, because they arise from a ventricular source.

Figure 32: Third-degree AV block.



Note: The P waves appear at regular intervals, as do the QRS complexes, but they have nothing to do with one another. The QRS complexes are wide, implying a ventricular origin.

Although a ventricular escape rhythm may look like a slow run of PVCs (slow ventricular tachycardia), there is one important difference: PVCs are premature, oc-

curring before the next expected beat, and even the slowest VT will be faster than the patient's normal rhythm. A ventricular escape beat occurs after a long pause and is therefore never premature, and a sustained ventricular escape rhythm is always slower than the normal beats. PVCs, being premature intrusions, can be suppressed with little clinical consequence. A ventricular escape rhythm, however, may be life saving, and suppression could be fatal.

The diagnosis of third-degree heart block requires the presence of AV dissociation in which the ventricular rate is slower than the sinus or atrial rate.

AV dissociation can also occur when there is a block high in the AV node, but in this case, there is an accelerated junctional rhythm to drive the heart that is faster than the sinus rhythm. This situation rarely requires a pacemaker. It occurs most often in patients undergoing an acute infarction and those who have received an overdose of an anti-arrhythmic medication.

Degenerative disease of the conduction system is the leading cause of third-degree heart block. It can also complicate an acute myocardial infarction. Pacemakers are virtually always required when third-degree heart block develops. It is a true medical emergency. Some forms of complete heart block develop prenatally (congenital heart block), and these are often associated with an adequate and stable ventricular escape rhythm. Permanent pacemakers are only implanted in these children if there is clear-cut developmental impairment that can be attributed to an inadequate cardiac output.

Bundle Branch Block

The term bundle branch block refers to a conduction block in either the left or right bundle branches. The figure below reviews the anatomy of the ventricular bundle branches.

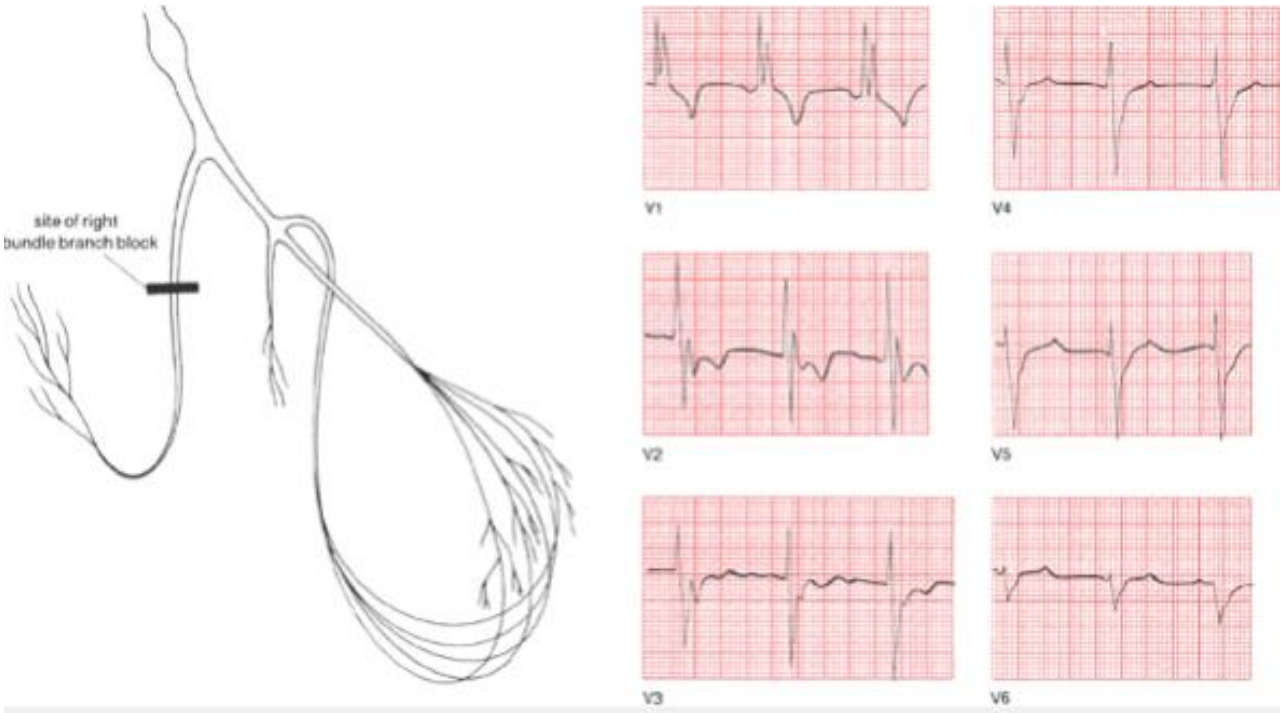
Right Bundle Branch Block

In right bundle branch block, conduction through the right bundle is obstructed. As a result, right ventricular depolarization is delayed; it does not begin until the left ventricle is almost fully depolarized. This causes two things to happen on the EKG:

The delay in right ventricular depolarization prolongs the total time for ventricular depolarization. As a result, the QRS complex widens beyond 0.12 seconds.

The wide QRS complex assumes a unique, virtually diagnostic shape in those leads overlying the right ventricle: V1 and V2. As you know, the normal QRS complex in these leads consists of a small positive R wave and a deep negative S wave, reflecting the electrical dominance of the left ventricle. With right bundle branch block, you can still see the initial R and S waves as the left ventricle depolarizes, but as the right ventricle then begins its delayed depolarization, unopposed by the now fully depolarized and electrically silent left ventricle, the electrical axis of current flow swings sharply back toward the right. This inscribes a second R wave, called R', in leads V1 and V2. The whole complex is called RSR', and its appearance has been likened to rabbit ears. Meanwhile, in the left lateral leads overlying the left ventricle (I, AVL, V5, and V6), late right ventricular depolarization causes reciprocal late deep S waves to be inscribed (Fig. 33).

Figure 33: Right bundle branch block.



Notes: The QRS complex in lead V1 shows the classic wide RSR9 configuration, too, the S waves in V5 and V6.

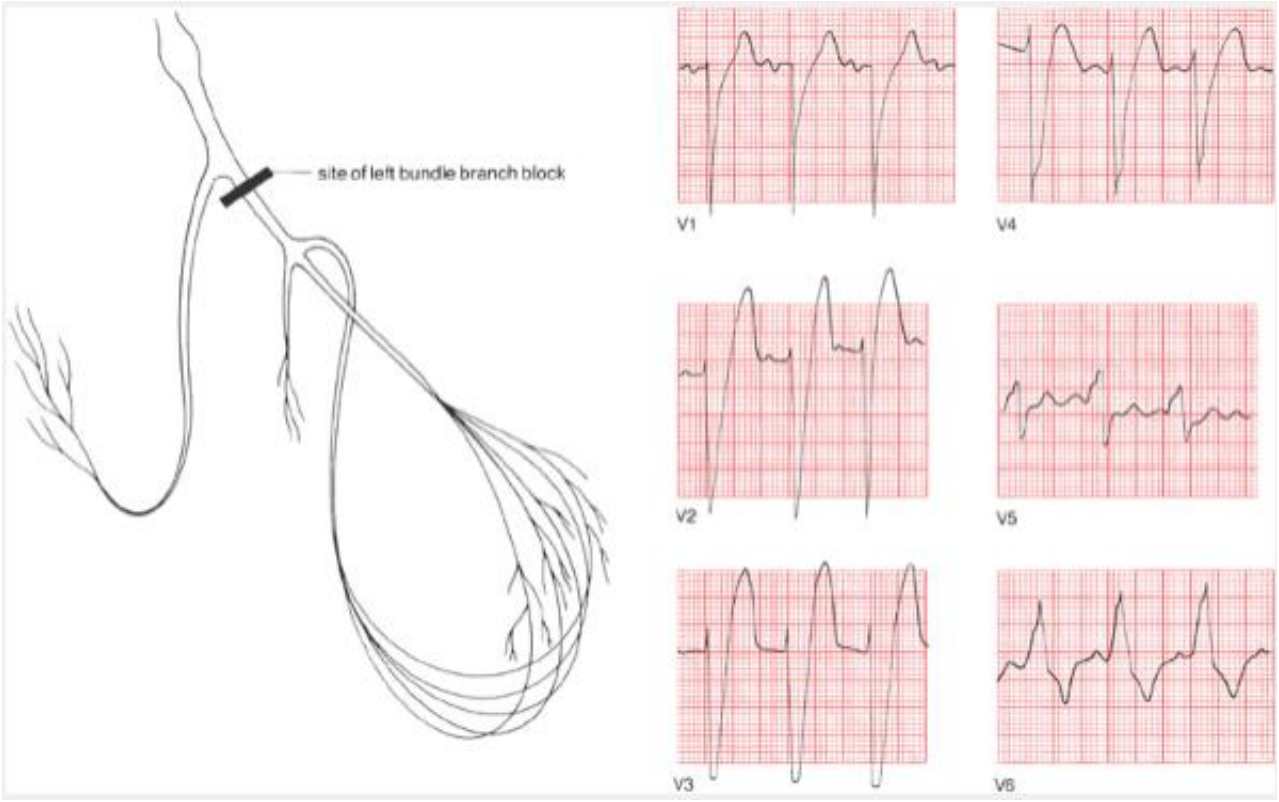
Left Bundle Branch Block

In left bundle branch block, it is left ventricular depolarization that is delayed. Again, there are two things to look for on the EKG:

The delay in left ventricular depolarization causes the QRS complex to widen beyond 0.12 seconds in duration.

The QRS complex in the leads overlying the left ventricle (I, AVL, V5, and V6) will show a characteristic change in shape. The QRS complexes in these leads already have tall R waves. Delayed left ventricular depolarization causes a marked prolongation in the rise of those tall R waves, which will either be broad on top or notched. True rabbit ears are less common than in right bundle branch block. Those leads overlying the right ventricle will show reciprocal, broad, deep S waves. The left ventricle is so dominant in left bundle branch block that left axis deviation may also be present, but this is variable (Fig. 34).

Figure 34: Left bundle branch block



Left Bundle Hemiblocks Cause Axis Deviation

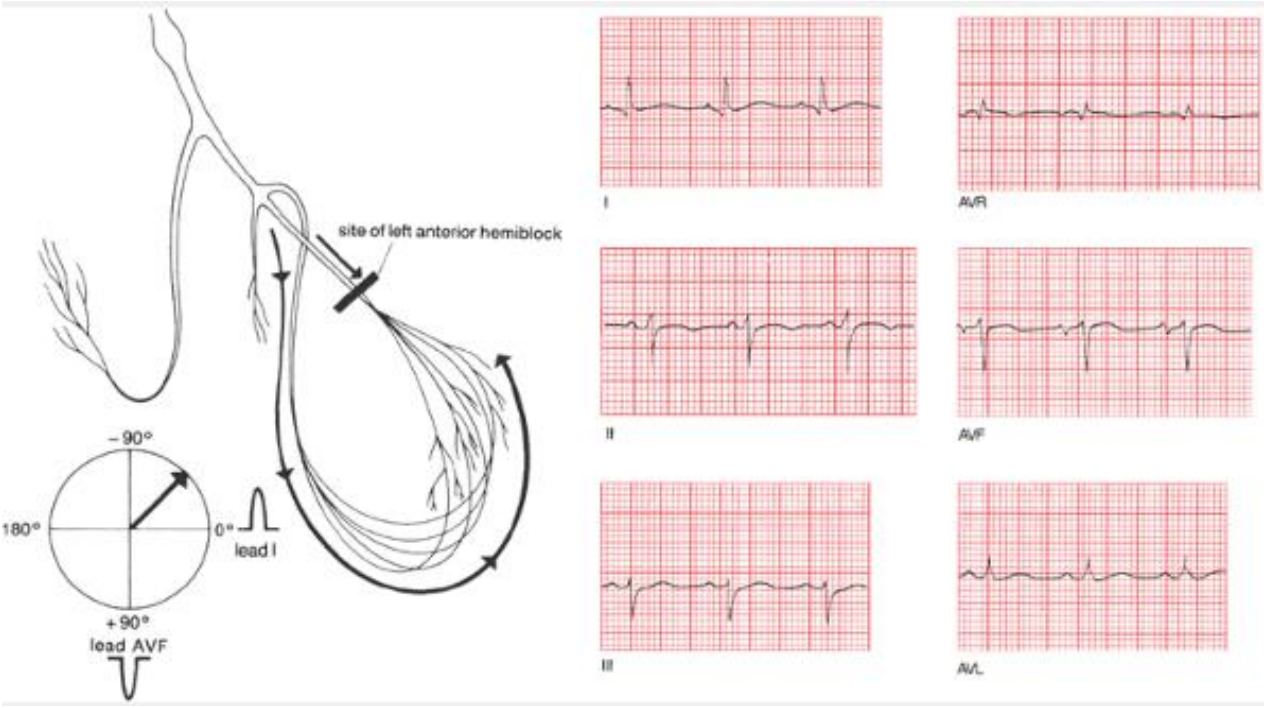
The major effect that hemiblocks have on the ECG is axis deviation. Here is why.

As shown on the previous page, the left anterior fascicle lies superiorly and laterally to the left posterior fascicle. With left anterior hemiblock, conduction down the left anterior fascicle is blocked. All the current, therefore, rushes down the left posterior fascicle to the inferior surface of the heart. Left ventricular myocardial depolarization then occurs, progressing in an inferior-to-superior and right-to-left direction.

The axis of ventricular depolarization is therefore redirected upward and slightly leftward, inscribing tall positive R waves in the left lateral leads and deep S waves inferiorly. This results in left axis deviation in which the electrical axis of ventricular depolarization is redirected between -30B° and -90B°.

The simplest method is to look at the QRS complex in leads I and AVF. The QRS complex will be positive in lead I and negative in lead AVF. However, this analysis will define a range from 0B° to -90B°.Therefore, look at lead II, which is angled at +60B°; if its QRS complex is negative, then the axis must lie more negative than -30B° (Fig. 35).

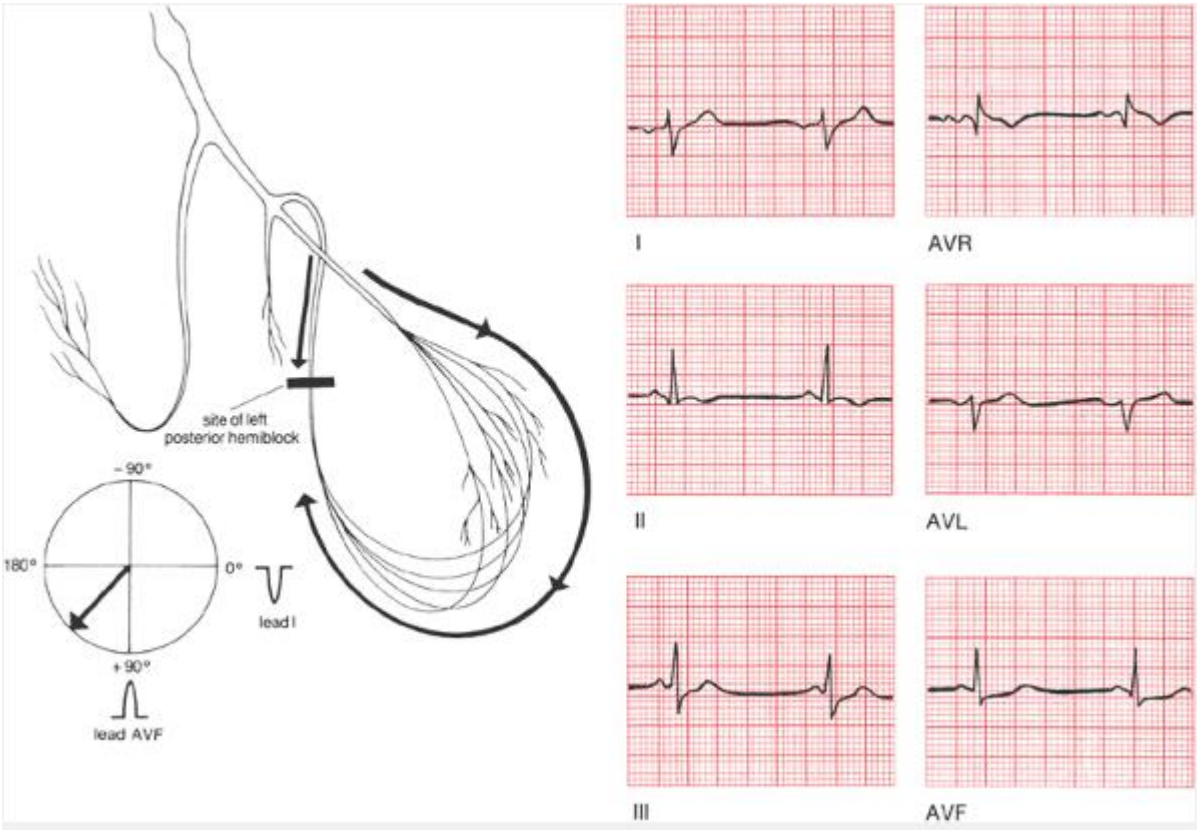
Figure 35: Left anterior hemiblock.



Notes: Current flow down the left anterior fascicle is blocked; hence, all the current must pass down the posterior fascicle. The resultant axis is redirected upward and leftward (left axis deviation).

In left posterior hemiblock, the reverse occurs. All of the current rushes down the left anterior fascicle, and ventricular myocardial depolarization then ensues in a superior-to-inferior and left-to-right direction (Fig. 36). The axis of depolarization is therefore directed downward and rightward, writing tall R waves inferiorly and deep S waves in the left lateral leads. The result is right axis deviation (i.e., the electrical axis of ventricular depolarization is between +90B° and 180B°).

Figure 36: Left posterior hemiblock.



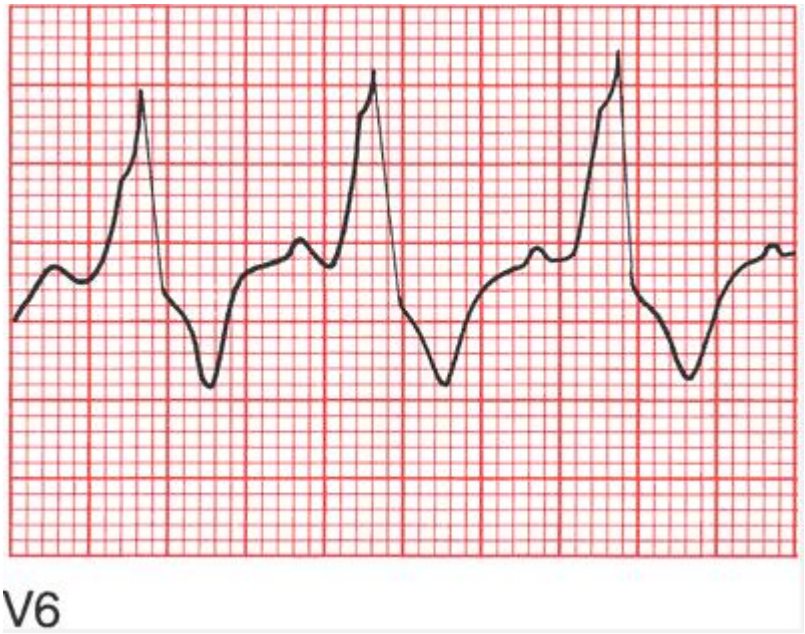
Notes: Current flow down the left posterior fascicle is blocked; hence, all the current must pass down the right anterior fascicle. The resultant axis is redirected downward and rightward (right axis deviation).

Bundle Branch Block and Repolarization

In both right and left bundle branch block, the repolarization sequence is also affected. In right bundle branch block, the right precordial leads will show ST seg-

ment depression and T wave inversion, just like the repolarization abnormalities that occur with ventricular hypertrophy. Similarly, in left bundle branch block, ST segment depression and T wave inversion can be seen in the left lateral leads (Fig. 37).
Although right bundle branch block can be caused by diseases of the conducting system, it is also a fairly common phenomenon in otherwise normal hearts.
Left bundle branch block, on the other hand, rarely occurs in normal hearts and almost always reflects significant underlying cardiac disease, such as degenerative disease of the conduction system or ischemic coronary artery disease.

Figure 37: ST segment depression and T wave inversion in lead V6 in a patient with left bundle branch block.



Critical Rate

Both right and left bundle branch block can be intermittent or fixed. In some individuals, bundle branch block only appears when a particular heart rate, called the critical rate, is achieved. In other words, the ventricles conduct normally at slow heart rates, but, above a certain rate, bundle branch block develops.
The development of a rate-related bundle branch block is directly related to the time it takes a particular bundle branch to repolarize and thus prepare itself for the next electrical impulse to come down the pass. If the heart rate is so rapid that a particular

bundle branch cannot repolarize in time, there will be a temporary block to conduction, resulting in the classic ECG appearance of a rate-related bundle branch block (Fig. 38).

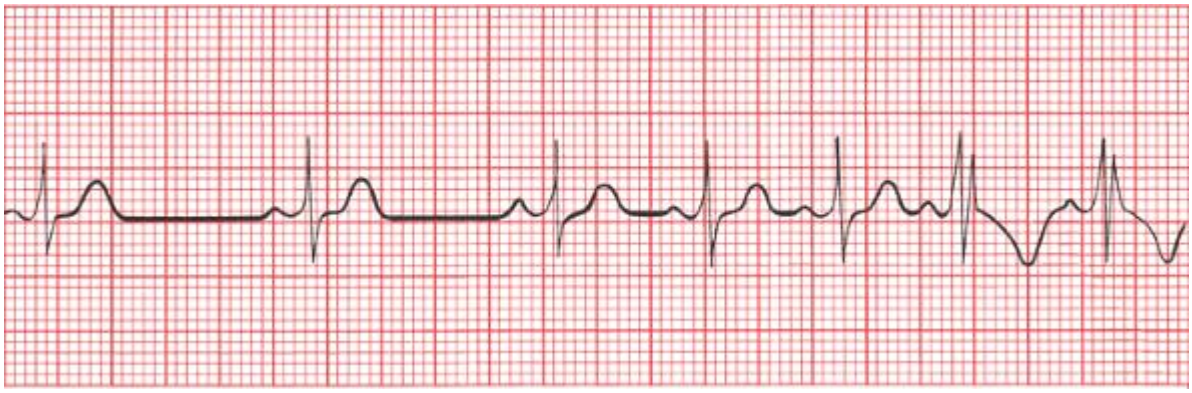
In summary, bundle branch block is diagnosed by looking at the width and configuration of the QRS complexes.

- QRS complex widened to greater than 0.12 seconds
- RSR' in V1 and V2 (rabbit ears) with ST segment depression and T wave inversion
- Reciprocal changes in V5, V6, I, and AVL.

Criteria for Left Bundle Branch Block

- QRS complex widened to greater than 0.12 seconds
- Broad or notched R wave with prolonged upstroke in leads V5, V6, I, and AVL, with ST segment depression and T wave inversion
- Reciprocal changes in V1 and V2
- Left axis deviation may be present.

Figure 38: An example of critical rate (lead V2). As the heart accelerates, the pattern of right bundle branch block appears.



Because bundle branch block affects the size and appearance of R waves, the criteria for ventricular hypertrophy discussed in Chapter 2 cannot be used if bundle branch block is present. Specifically, right bundle branch block precludes the diagnosis of right ventricular hypertrophy, and left bundle branch block precludes the diagnosis of left ventricular hypertrophy.

Combining Right Bundle Branch Block and Hemiblocks

Right bundle branch block and hemiblocks can occur together. The term bifascicular block refers to the combination of either left anterior or left posterior hemiblock with right bundle branch block. In bifascicular block, only one fascicle of the left bundle branch is supplying the bulk of both ventricles. The ECG findings include a combination of features of both hemiblock and right bundle branch block.

Preexcitation Syndromes

With normal conduction, the major delay between the atria and the ventricles is in the AV node, where the wave of depolarization is held up for about 0.1 second, long enough for the atria to contract and empty their contents into the ventricles. In the preexcitation syndromes, there are accessory pathways by which the current can bypass the AV node and thus arrive at the ventricles ahead of time.

A number of different accessory pathways have been discovered. Probably fewer than 1% of individuals possess one of these pathways. There is a decided male preponderance. Accessory pathways may occur in normal healthy hearts as an isolated finding, or they may occur in conjunction with mitral valve prolapse, hypertrophic obstructive cardiomyopathy (HOCM), and various congenital disorders.

There are two major preexcitation syndromes: Wolff-Parkinson-White (WPW) syndrome and Lown-Ganong-Levine (LGL) syndrome. They are both easily diagnosed on the ECG. In both syndromes, the accessory conduction pathways act as short circuits, allowing the atrial wave of depolarization to bypass the AV node and activate the ventricles prematurely.

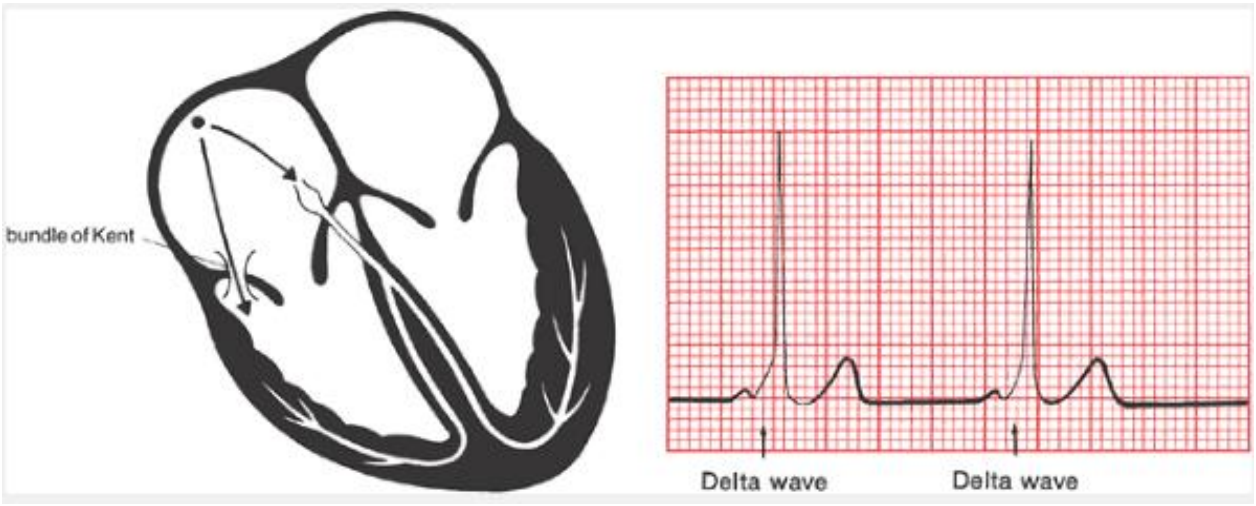
Wolff-Parkinson-White Syndrome

In WPW syndrome, the bypass pathway has been named the bundle of Kent. It is a discrete aberrant conducting pathway that connects the atria and ventricles (Fig. 39). It can be left sided (connecting the left atrium and left ventricle) or right sided (connecting the right atrium and right ventricle).

Premature ventricular depolarization through the bundle of Kent causes two things to happen on the ECG:

- The PR interval, representing the time from the start of atrial depolarization to the start of ventricular depolarization, is shortened. The criterion for diagnosis is a PR interval less than 0.12 seconds.
- The QRS complex is widened to more than 0.1 second. Unlike bundle branch block, in which the QRS complex is widened because of delayed ventricular activation, in WPW, it is widened because of premature activation. The QRS complex in WPW actually represents a fusion beat: most of the ventricular myocardium is activated through the normal conduction pathways, but a small region is depolarized early through the bundle of Kent. This small region of myocardium that is depolarized early gives the QRS complex a characteristic slurred initial upstroke called a delta wave. A true delta wave may be seen in only a few leads, so scan the entire ECG.

Figure 39: Wolff-Parkinson-White (WPW) syndrome.



Notes: Current is held up by the normal delay at the AV node but races unimpeded down the bundle of Kent. The EKG shows the short PR interval and delta wave.

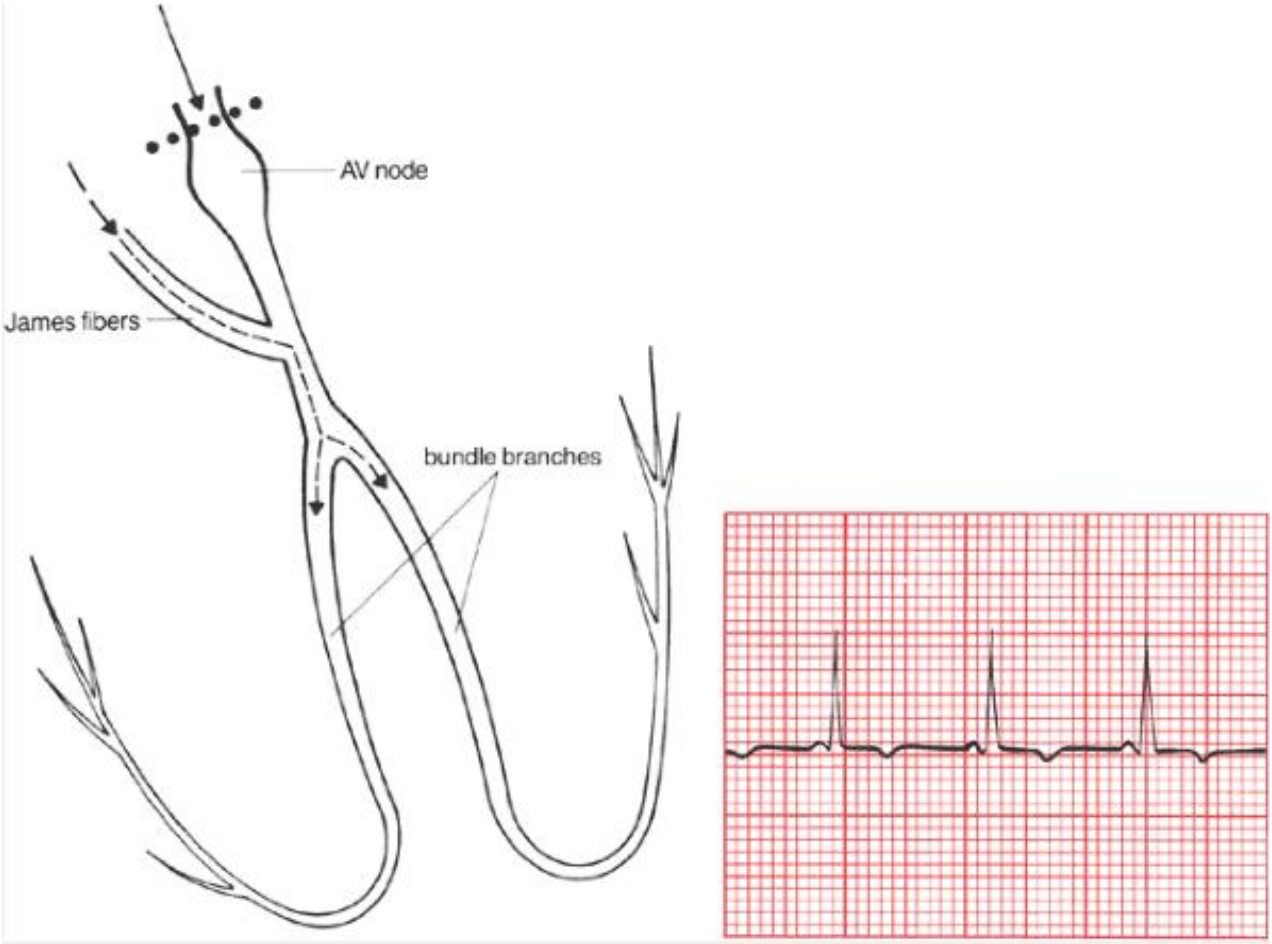
Lown-Ganong-Levine Syndrome

In LGL syndrome, the accessory pathway (called James fibers) is effectively intranodal. The James fibers bypass the delay within the AV node. All ventricular conduction occurs through the usual ventricular conduction pathways; unlike WPW, there is no small region of ventricular myocardium that is depolarized independently of the rest of the ventricles (Fig. 40).

Therefore, there is no delta wave, and the QRS complex is not widened. The only electrical manifestation of LGL is a shortening of the PR interval as a result of the accessory pathway bypassing the delay within the AV node.

- The criteria for the diagnosis of LGL are:
- The PR interval is shortened to less than 0.12 seconds
- The QRS complex is not widened
- There is no delta wave.

Figure 40: In Lown-Ganong-Levine (LGL) syndrome, the PR interval is short, but there is no delta wave



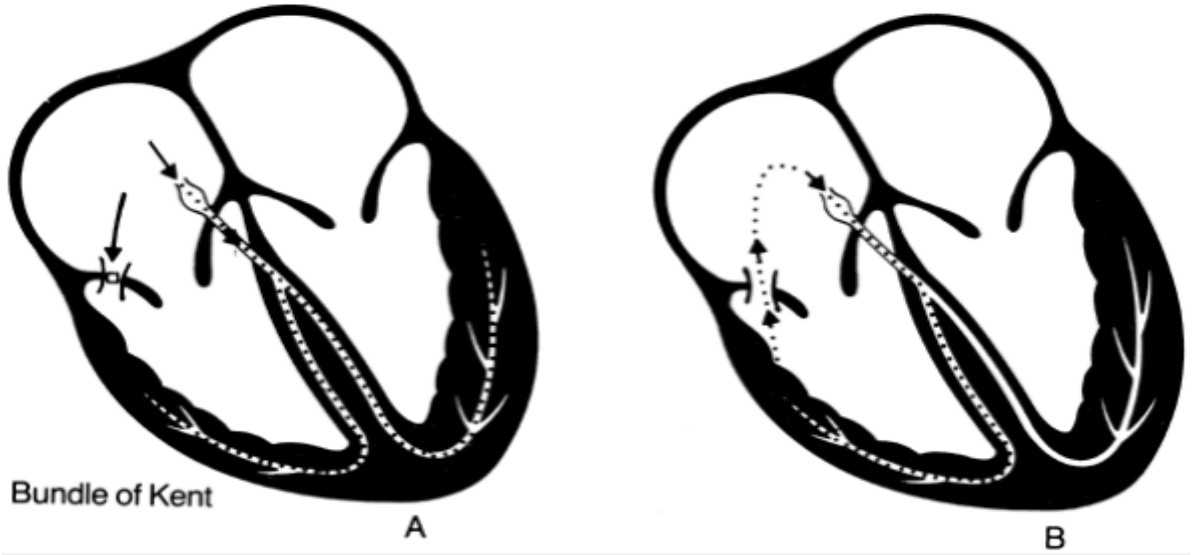
In many individuals with WPW or LGL, preexcitation poses few, if any, clinical problems. However, it is now well established that preexcitation does predispose to various tachyarrhythmias. This predisposition has been most clearly documented in WPW, where it is estimated that 50% to 70% of individuals experience at least one supraventricular arrhythmia.

Paroxysmal Supraventricular Tachycardia in WPW

In normal hearts, paroxysmal supraventricular tachycardia (PSVT) usually arises through a reentrant mechanism. The same is true in WPW. In fact, the presence of an accessory bundle an alternate pathway of conduction is the perfect substrate for reentry. Here is how it works.

We have already seen how, in WPW, a normal beat generates a QRS complex that is a fusion of two waves, one conducted through the bundle of Kent (the delta wave) and one through the normal route of conduction. Although the bundle of Kent usually conducts current faster than the AV node, it also tends to have a longer refractory period once it has been depolarized. What happens, then, if a normal sinus impulse is followed abruptly by a premature atrial beat? This premature beat will be conducted normally through the AV node, but the bundle of Kent may still be refractory, blocking conduction through the alternate route (Fig. 41). The wave of depolarization will then move through the AV node and into the bundle branches and ventricular myocardium. By the time it encounters the bundle of Kent on the ventricular side, it may no longer be refractory, and the current can pass back into the atria. It is then free to pass right back down through the AV node, and a self-sustaining, revolving reentrant mechanism has been established. The result is PSVT. The QRS complex is narrow because ventricular depolarization occurs through the normal bundle branches.

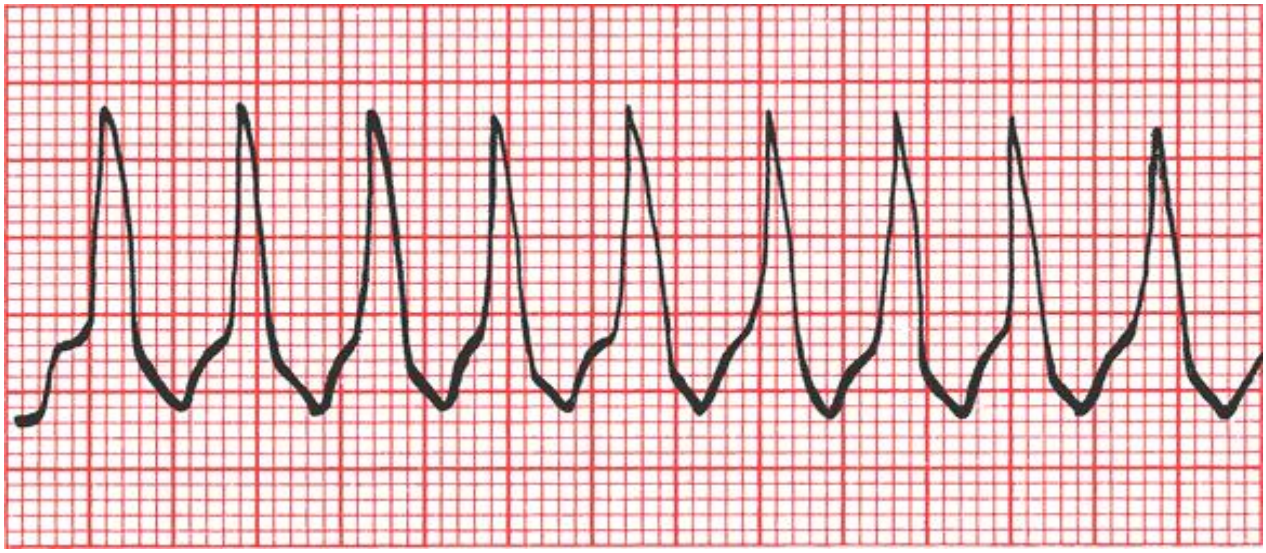
Figure 41: The formation of a reentry circuit in WPW syndrome.



Notes: Current passes down the normal conduction pathways (A) and circles back through the bundle of Kent to form a complete reentrant circuit (B).

Less commonly, the reentrant mechanism circles the other way, that is, down the bundle of Kent and back up through the AV node. The result, again, is PSVT; but in this case, the QRS complex is wide and bizarre because ventricular depolarization does not occur through the normal bundle branches. This arrhythmia may be indistinguishable from ventricular tachycardia on the ECG (Fig. 42).

Figure 42: Wide-complex PSVT in WPW syndrome



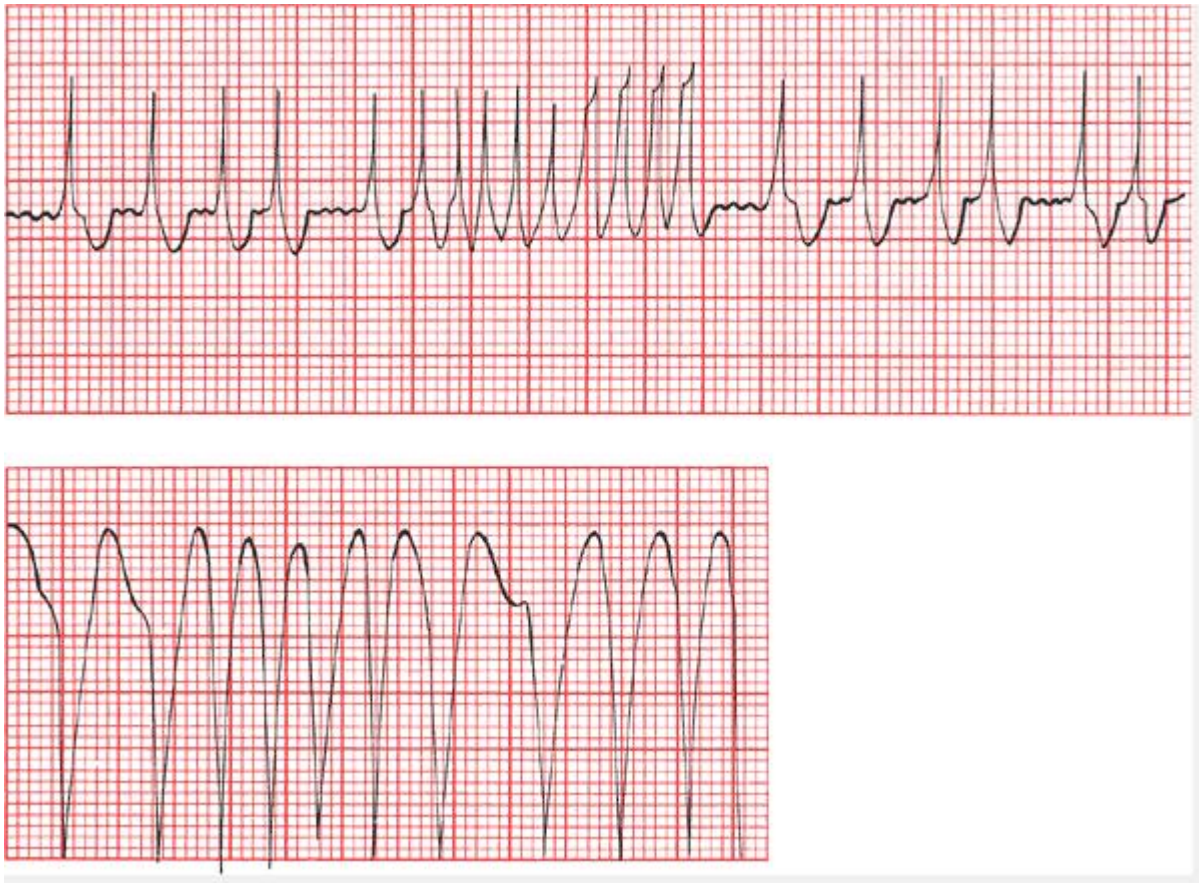
In 10% to 15% of patients with WPW, there is more than one accessory pathway, permitting the formation of multiple reentry loops as the current passes up and down through the different Kent bundles and the AV node.

Atrial fibrillation and WPW

Atrial fibrillation, the other arrhythmia commonly seen in WPW, can be particularly devastating. The bundle of Kent can act as a free conduit for the chaotic atrial activity. Without the AV node to act as a barrier between the atria and ventricles, ventricular rates can rise as high as 300 beats per minute (Fig. 43). The precise rate will depend on the refractory period of the bundle of Kent. This rapid atrial fibrillation has been known to induce ventricular fibrillation, a lethal arrhythmia. Fortunately, this lethal form of atrial fibrillation is rare in WPW, but it must be considered a diagnostic

possibility in patients who have been resuscitated from an episode of sudden death or syncope and are found to have preexcitation on their cardiograms.

Figure 43: Two examples of atrial fibrillation in WPW syndrome. The ventricular rate is extremely fast.



Mapping the aberrant pathways in patients with WPW can be accomplished during EPS, and has become quite routine in affected patients who are symptomatic or have documented arrhythmias. During the mapping procedure, the atrial-ventricular connection can be ablated, thereby resolving the problem.

References:

1. Thaler, Malcolm S. Title: Only EKG Book You'll Ever Need, The, 5th Edition. Copyright B©2007 Lippincott Williams & Wilkins.

5. Topic 9. Practical skills for the topic №14 «Acute heart failure. Chronic heart failure»

Heart falure (HF) is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and / or elevated intracardiac pressures at rest or during stress. The current definition of HF restricts itself to stages atwhich clinical symptoms are apparent. Before clinical symptoms become apparent, patients canpresentwithasymptomatic structuralorfunctional cardiac abnormalities [systolic or diastolic left ventricular (LV) dysfunction], which are precursors ofHF.Recognitionof these precursors is important because they are related to poor outcomes, and starting treatment at the precursor stage may reduce mortality in patients with asymptomatic systolic LV dysfunction.

The main terminology used to describe HF is historical and is based on measurement of the LVEF. HF comprises a wide range of patients, from those with normal LVEF [typically considered as ≥50%; HF with preserved EF (HFpEF)] to those with reduced LVEF [typically considered as <40%; HF with reduced EF (HFrEF)]. Patients with an LVEF in the range of 40–49% represent a ‘grey area’, which we now define as HFmrEF. Differentiation of patients with HF based on LVEF is important due to different underlying aetiologies, demographics, co-morbidities and response to therapies.6 Most clinical trials published after 1990 selected patients based on LVEF [usually measured using echocardiography, a radionuclide technique or cardiac magnetic resonance (CMR)], and it is only in patients with HFrEF that therapies have been shown to reduce both morbidity and mortality. The diagnosis of HFpEF is more challenging than the diagnosis of HFrEF. Patients with HFpEF generally do not have a dilated LV, but instead often have an increase in LV wall thickness and/or increased left atrial (LA) size as a sign of increased filling pressures. Most have additional ‘evidence’ of impaired LV filling or suction capacity, also classified as diastolic dysfunction, which is generally accepted as the likely cause of HF in these patients (hence the

term ‘diastolic HF’). However, most patients with HFrEF (previously referred to as ‘systolic HF’) also have diastolic dysfunction, and subtle abnormalities of systolic function have been shown in patients with HFpEF. Hence the preference for stating preserved or reduced LVEF over preserved or reduced ‘systolic function’. Patients with HFmrEF most probably have primarily mild systolic dysfunction, but with features of diastolic dysfunction.

Patients without detectable LV myocardial disease may have other cardiovascular causes for HF (e.g. pulmonary hypertension, valvular heart disease, etc.). Patients with non-cardiovascular pathologies (e.g. anaemia, pulmonary, renal or hepatic disease) may have symptoms similar or identical to those of HF and each may complicate or exacerbate the HF syndrome.

The patient who has never exhibited the typical symptoms and/or signs of HF and with a reduced LVEF is described as having asymptomatic LV systolic dysfunction. Patients who have had HF for some time are often said to have ‘chronic HF’.

A treated patient with symptoms and signs that have remained generally unchanged for at least 1 month is said to be ‘stable’. If chronic stable HF deteriorates, the patient may be described as ‘decompensated’ and this may happen suddenly or slowly, often leading to hospital admission, an event of considerable prognostic importance. New-onset (‘de novo’) HF may also present acutely, for example, as a consequence of acute myocardial infarction (AMI), or in a subacute (gradual) fashion, for example, in patients with a dilated cardiomyopathy (DCM), who often have symptoms for weeks or months before the diagnosis becomes clear. Although symptoms and signs of HF may resolve, the underlying cardiac dysfunction may not, and patients remain at the risk of recurrent ‘decompensation’. Occasionally, however, a patient may have HF due to a problem that resolves completely (e.g. acute viral myocarditis, takotsubo cardiomyopathy or tachycardiomyopathy). Other patients, particularly those with ‘idiopathic’ DCM, may also show substantial or even complete recovery of LV systolic function with modern diseasemodifying therapy [including angiotensin-converting enzyme inhibitor, beta-blocker, mineralocorticoid receptor antagonist, ivabradine and/or CRT]. ‘Congestive HF’ is a term that is sometimes used,

and may describe acute or chronic HF with evidence of volume overload. Many or all of these terms may be accurately applied to the same patient at different times, depending upon their stage of illness.

Heart failure should never be the only diagnosis. The etiology of heart failure and the presence of exacerbating factors or other diseases that may have an important influence on management should be carefully considered in all cases. The extent to which the cause of heart failure should be pursued by further investigation will depend on the resources available and the likelihood that diagnosis will influence management. CHF may be caused by myocardial dysfunction, valve abnormalities, pericardial disease, or it may be induced by rhythm disturbances. Acute ischaemia, anaemia, renal or thyroid dysfunction, and cardio-depressant drugs may exacerbate, or more rarely, cause heart failure. Acute pulmonary oedema and cardiogenic shock have a similar etiological spectrum as CHF, though pulmonary oedema may be more often associated with a hypertensive crisis and normal left ventricular systolic function. Standard textbooks of cardiology should be consulted for a more extensive list of the causes of heart failure. In Europe, myocardial dysfunction secondary to coronary artery disease, usually as a consequence of myocardial infarction, is the most common cause of heart failure among patients under the age of 75 years and clear abnormalities in systolic function are usually present. Concomitant hypertension is the most important condition in this context for the development of heart failure. Among elderly patients who are often less intensively investigated, an accurate diagnosis of the presence and the etiology of heart failure is more difficult and obscured by multiple other diagnoses. Systolic hypertension and cardiac hypertrophy, as well as cell loss and fibrosis may be more important causes of heart failure in the elderly and may be more likely to manifest predominantly as abnormalities of diastolic function. Importance of identifying potentially reversible exacerbating factors In patients with pre-existing cardiac dysfunction, symptoms of CHF may be caused or exacerbated by poor compliance to treatment, myocardial ischaemia, hypertension, tachy- or bradyarrhythmia, changes in valvular regurgitation, pulmonary embolism, aortic dissection, infection, renal dysfunction, side effects of drug therapy, and excessive fluid or

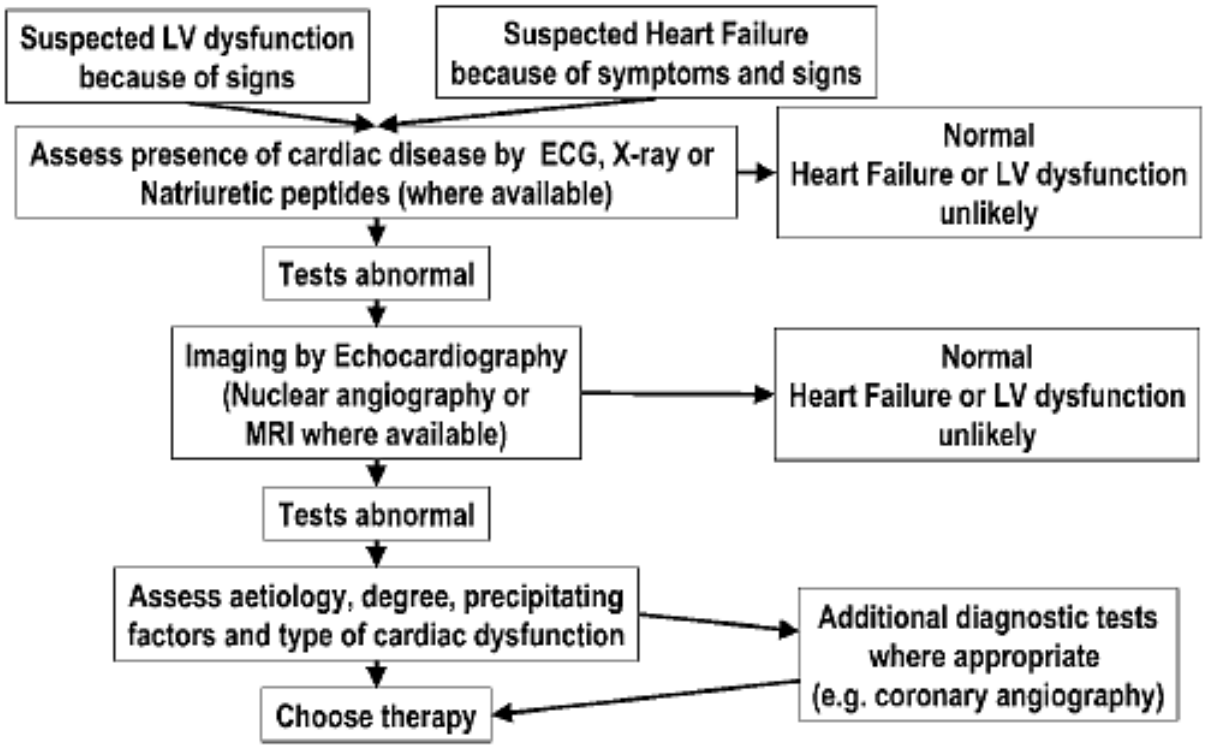
sodium intake. It is important to identify any reversible factors in order to treat heart failure optimally.

Aspects of the pathophysiology of the symptoms of heart failure relevant to diagnosis The origin of the symptoms of heart failure is not fully understood. Increased pulmonary capillary pressure is undoubtedly responsible for pulmonary oedema in part, but studies conducted during exercise in patients with CHF demonstrate only a weak relationship between capillary pressure and exercise performance. This suggests that raised pulmonary capillary pressure is not the only factor responsible for exertional breathlessness. In this context, variation in the degree of dynamic mitral regurgitation will influence breathlessness. Abnormalities of alveolar-capillary gas diffusion, peripheral or respiratory skeletal muscle deconditioning, and non-cardiac causes of dyspnoea, such as obesity or pulmonary disease, should always be considered. Peripheral oedema is poorly related to right heart pressures: capillary permeability for fluid and small proteins may be important additional factors. Venous insufficiency and drug therapy (calcium channel blockers) should be considered.

Although impairment of cardiac function is central to the development of heart failure, altered peripheral blood flow, especially to the kidney and skeletal muscle, is typical and probably of major pathophysiological importance. Similarly, activation of a number of neuroendocrine systems is characteristic of heart failure. Baroreceptor dysfunction is an important link between vasomotor and neuroendocrine dysfunction. The understanding of CHF has moved from a haemodynamic concept into accepting the importance of neuroendocrine pathophysiological changes as important for the progression as well as the treatment of heart failure. Activation of various inflammatory pathways may also contribute to cardiac dysfunction and to the clinical syndrome, particularly in more advanced stages.

Possible methods for the diagnosis of heart failure in clinical practice Symptoms and signs in the diagnosis of heart failure. Symptoms and signs are important as they alert the observer to the possibility that heart failure exists. The clinical suspicion of heart failure must be confirmed by more objective tests particularly aimed at assessing cardiac function (Fig. 44).

Figure 44: Algorithm for the diagnosis of heart failure or left ventricular dysfunction



5.1. Mastering the skills of interpretation of blood tests in the field of the topic **(brain natriuretic peptides).**

The following laboratory investigations are recommended as part of a routine diagnostic evaluation of patients with CHF: complete blood count (Hb, leukocytes, and platelets), S-electrolytes, S-creatinine, S-glucose, S-hepatic enzymes, and urinanalysis. Additional tests to consider include C-reactive protein, thyroid stimulating hormone (TSH), S-uric acid, and S-urea. In acute exacerbations, it is important to exclude acute myocardial infarction by myocardial biomarkers. Anaemia may exacerbate pre-existing heart failure and is associated with increased risk for morbidity and mortality. A raised haematocrit suggests that breathlessness may be caused by pulmonary disease, cyanotic congenital heart disease, or a pulmonary arteriovenous malformation.

Elevated serum creatinine can be caused by primary renal disease, which may induce all the features of heart failure by volume overload. Heart failure and renal

dysfunction often coincide because of the underlying diseases, such as diabetes and hypertension, or as a consequence of impaired kidney perfusion by reduction in cardiac output during the progression of heart failure. Treatment with diuretics and/or ACE-inhibitors sometimes together with potassium-sparing diuretics is another reason for a high S-creatinine value. Further, age alone can be a cause of reduced creatinine clearance.

Plasma concentrations of certain natriuretic peptides or their precursors, especially BNP and NT-proBNP, are helpful in the diagnosis of heart failure. A low-normal concentration in an untreated patient makes heart failure unlikely to be the cause of symptoms.

BNP and NT-proBNP have considerable prognostic potential though evaluation of their role in treatment monitoring remains to be determined. Several clinical and epidemiological studies have demonstrated a direct relationship between increasing plasma concentrations of natriuretic peptides and decreasing cardiac (usually left ventricular) function. Although this applies to atrial natriuretic peptides (ANP), B-type natriuretic peptide (BNP) and its precursor NT-proBNP, for which there are now commercially available assays, have been much more extensively characterized in clinical practice. Conclusive evidence of diagnostic accuracy is now available from well-conducted clinical trials. Patients who were referred to a rapid access heart failure clinic from primary care BNP performed extremely well when compared with the gold standard diagnoses made by a panel of three cardiologists with all available clinical information. In particular, the negative predictive accuracy was 97%, i.e. to rule out the diagnosis, whereas this population with a high a priori likelihood of heart failure, the positive predictive value was also high at 70%. Thus, the diagnostic potential of both BNP and NT-proBNP in primary care is high, a setting in which only about one-third of patients with suspected heart failure has the presence of heart failure subsequently confirmed. A large study has recently confirmed that BNP could help differentiate cardiac from respiratory acute breathlessness in the emergency room setting. The predictive accuracy of BNP for heart failure was similar to or better than other clinical variables, including the chest X-ray.

Although the diagnostic potential of natriuretic peptides is less clear-cut when systolic function is normal, there is increasing evidence that their elevation can indicate that diastolic dysfunction is present. Other common cardiac abnor-malities that may cause elevated natriuretic peptide levels include left ventricular hypertrophy, valvular heart disease, acute or chronic ischaemia, hypertension, and pulmonary embolism. Although rarely high BNP may also signifys noncardiac disease with the most common being renal impairment, it is important to recognize that female gender and increasing age also elevate the plasma levels, factors that must be taken into account when setting cut points. It needs also to be stressed that, as with troponin measurements, these values are assay specific and not interchangeable among assays.

In considering the use of BNP and NT-proBNP as diagnostic aids, it should be emphasized that a ‘normal’ value cannot completely exclude cardiac disease, but a normal or low concentration in an untreated patient makes heart failure unlikely as the cause of symptoms. Nevertheless, values in the normal range are associated with an excellent prognosis and alternative causes of the symptoms should be sought in the first instance. Most importantly, it must be recognized that elevated levels are powerful predictors of death and future major cardiac events. Therefore, such an observation confers ‘high risk’ status and mandates further cardiological investigation to elucidate the cause. In the first instance, this is likely to be an ECG, which may provide the explanation and indicate a management plan. In clinical practice today, the place of BNP and NTproBNP is as ‘rule out’ tests to exclude significant cardiac disease. Particularly in primary care but also in certain aspects of secondary care (e.g. the emergency room and clinics), the cost-effectiveness of the test suggests that a normal result should obviate the need for further cardiological tests such as in the first instance, echocardiography as well as more expensive investigations.

Thus, the plasma concentration of NPs can be used as an initial diagnostic test, especially in the non-acute setting when echocardiography is not immediately available. Elevated NPs help establish an initial working diagnosis, identifying those who require further cardiac investigation; patients with values below the cutpoint for the exclusion of important cardiac dysfunction do not require echocardiography. Patients

with normal plasma NP concentrations are unlikely to have HF. The upper limit of normal in the non-acute setting for BNP is 35 pg/mL and for NT-proBNP it is 125 pg/mL; in the acute setting, higher values should be used [BNP < 100 pg/mL, NT-proBNP < 300 pg/mL and mid-regional pro A-type natriuretic peptide (MR-proANP) < 120 pmol/L]. Diagnostic values apply similarly to HFrEF and HFpEF; on average, values are lower for HFpEF than for HFrEF. At the mentioned exclusionary cut-points, the negative predictive values are very similar and high in both the non-acute and acute setting, but the positive predictive values are lower both in the non-acute setting and in the acute setting). Therefore, the use of NPs is recommended for ruling-out HF, but not to establish the diagnosis. There are numerous cardiovascular and non-cardiovascular causes of elevated NPs that may weaken their diagnostic utility in HF. Among them, AF, age and renal failure are the most important factors impeding the interpretation of NP measurements. On the other hand, NP levels may be disproportionally low in obese patients.

5.2. Mastering the skills of ECG and echocardiogramms' interpretation in the field of the topic

Electrocardiogram

A normal electrocardiogram (ECG) suggests that the diagnosis of CHF should be carefully reviewed. Electrocardiographic changes in patients with heart failure are frequent. The negative predictive value of normal ECG to exclude left ventricular systolic dysfunction exceeds 90%. On the other hand, the presence of anterior Q-waves and a left bundle branch block in patients with ischaemic heart disease are good predictors of a decreased ejection fraction. ECG signs of left atrial overload or left ventricular hypertrophy may be associated with systolic as well as isolated diastolic dysfunction, but they have a low predictive value. A QRS width .120 ms suggests that cardiac dyssynchrony may be present and a target for treatment.

The ECG is crucial for detecting atrial fibrillation or flutter, and sometimes ventricular arrhythmia, all of which are considered causative or contributing factors

for heart failure. The diagnostic contribution of ECG anomalies markedly increases if clinical symptoms and signs of heart failure co-exist. ECG recordings do not need to be repeated in the absence of changes of clinical status. Indeed, an abnormal ECG increases the likelihood of the diagnosis of HF, but has low specificity. Some abnormalities on the ECG provide information on aetiology (e.g. myocardial infarction), and findings on the ECG might provide indications for therapy (e.g. anticoagulation for AF, pacing for bradycardia, CRT if broadened QRS complex). HF is unlikely in patients presenting with a completely normal ECG. Therefore, the routine use of an ECG is mainly recommended to rule out HF.

Echocardiography

Echocardiography is the preferred method for the documentation of cardiac dysfunction at rest. The most important measurement of ventricular function is the LVEF for distinguishing patients with cardiac systolic dysfunction from patients with preserved systolic function. The access to and use of echocardiography is encouraged for the diagnosis of heart failure. Transthoracic Doppler echocardiography (TDE) is rapid, safe, and widely available. It is a non-invasive technique that allows the assessment of chamber dimensions, wall thicknesses and geometry, indices of regional and global, systolic and diastolic ventricular function.

Echocardiography also provides rapid and semi-quantitative assessment of valvular function, especially of mitral, tricuspid and aortic stenosis and regurgitation, grading of mitral regurgitation and the velocity of secondary tricuspid regurgitation for the estimate of systolic pulmonary artery pressure. Although M-mode measurements benefit from high temporal resolution, they are inaccurate in patients with spherical ventricles and regional dysfunction. The apical biplane summation of discs method - modified Simpson’s method - is validated but relies on accurate endocardial definition. Although quantitative visual assessment has been shown to detect low LVEF with good sensitivity and specificity, this procedure is reliable only with experienced observers. Other measurements include fractional shortening, sphericity index, atrioventricular plane displacement, myocardial performance index, and left ventricular wall motion index.

The interpretation of ejection fraction with any technique shortly after an acute myocardial infarction or in the context of a mitral regurgitation is more uncertain. Reproducibility of ejection fraction among different observers is poor, even when the same techniques are used.

Assessment of LV diastolic function

Assessment of diastolic function may be clinically useful in detecting abnormalities of diastolic function in patients who present with CHF and normal LVEF, in determining prognosis in heart failure patients, in providing a non-invasive estimate of left ventricular diastolic pressure, and in diagnosing constrictive pericarditis and restrictive cardiomyopathy also.

Diagnostic criteria of diastolic dysfunction

According to recommendations from the ESC Working Group on Myo-cardial Function, a diagnosis of primary diastolic heart failure requires three con-ditions to be simultaneously satisfied:

- presence of signs or symptoms of CHF,
- presence of normal or only mildly abnormal left ventricular systolic function (LVEF ≤ 45–50%),
- evidence of abnormal left ventricular relaxation, diastolic distensibility, or diastolic stiffness.

The third criterion may be the most difficult to satisfy because of limitations in the diagnostic methods. Furthermore, it is essential to exclude pulmonary disease. The two hallmarks of left ventricular diastolic dysfunction are impaired relaxation and decreased diastolic compliance. Quantification of rate of relaxation and compliance requires invasive methods and is therefore not practical in clinical routine. Instead, different echocardiography indices of diastolic filling may be used. Importantly, these indices do not directly measure diastolic function, but serve as markers of impaired diastolic function. The approaches which are most useful are the measurement of transmitral and pulmonary venous flow velocities by pulsed Doppler echocardiography and mitral annular velocities by tissue Doppler imaging (TDI). The

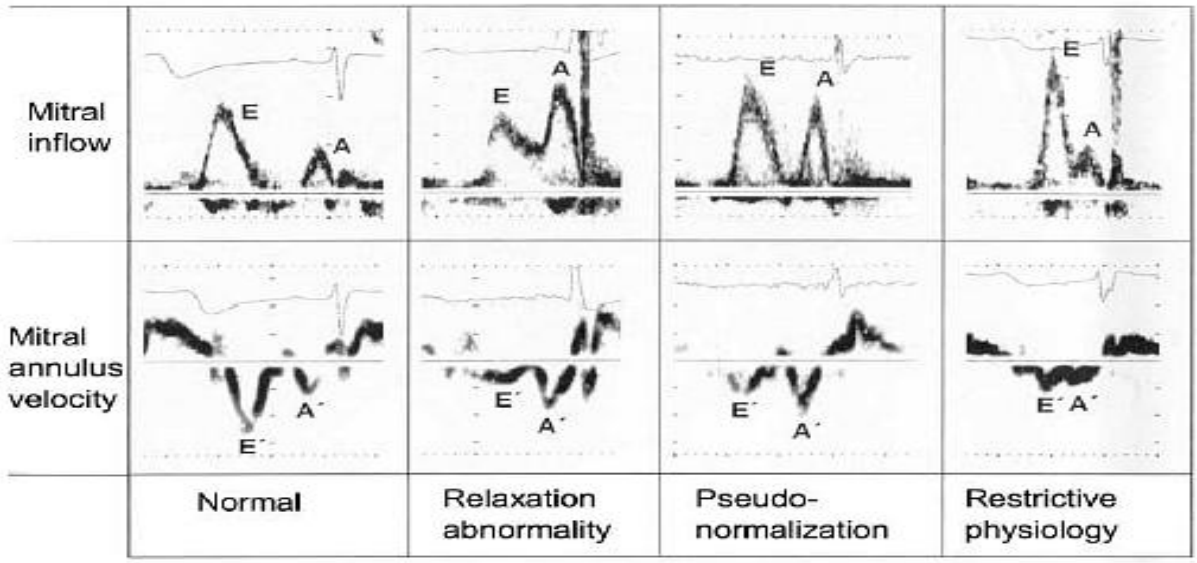
peak early diastolic mitral flow velocity (E) is directly related to the transmitral pressure gradient and left atrial pressure and is therefore markedly load-dependent. The peak early diastolic mitral annular velocity (E0) is less load-dependent and is related to the rate of left ventricular relaxation. One should also look for cardiac structural changes that may be consistent with diastolic dysfunction, in particular, left atrial enlargement and left ventricular hypertrophy. Filling patterns and staging of diastolic dysfunction In patients with cardiac disease, three abnormal left ventricular filling patterns have been described. At an early stage of diastolic dysfunction, there is typically a pattern of impaired myocardial relaxation with a decrease in peak transmitral E-velocity, a compensatory increase in the atrial-induced (A) velocity, and therefore a decrease in the E/A ratio. In patients with advanced cardiac disease there may be a pattern of ‘re-strictive filling’, with an elevated peak E-velocity, a short E-deceleration time, and a markedly increased E/A ratio. The elevated peak E-velocity is due to elevated left atrial pressure that causes an increase in the early-diastolic transmitral pressure gradient. The short E-deceleration time is due to reduced left ventricular chamber compliance that leads to rapid deceleration of transmi-tral flow.

In patients with an intermediate pattern between impaired relaxation and restrictive filling, the E/A ratio and the deceleration time may be normal, a so-called ‘pseudonormalized filling pattern’. This pattern may be distinguished from normal filling by the demonstration of reduced peak E1-velocity by TDI and by some other diagnostic approaches.

The three filling patterns ‘impaired relaxation’, ‘pseudonormalized filling’, and ‘restrictive filling’ represent mild, moderate, and severe diastolic dysfunction, respectively. Thus, by using the combined assessment of transmitral blood flow velocities and mitral annular velocities, it becomes possible to perform staging of diastolic dysfunction during a routine echocardiographic examination (Figure 45). In a given patient, however, the pattern may change over time because of changes in intrinsic myocardial function and in response to medication that modifies loading conditions. Importantly, the absolute value of E0 is dependent on the equipment that is used and instrument settings. Furthermore, transmitral velocities and mitral annular velocities

are age-dependent, and any given value should be compared with age-adjusted reference values. We still lack prospective outcome studies that investigate if assessment of diastolic function by these criteria may improve management of heart failure patients.

Figure 45. The three filling patterns ‘impaired relaxation’, ‘pseudonormalized filling’, and ‘restrictive filling’ represent mild, moderate, and severe diastolic dysfunction, respectively



Estimation of LV diastolic pressure

The marked sensitivity of left ventricular filling velocities to loading condi-tions represents a limitation when Doppler velocities are used as markers of diastolic function. The load sensitivity, however, makes it possible to estimate left ventricular diastolic pressure from the Doppler indices of filling. One of the most useful of these approaches is to compare the durations of antegrade transmitral flow with reversed pulmonary venous flow during atrial contraction. A pulmonary venous reverse A-wave duration that exceeds transmitral A-wave duration by 0.30 ms is a marker of elevated LV EDP. Because peak early mitral annular velocity is less preload-dependent than peak early transmitral velocity, the E/E0 ratio can be used to estimate left ventricular filling pressure. Persistence of a restrictive filling pattern of left ventricular filling after medical treatment is associated with increased mortality. Transoesophageal echocardiography is not recommended routinely and can only be advo-

cated in patients who have an inadequate echo window, in complicated valvular patients, in patients with suspected dysfunction of mechanical mitral valve prosthesis, or when it is mandatory to identify or exclude a thrombus in the atrial appendage. Repeated echocardiography can be recommended in the follow-up of patients with heart failure only when there is an important change in the clinical status suggesting significant improvement or deterioration in cardiac function.

Additional non-invasive tests to be considered in patients in which echocardiography at rest has not provided enough information and in patients with coronary artery disease (e.g. severe or refractory CHF and coronary artery disease) further non-invasive imaging may include the following techniques.

Stress echocardiography

Exercise or pharmacological stress echocardiography may be useful for detecting ischaemia as a cause of reversible or persistent dysfunction and in determining the viability of akinetic myocardium. Graded dobutamine infusion may be used to recruit contractile reserve. Sustained contractile improvement is observed when flow reserve is appropriate, in the presence of stunning or nontransmural infarction. A biphasic response indicates that flow reserve is blunted and suggests the presence of myocardial hibernation. Although several noncontrolled studies have shown that revascularization can improve regional function, clinical status, and survival in patients with a significant amount of hibernating myocardium, a systematic assessment of myocardial viability in patients with coronary artery disease and heart failure with systolic dysfunction cannot yet be recommended.

Nuclear cardiology

Radionuclide angiography (RNA) provides reasonably accurate measure-ments of left and, to a lesser extent, right ventricular ejection fraction (RVEF) and cardiac volumes. Left ventricular filling dynamics can also be analysed. In none of these are the measurements reliable in the presence of atrial fibrillation. Planar myocardial scintigraphy or single photon emission computed tomography (SPECT) can be performed at rest or during stress using infusion of different agents, such as thallium201 or 99 technetium sestamibi. The presence and extent of ischaemia can be evaluated.

Although each of these imaging modalities may have certain diagnostic and prognostic value, the routine use of nuclear cardiology cannot be recommended. As with echocardiography, values of ejection fraction vary with the technique used. Thus, analysis using a single region of interest gives values significantly lower than when two regions are used. However, reproducibility is better than with echocardiography.

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