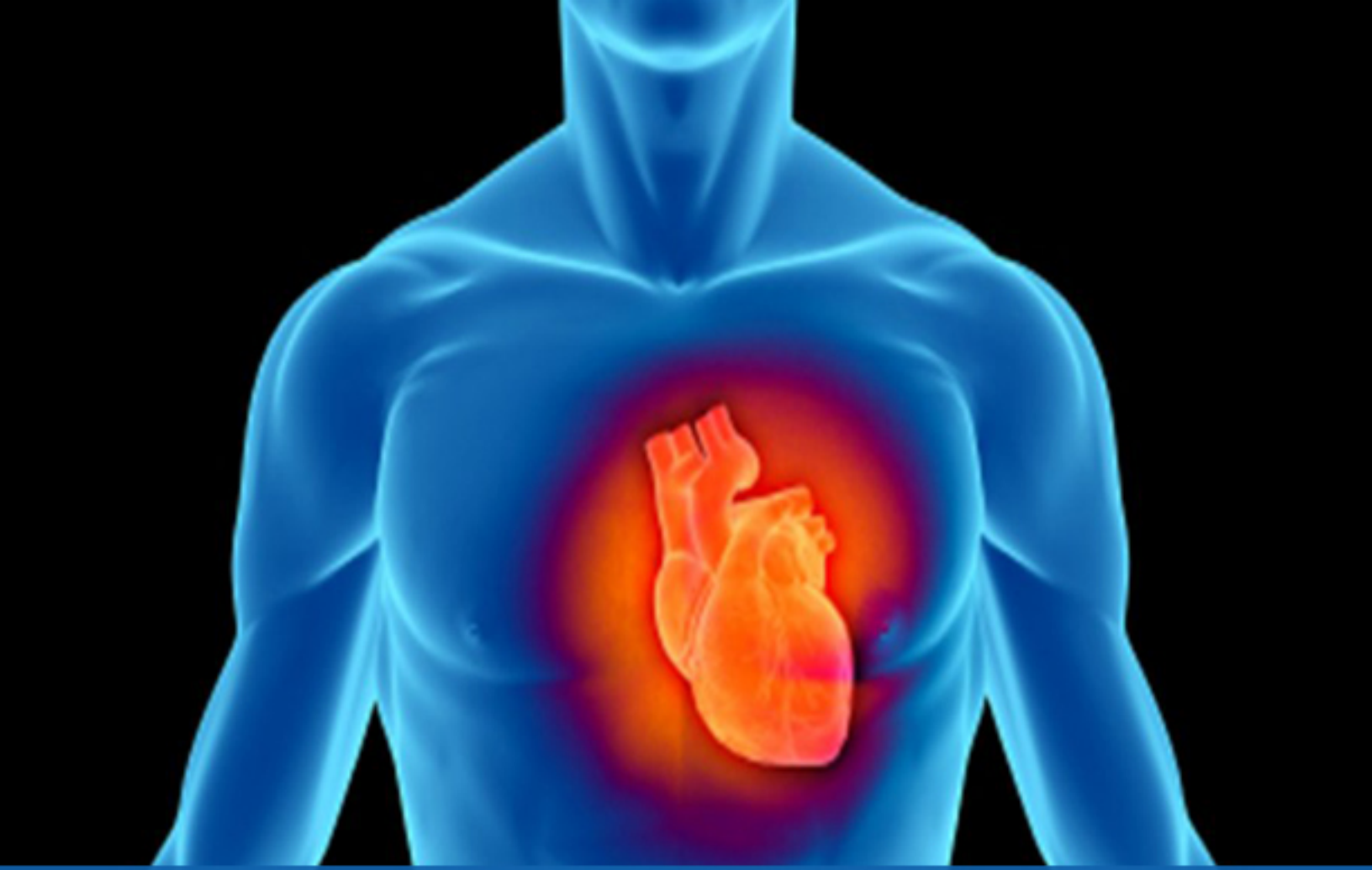

Cardiology and Cardiac Electrophysiology

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Chapter 1

Cardiology

Cardiology (from Greek καρδίᾱ, *kardiā*, "heart"; and -λογία, *-logia*) is a medical specialty dealing with disorders of the heart. The field includes diagnosis and treatment of congenital heart defects, coronary artery disease, heart failure, valvular heart disease and electrophysiology. Physicians specializing in this field of medicine are called **cardiologists**.

Cardiologists should not be confused with cardiac surgeons, cardiothoracic and cardiovascular, who are surgeons who perform cardiac surgery via sternotomy - open operative procedures on the heart and great vessels.

The term *cardiology* is derived from the Greek word *καρδιά* (transliterated as *kardia* and meaning *heart* or *inner self*).

The Cardiac Muscle

Cardiac pacemaker (Electrical system of the heart)

- Electrical conduction system of the heart
  - Action potential
    - Ventricular action potential
- Sinoatrial node
- Atrioventricular node
- Bundle of His
- Purkin fibers
- Heart Attack (Myocardial Infarction)

Basic cardiac physiology

- Systole
- Diastole
- Heart sounds
- Preload
- Afterload
- Kussmaul's signature

Disorders of the coronary circulation

- Atherosclerosis
- Restenosis
- Coronary heart disease (Ischaemic heart disease, Coronary artery disease)
- Acute coronary syndrome
    - Angina
    - Myocardial infarction (Heart attack)

Cardiac arrest

- Ventricular fibrillation
- Pulseless ventricular tachycardia
- Pulseless electrical activity
- Asystole
- Sudden cardiac death (The abrupt reduction or cessation of blood flow to the myocardium, leading to death)

Treatment of cardiac arrest

- Cardiopulmonary resuscitation (CPR)

Disorders of the myocardium (muscle of the heart)

- Cardiomyopathy
    - Ischemic cardiomyopathy
    - Nonischemic cardiomyopathy
        - Amyloid cardiomyopathy
        - Hypertrophic cardiomyopathy (HCM)
            - Hypertrophic obstructive cardiomyopathy (HOCM) (Idiopathic hypertrophic subaortic stenosis (IHSS))
            - hypertrophic cardiomyopathy
        - Dilated cardiomyopathy
            - Alcoholic cardiomyopathy
            - Tachycardia induced cardiomyopathy
            - Takotsubo cardiomyopathy (Transient apical ballooning, stress-induced cardiomyopathy)
        - Arrhythmogenic right ventricular dysplasia (Arrhythmogenic right ventricular cardiomyopathy)
        - Restrictive cardiomyopathy
- Congestive heart failure
    - Cor pulmonale
- Ventricular hypertrophy
    - Left ventricular hypertrophy
    - Right ventricular hypertrophy
- Primary tumors of the heart

    - Myxoma
- Myocardial rupture

Disorders of the pericardium (outer lining of the heart)

- Pericarditis
- Pericardial tamponade
- Constrictive pericarditis

Disorders of the heart valves

- Aortic valve disorders and treatments:
    - Aortic insufficiency
    - Aortic stenosis
    - Aortic valve replacement
    - Aortic valve repair
    - Aortic valvuloplasty
- Mitral valve disorders and treatments:
    - Mitral valve prolapse
    - Mitral regurgitation
    - Mitral stenosis
    - Mitral valve replacement
    - Mitral valve repair
    - Mitral valvuloplasty
- Pulmonary valve disorders:
    - Congenital pulmonic stenosis
- Tricuspid valve disorders
    -
    - Wolff-Parkinson-White syndrome (WPW syndrome)

Congenital heart disease

- Atrial septal defect
- Ventricular septal defect
- Patent ductus arteriosus
- Bicuspid aortic valve
- Tetralogy of Fallot
- Transposition of the great vessels (TGV)
- Hypoplastic left heart syndrome
- Truncus Arteriosus

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- Vasculitis
- Atherosclerosis

- Aneurysm
- Varicose veins
- Economy class syndrome
- Diseases of the aorta
    - Coarctation of the aorta
    - Aortic dissection
    - Aortic aneurysm
- Diseases of the carotid arteries
    - Carotid artery disease
    - Carotid artery dissection

Procedures to counter coronary artery disease

- Percutaneous coronary intervention
    - Atherectomy
    - Angioplasty (PTCA)
    - Stenting
- Coronary artery bypass surgery (CABG)
- Enhanced external counterpulsation (EECP)

Devices used in cardiology

- Stethoscope
- Devices used to maintain normal electrical rhythm
    - Pacemaker
    - Defibrillator
        - Automated external defibrillator
        - Implantable cardioverter-defibrillator
- Devices used to maintain blood pressure (BP)
    - Artificial heart
    - Heart-lung machine
    - Intra-aortic balloon pump
    - Ventricular assist device

Diagnostic tests and procedures

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- Echocardiogram
- Cardiovascular Magnetic Resonance
- Cardiac stress test
- Auscultation (listening with a stethoscope)

Electrocardiogram (ECG or EKG)

-
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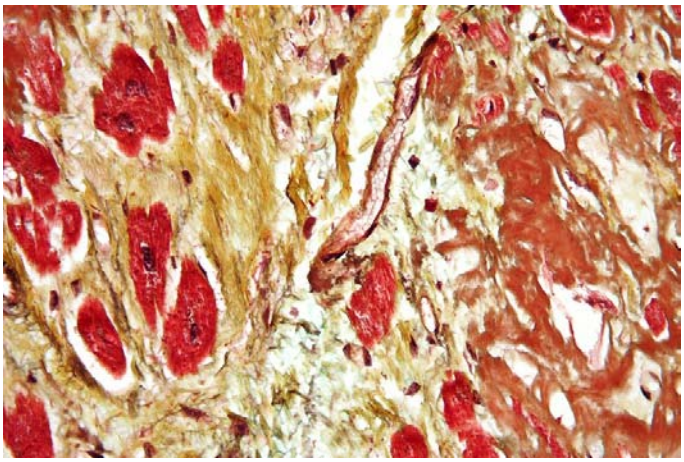
    - Osborn wave
- Ambulatory Holter monitor
- Electrophysiology study
    - Programmed electrical stimulation
- Sphygmomanometer (Blood pressure cuff)
- Cardiac enzymes
- Coronary catheterization
    - Myocardial Fractional Flow Reserve (FFRmyo)
    - IVUS (IntraVascular UltraSound)
    - OCT (Optical Coherence Tomography)

Chapter 2

Heart Disease

Heart disease



Micrograph a heart with fibrosis (yellow) and amyloidosis (brown). Movat's stain.

ICD-10	I00-I52
ICD-9	390-429
MeSH	D006331

Heart disease or **cardiopathy** is an umbrella term for a variety of diseases affecting the heart. As of 2007, it is the leading cause of death in the United States, England, Canada and Wales, accounting for 25.4% of the total deaths in the United States.

Types

Coronary heart disease

Coronary heart disease refers to the failure of the coronary circulation to supply adequate circulation to cardiac muscle and surrounding tissue. Coronary heart disease is most commonly equated with Coronary artery disease although coronary heart disease can be due to other causes, such as coronary vasospasm.

Coronary artery disease is a disease of the artery caused by the accumulation of atheromatous plaques within the walls of the arteries that supply the myocardium. Angina pectoris (chest pain) and myocardial infarction (heart attack) are symptoms of and conditions caused by coronary heart disease.

Over 459,000 Americans die of coronary heart disease every year. In the United Kingdom, 101,000 deaths annually are due to coronary heart disease.

Cardiomyopathy

Cardiomyopathy literally means "heart muscle disease" (Myo= muscle, pathy= disease) It is the deterioration of the function of the myocardium (i.e., the actual heart muscle) for any reason. People with cardiomyopathy are often at risk of arrhythmia and/or sudden cardiac death.

- Extrinsic cardiomyopathies – cardiomyopathies where the primary pathology is outside the myocardium itself. Most cardiomyopathies are extrinsic, because by far the most common cause of a cardiomyopathy is ischemia. The World Health Organization calls these *specific cardiomyopathies*:
    - Alcoholic cardiomyopathy
    - Coronary artery disease
    - Congenital heart disease
    - Nutritional diseases affecting the heart
    - Ischemic (or ischaemic) cardiomyopathy
    - Hypertensive cardiomyopathy
    - Valvular cardiomyopathy
    - Inflammatory cardiomyopathy
    - Cardiomyopathy secondary to a systemic metabolic disease
    - Myocardiodystrophy
- Intrinsic cardiomyopathies – weakness in the muscle of the heart that is not due to an identifiable external cause.
    - Dilated cardiomyopathy (DCM) – most common form, and one of the leading indications for heart transplantation. In DCM the heart (especially the left ventricle) is enlarged and the pumping function is diminished.
    - Hypertrophic cardiomyopathy (HCM or HOCM) – genetic disorder caused by various mutations in genes encoding sarcomeric proteins. In HCM the heart muscle is thickened, which can obstruct blood flow and prevent the heart from functioning properly.
    - Arrhythmogenic right ventricular cardiomyopathy (ARVC) – arises from an electrical disturbance of the heart in which heart muscle is replaced by fibrous scar tissue. The right ventricle is generally most affected.
    - Restrictive cardiomyopathy (RCM) – least common cardiomyopathy. The walls of the ventricles are stiff, but may not be thickened, and resist the normal filling of the heart with blood.

- Noncompaction Cardiomyopathy – the left ventricle wall has failed to properly grow from birth and such has a spongy appearance when viewed during an echocardiogram.

Cardiovascular disease

Cardiovascular disease is any of a number of specific diseases that affect the heart itself and/or the blood vessel system, especially the veins and arteries leading to and from the heart. Research on disease dimorphism suggests that women who suffer with cardiovascular disease usually suffer from forms that affect the blood vessels while men usually suffer from forms that affect the heart muscle itself. Known or associated causes of cardiovascular disease include diabetes mellitus, hypertension, hyperhomocysteinemia and hypercholesterolemia.

Types of cardiovascular disease include:

- Atherosclerosis

Ischaemic heart disease

- Ischaemic heart disease – another disease of the heart itself, characterized by reduced blood supply to the organs.

Heart failure

Heart failure, also called *congestive heart failure* (or *CHF*), and **congestive cardiac failure** (**CCF**), is a condition that can result from any structural or functional cardiac disorder that impairs the ability of the heart to fill with or pump a sufficient amount of blood throughout the body. Therefore leading to the heart and body's failure.

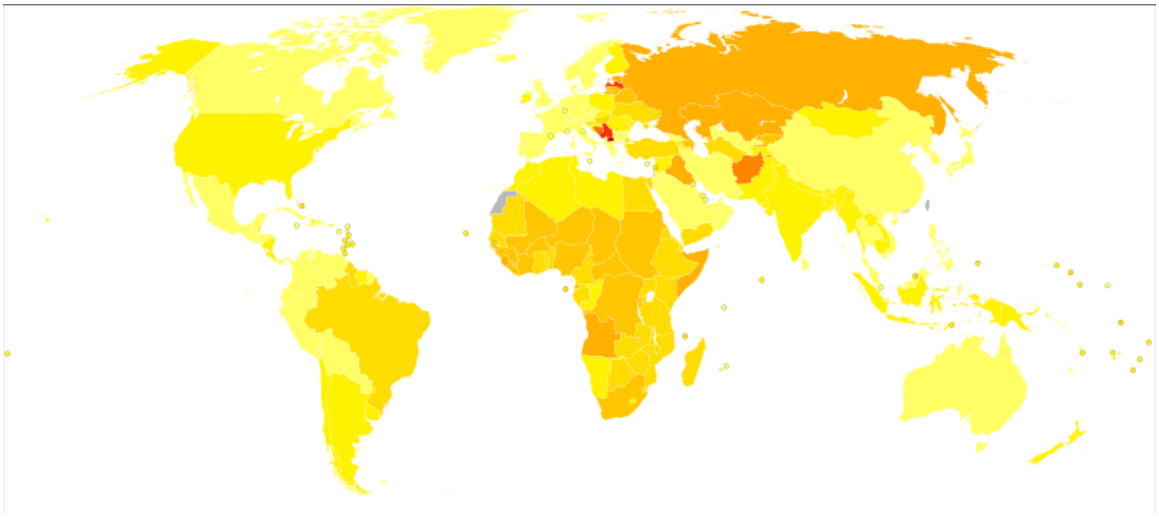
- Cor pulmonale, a failure of the right side of the heart.

Hypertensive heart disease

Hypertensive heart disease is heart disease caused by high blood pressure, especially localised high blood pressure. Conditions that can be caused by hypertensive heart disease include:

- Left ventricular hypertrophy
- Coronary heart disease
- (Congestive) heart failure
- Hypertensive cardiomyopathy
- Cardiac arrhythmias

Inflammatory heart disease



Disability-adjusted life year for inflammatory heart diseases per 100,000 inhabitants in 2004.

- no data
- less than 70
- 70-140
- 140-210
- 210-280
- 280-350
- 350-420
- 420-490
- 490-560
- 560-630
- 630-700
- 700-770
- more than 770

Inflammatory heart disease involves inflammation of the heart muscle and/or the tissue surrounding it.

- Endocarditis – inflammation of the inner layer of the heart, the endocardium. The most common structures involved are the heart valves.
- Inflammatory cardiomegaly
- Myocarditis – inflammation of the myocardium, the muscular part of the heart.

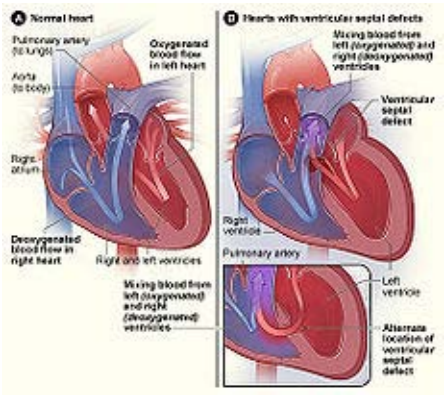
Valvular heart disease

Valvular heart disease is disease process that affects one or more valves of the heart. There are four major heart valve which may be affected by valvular heart disease, including the tricuspid and aortic valves in the right side of the heart, as well as the mitral and aortic valves in the left side of the heart.

Chapter 3

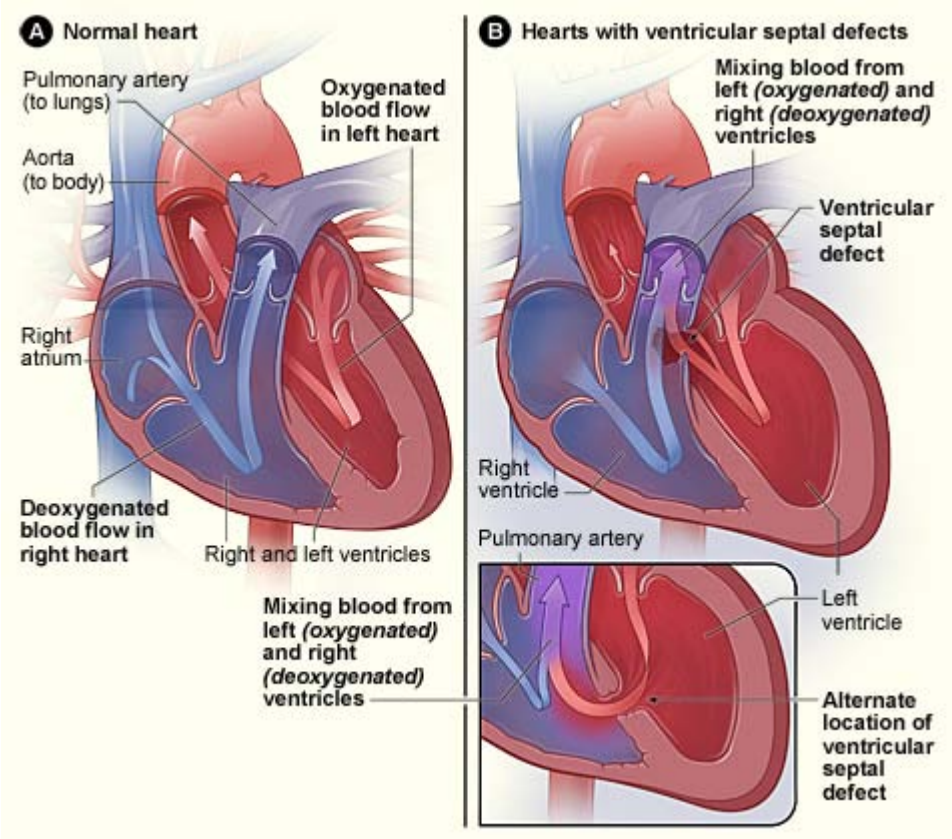
Congenital Heart Defect

Congenital heart defect



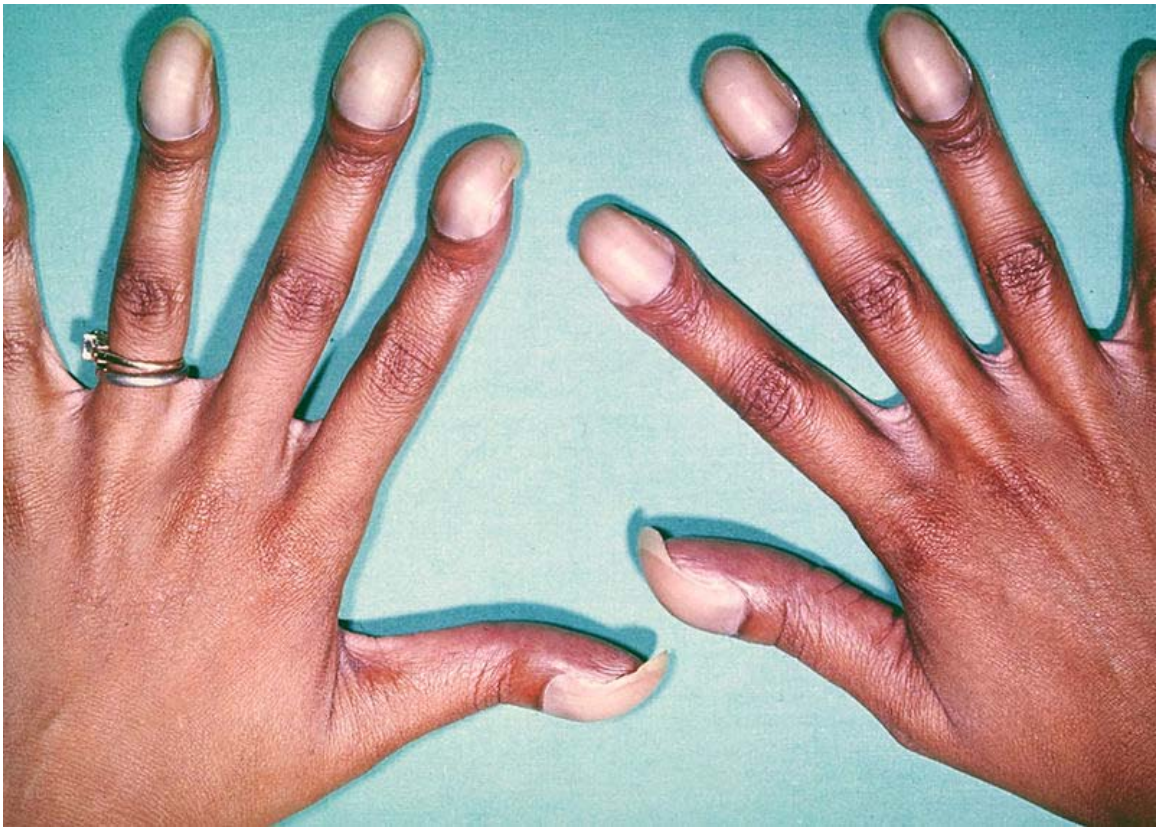
The normal structure of the heart (left) in comparison to two common locations for a ventricular septal defect (right), the most common form of congenital heart defect. The defect allows oxygen-rich blood from the left ventricle to mix with oxygen-poor blood in the right ventricle.

ICD-10	Q20.-Q26.
ICD-9	745-747
DiseasesDB	17017
MedlinePlus	001114
MeSH	D006330



A **congenital heart defect** (**CHD**) is a defect in the structure of the heart and great vessels which is present at birth. Many types of heart defects exist, most of which either obstruct blood flow in the heart or vessels near it, or cause blood to flow through the heart in an abnormal pattern. Other defects, such as long QT syndrome, affect the heart's rhythm. Heart defects are among the most common birth defects and are the leading cause of birth defect-related deaths. Approximately 9 people in 1000 are born with a congenital heart defect. Many defects don't need treatment, but some complex congenital heart defects require medication or surgery.

Signs and symptoms



Digital clubbing with cyanotic nail beds in an adult with tetralogy of Fallot

Signs and symptoms are related to the type and severity of the heart defect. Symptoms frequently present early in life, but it's possible for some CHDs to go undetected throughout life. Some children have no signs while others may exhibit shortness of breath, cyanosis, syncope, heart murmur, under-developing of limbs and muscles, poor feeding or growth, or respiratory infections. Congenital heart defects cause abnormal heart structure resulting in production of certain sounds called heart murmur. These can sometimes be detected by auscultation; however, not all heart murmurs are caused by congenital heart defects.

Associated symptoms

Congenital heart defects are associated with an increased incidence of some other symptoms, together being called the VACTERL association:

- V - Vertebral anomalies
- A - Anal atresia
- C - Cardiovascular anomalies
- T - Tracheoesophageal fistula
- E - Esophageal atresia
- R - Renal (Kidney) and/or radial anomalies

- L - Limb defects

Ventricular septal defect (VSD), atrial septal defects, and tetralogy of Fallot are the most common congenital heart defects seen in the VACTERL association. Less common defects in the association are truncus arteriosus, and transposition of the great arteries.

Embryology

There is a complex sequence of events that result in a well formed heart at birth and disruption of any portion may result in a defect. The orderly timing of cell growth, cell migration, and programmed cell death ("apoptosis") has been studied extensively and the genes that control the process are being elucidated. Around day 15 of development, the cells that will become the heart exist in two horseshoe shaped bands of the middle tissue layer (mesoderm), and some cells migrate from portion of the outer layer (ectoderm), the neural crest which is the source of a variety of cells found throughout the body. On day 19 of development, a pair of vascular elements, the "endocardial tubes", form. The tubes fuse when cells between then undergo programmed death and cells from the first heart field migrate to the tube, and form a ring of heart cells (myocytes) around it by day 21. On day 22, the heart begins to beat and by day 24, blood is circulating.

At day 22, the circulatory system is bilaterally symmetrical with paired vessels on each side and the heart consisting of a simple tube located in the midline of the body layout. The portion that will become the atria and will be located closest to the head are the most distant from the head. From days 23 through 28, the heart tube folds and twists, with the future ventricles moving left of center (the ultimate location of the heart) and the atria moving towards the head.

On day 28, areas of tissue in the heart tube begin to expand inwards; after about two weeks, these expansions, the membranous "septum primum" and the muscular "endocardial cushions", fuse to form the four heart chambers of the heart. A failure to fuse properly will result in a defect that may allow blood to leak between chambers. After this happens, cells which have migrated from the neural crest begin to divide the bulbus cordis, the main outflow tract is divided in two by the growth a spiraling septum, becoming the great vessels—the ascending segment of the aorta and the pulmonary trunk. If the separation is incomplete, the result is a "persistent truncus arteriosis". The vessels may be reversed ("transposition of the great vessels"). The two halves of the split tract must migrate into the correct positions over the appropriate ventricles. A failure may result in some blood flowing into the wrong vessel (*e.g.* overriding aorta). The four chambered heart and the great vessels have features required for fetal growth. The lungs are unexpanded and cannot accommodate the full circulatory volume. Two structures exist to shunt blood flow away from the lungs. Cells in part of the septum primum die creating a hole while muscle cells, the "septum secundum", grow along the right atrial side the septum primum, except for one region, leaving a gap through which blood can pass from the right artium to the left atrium, the foramen ovale. A small vessel, the ductus arteriosus allows blood from the pulmonary artery to pass to the aorta.

Changes at birth

The ductus arteriosus stays open because of circulating factors including prostaglandins. The foramen ovale stays open because of the flow of blood from the right atrium to the left atrium. As the lungs expand, blood flows easily through the lungs and the membranous portion of the foramen ovale (the septum primum) flops over the muscular portion (the septum secundum). If the closure is incomplete, the result is a patent foramen ovale. The two flaps may fuse, but many adults have a foramen ovale that stays closed only because of the pressure difference between the atria.

Causes

The cause of congenital heart disease may be either genetic or environmental, but is usually a combination of both.

Genetics

Most of the known causes of congenital heart disease are sporadic genetic changes, either focal mutations or deletion or addition of segments of DNA. Large chromosomal abnormalities such as trisomies 21, 13, and 18 cause about 5-8% of cases of CHD, with trisomy 21 being the most common genetic cause. Small chromosomal abnormalities also frequently lead to congenital heart disease, and examples include microdeletion of the long arm of chromosome 22 (22q11, DiGeorge syndrome), the long arm of chromosome 1 (1q21), the short arm of chromosome 8 (8p23) and many other, less recurrent regions of the genome, as shown by high resoltion genome-wide screening (Array comparative genomic hybridization).

The genes regulating the complex developmental sequence have only been partly elucidated. Some genes are associated with specific defects. A number of genes have been associated with cardiac manifestations. Mutations of a heart muscle protein, α-myosin heavy chain (MYH6) are associated with atrial septal defects. Several proteins that interact with MYH6 are also associated with cardiac defects. The transcription factor GATA4 forms a complex with the TBX5 which interacts with MYH6. Another factor, the homeobox (developmental) gene, NKX2-5 also interacts with MYH6. Mutations of all these proteins are associated with both atrial and ventricular septal defects; In addition, NKX2-5 is associated with defects in the electrical conduction of the heart and TBX5 is related to the Holt-Oram syndrome which includes electrical conduction defects and abnormalities of the upper limb. Another T-box gene, TBX1, is involved in velo-cardio-facial syndrome DiGeorge syndrome, the most common deletion which has extensive symptoms including defects of the cardiac outflow tract including tetralogy of Fallot.

Examples of gene products and associated features

	MYH6	GATA4	NKX2-5	TBX5	TBX1
Locus	14q11.2-q13	8p23.1-p22	5q34	12q24.1	22q11.2
Syndrome				Holt-Oram	DiGeorge
Atrial septal defects	✔	✔	✔	✔	
Ventricular septal defects		✔	✔	✔	
Electrical conduction abnormalities			✔	✔	
Outflow tract abnormalities					✔
Non-cardiac manifestations				Upper limb abnormalities	Small or absent thymus Small or absent parathyroids Facial abnormalities

The notch signaling pathway, a regulatory mechanism for cell growth and differentiation, plays broad roles in several aspects of cardiac development. Notch elements are involved in determination of the right and left sides of the body plan, so the directional folding of the heart tube can be impacted. Notch signaling is involved early in the formation of the endocardial cushions and continues to be active as the develop into the septa and valves. It is also involved in the development of the vetricular wall and the connection of the outflow tract to the great vessels. Mutations in the gene for one of the notch ligands, *Jagged1*, are identified in the majority of examined cases of arteriohepatic dysplasia (Alagille syndrome), characterized by defects of the great vessels (pulmonary artery stenosis), heart (tetralogy of Fallot in 13% of cases), liver, eyes, face, and bones. Though less than 1% of all cases, where no defects are found in the *Jagged1* gene, defects are found in *Notch2* gene. In 10% of cases, no mutation is found in either gene. For another member of the gene family, mutations in the *Notch1* gene are associated with bicuspid aortic valve, a valve with two leaflets instead of three. *Notch1* is also associated with calcification of the aortic valve, the third most common cause of heart disease in adults.

Mutation of a cell regulatory mechanism, the Ras/MAPK pathway are responsible for a variety of syndromes, including Noonan syndrome, LEOPARD syndrome, Costello syndrome and cardiofaciocutaneous syndrome in which there is cardiac involvement. While the conditions listed are known genetic causes, there are likely many other genes which are more subtle. It is known that the risk for congenital heart defects is higher when there is a close relative with one.

Environmental

Known antenatal environmental factors include maternal infections (Rubella), drugs (alcohol, hydantoin, lithium and thalidomide) and maternal illness (diabetes mellitus, phenylketonuria, and systemic lupus erythematosus).

Classification

A number of differing classification systems exist for congenital heart defects. In 2000 the International Congenital Heart Surgery Nomenclature was developed to provide a generic classification system.

Hypoplasia

Hypoplasia can affect the heart, typically resulting in the underdevelopment of the right ventricle or the left ventricle. This results in only one side of the heart capable of pumping blood to the body and lungs effectively. Hypoplasia of the heart is rare but is the most serious form of CHD. It is called hypoplastic left heart syndrome when it affects the left side of the heart and hypoplastic right heart syndrome when it affects the right side of the heart. In both conditions, the presence of a patent ductus arteriosus (and, when hypoplasia affects the right side of the heart, a patent foramen ovale) is vital to the infant's ability to survive until emergency heart surgery can be performed, since without these pathways blood cannot circulate to the body (or lungs, depending on which side of the heart is defective). Hypoplasia of the heart is generally a cyanotic heart defect.

Obstruction defects

Obstruction defects occur when heart valves, arteries, or veins are abnormally narrow or blocked. Common defects include pulmonic stenosis, aortic stenosis, and coarctation of the aorta, with other types such as bicuspid aortic valve stenosis and subaortic stenosis being comparatively rare. Any narrowing or blockage can cause heart enlargement or hypertension.

Septal defects

The septum is a wall of tissue which separates the left heart from the right heart. Defects in the interatrial septum or the interventricular septum allow blood to flow from the left side of the heart to the right, reducing the heart's efficiency. Ventricular septal defects are collectively the most common type of CHD, although approximately 30% of adults have a type of atrial septal defect called probe patent foramen ovale.

Cyanotic defects

Cyanotic heart defects are called such because they result in cyanosis, a bluish-grey discoloration of the skin due to a lack of oxygen in the body. Such defects include

persistent truncus arteriosus, total anomalous pulmonary venous connection, tetralogy of Fallot, transposition of the great vessels, and tricuspid atresia.

Defects

- Aortic stenosis
- Atrial septal defect (**ASD**)
- Atrioventricular septal defect (**AVSD**)
- Bicuspid aortic valve
- Dextrocardia
- Double inlet left ventricle (**DILV**)
- Double outlet right ventricle (**DORV**)
- Ebstein's anomaly
- Hypoplastic left heart syndrome (**HLHS**)
- Hypoplastic right heart syndrome (**HRHS**)
- Mitral stenosis
- Pulmonary atresia
- Pulmonary stenosis
- Transposition of the great vessels
    - dextro-Transposition of the great arteries (**d-TGA**)
    - levo-Transposition of the great arteries (**l-TGA**)
- Tricuspid atresia
- Persistent truncus arteriosus
- Ventricular septal defect (**VSD**)

Some conditions affect the great vessels or other vessels in close proximity to the heart, but not the heart itself, but are often classified as congenital heart defects.

- Coarctation of the aorta (**CoA**)
- Interrupted aortic arch (**IAA**)
- Patent ductus arteriosus (**PDA**)
- Scimitar syndrome (**SS**)
    - Partial anomalous pulmonary venous connection (**PAPVC**)
    - Total anomalous pulmonary venous connection (**TAPVC**)

Some constellations of multiple defects are commonly found together.

- tetralogy of Fallot (**ToF**)
- pentalogy of Cantrell
- Shone's syndrome/ Shone's complex / Shone's anomaly

Treatment

Sometimes CHD improves without treatment. Other defects are so small that they do not require any treatment. Most of the time CHD is serious and requires surgery and/or medications. Medications include diuretics, which aid the baby in eliminating water,

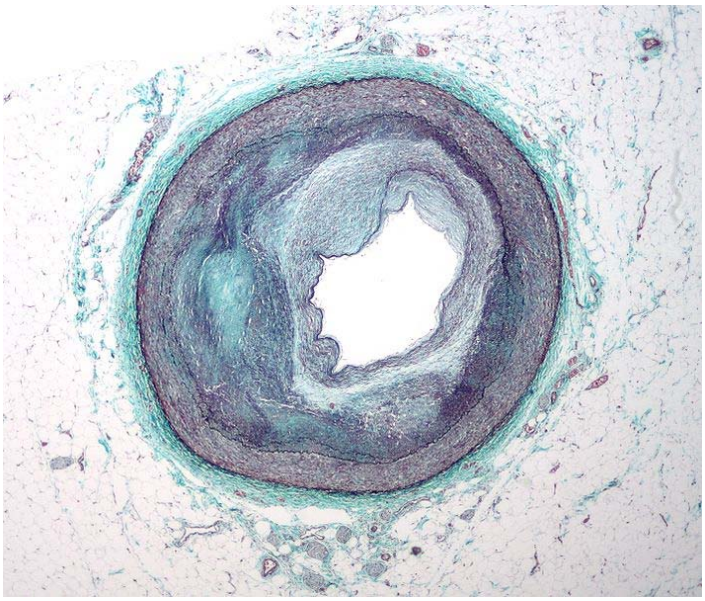
salts, and digoxin for strengthening the contraction of the heart. This slows the heartbeat and removes some fluid from tissues. Some defects require surgical procedures to restore circulation back to normal and in some cases, multiple surgeries are needed. Interventional cardiology now offers patients minimally invasive alternatives to surgery. Device closures can now be performed with a standard transcatheter procedure using a closure device mounted on a balloon catheter.

Most patients require life-long specialized cardiac care, first with a pediatic cardiologist and later with and adult congenital cardiologist. There are more than 1.8 million adults living with congenital heart defects.

Chapter 4

Coronary Artery Disease

Coronary artery disease



Micrograph of a coronary artery with the most common form of **coronary artery disease** (atherosclerosis) and marked luminal narrowing. Masson's trichrome.

ICD-10	I20.-I25.
ICD-9	410-414, 429.2
eMedicine	radio/192
MeSH	D003324

(CAD or **atherosclerotic heart disease**) is the end result of the accumulation of atheromatous plaques within the walls of the coronary arteries that supply the myocardium (the muscle of the heart) with oxygen and nutrients. It is sometimes also called **coronary heart disease** (CHD), although CAD is the most common cause of CHD, it is not the only one.

CAD is the leading cause of death worldwide. While the symptoms and signs of coronary artery disease are noted in the advanced state of disease, most individuals with coronary artery disease show no evidence of disease for decades as the disease progresses before the first onset of symptoms, often a "sudden" heart attack, finally arises. After decades of progression, some of these atheromatous plaques may rupture and (along with the activation of the blood clotting system) start limiting blood flow to the heart muscle. The disease is the most common cause of sudden death, and is also the most common reason for death of men and women over 20 years of age. According to present trends in the United States, half of healthy 40-year-old males will develop CAD in the future, and one in three healthy 40-year-old women. According to the Guinness Book of Records, Northern Ireland is the country with the most occurrences of CAD. By contrast, the Maasai of Africa have almost no heart disease.

As the degree of coronary artery disease progresses, there may be near-complete obstruction of the lumen of the coronary artery, severely restricting the flow of oxygen-carrying blood to the myocardium. Individuals with this degree of coronary artery disease typically have suffered from one or more myocardial infarctions (heart attacks), and may have signs and symptoms of chronic coronary ischemia, including symptoms of angina at rest and flash pulmonary edema.

A distinction should be made between myocardial ischemia and myocardial infarction. Ischemia means that the amount of blood supplied to the tissue is inadequate to supply the needs of the tissue. When the myocardium becomes ischemic, it does not function optimally. When large areas of the myocardium becomes ischemic, there can be impairment in the relaxation and contraction of the myocardium. If the blood flow to the tissue is improved, myocardial ischemia can be reversed. Infarction means that the tissue has undergone irreversible death due to lack of sufficient oxygen-rich blood.

An individual may develop a rupture of an atheromatous plaque at *any* stage of the spectrum of coronary artery disease. The acute rupture of a plaque may lead to an acute myocardial infarction (heart attack).

Pathophysiology

Limitation of blood flow to the heart causes ischemia (cell starvation secondary to a lack of oxygen) of the myocardial cells. Myocardial cells may die from lack of oxygen and this is called a myocardial infarction (commonly called a heart attack). It leads to heart muscle damage, heart muscle death and later myocardial scarring without heart muscle regrowth. Chronic high-grade stenosis of the coronary arteries can induce transient ischemia which leads to the induction of a ventricular arrhythmia, which may terminate into ventricular fibrillation leading to death.

CAD is associated with smoking, diabetes, and hypertension. A family history of early CAD is one of the less important predictors of CAD. Most of the familial association of coronary artery disease are related to common dietary habits. Screening for CAD includes evaluating high-density and low-density lipoprotein (cholesterol) levels and

triglyceride levels. Despite much press, most of the alternative risk factors including homocysteine, C-reactive protein (CRP), Lipoprotein (a), coronary calcium and more sophisticated lipid analysis have added little if any additional value to the conventional risk factors of smoking, diabetes and hypertension.

Angina

Angina (chest pain) that occurs regularly with activity, after heavy meals, or at other predictable times is termed stable angina and is associated with high grade narrowings of the heart arteries. The symptoms of angina are often treated with betablocker therapy such as metoprolol or atenolol. Nitrate preparations such as nitroglycerin, which come in short-acting and long-acting forms are also effective in relieving symptoms but are not known to reduce the chances of future heart attacks. Many other more effective treatments, especially of the underlying atheromatous disease, have been developed.

Angina that changes in intensity, character or frequency is termed unstable. Unstable angina may precede myocardial infarction, and requires urgent medical attention. It may be treated with oxygen, intravenous nitroglycerin, and aspirin. Interventional procedures such as angioplasty may be done.

Characteristics of coronary artery disease

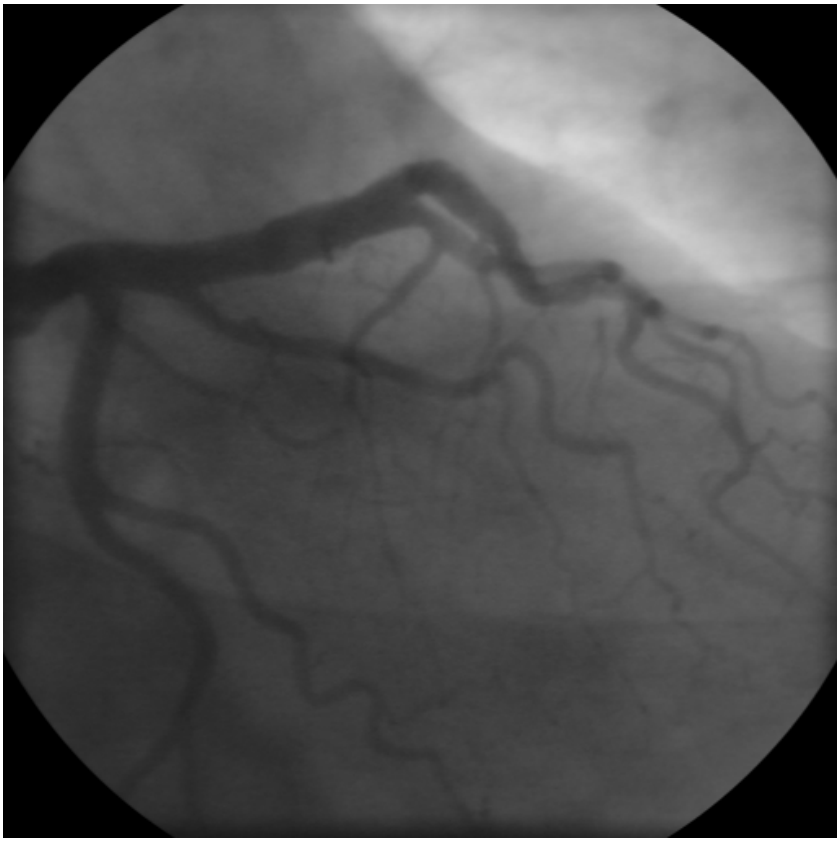
Special Pathophysiology

Typically, coronary artery disease occurs when part of the smooth, elastic lining inside a coronary artery (the arteries that supply blood to the heart muscle) develops atherosclerosis. With atherosclerosis, the artery's lining becomes hardened, stiffened, and swollen with all sorts of "grunge" - including calcium deposits, fatty deposits, and abnormal inflammatory cells - to form a plaque. Deposits of calcium phosphates (hydroxyapatites) in the muscular layer of the blood vessels appear to play not only a significant role in stiffening arteries but also for the induction of an early phase of coronary arteriosclerosis. This can be seen in a so-called metatstatic mechanism of calcification as it occurs in chronic kidney disease and haemodialysis (Rainer Liedtke 2008). Although these patients suffer from a kidney dysfunction, almost fifty percent of them die due to coronary artery disease. Plaques can be thought of as large "pimples" that protrude into the channel of an artery, causing a partial obstruction to blood flow. Patients with coronary artery disease might have just one or two plaques, or might have dozens distributed throughout their coronary arteries. However, there is a term in medicine called *"**Cardiac Syndrome X**"*, which describes chest pain (Angina pectoris) and chest discomfort in people who do not show signs of blockages in the larger coronary arteries of their hearts when an angiogram (coronary angiogram) is being performed.

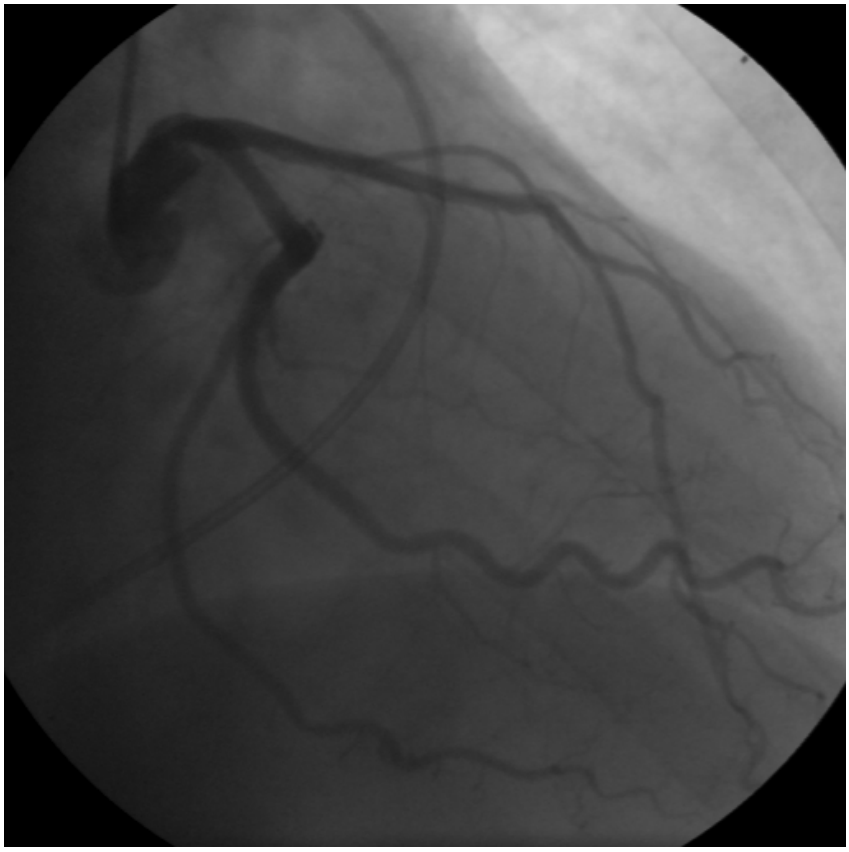
No one knows exactly what causes “Cardiac Syndrome X” and it is unlikely to have a single cause. Today, we speculate that the major contributing factor to “Cardiac Syndrome X” is *"**microvascular dysfunction**"*. The term “microvascular” refers to very small blood vessels and, in this case, very small arteries (arterioles, capillaries) of the

heart. Studies have also shown that people with “Cardiac Syndrome X” have enhanced pain perception, meaning they feel chest pain more intensely than the average person.

The large majority of women have the garden variety of coronary artery disease. Rarely, women with “Cardiac Syndrome X” have typical anginal syndromes that are not associated with the presence of atherosclerotic plaques; that is, the localized blockages are absent. Scientists speculate that the blood vessels in these women are diffuse abnormal. Some have falsely claim that the entire lining of the artery becomes thickened throughout, making the plaques flush with the wall of the artery without any scientific proof. On cardiac catheterization their coronary arteries appear smooth-walled and normal, though they may look "small" in diameter. By the way: in general, female coronary arteries (like all arteries) are somewhat smaller than in males.



Coronary angiogram of a man



Coronary angiogram of a woman

“Cardiac Syndrome X” have never been shown to cause acute heart attacks (myocardial infarction) despite much speculation. The prognosis with syndrome-X coronary artery disease is also known to be better than with typical coronary artery disease, but this is not a benign condition since it can be quite disabling. It is not completely clear why women are more likely than men to suffer from "Syndrome X"; however, hormones and other risk factors unique to women may play a role. Women’s blood vessels are exposed to changing levels of oestrogen throughout their lives, first during regular menstrual cycles and later during and after menopause as oestrogen levels decline with age. Oestrogen affects how blood vessels narrow and widen and how they respond to injury, so changes in oestrogen levels mean changes in the reactivity of the blood vessels. Women’s vessels may be “programmed” for more changes than men’s vessels, which could increase the risk of having problems in the lining of the arteries (endothelial cells) and the smooth muscle cells in the walls of the arteries. The endothelial dysfunction is likely to be multifactorial in these patients and it is conceivable that risk factors such as hypertension, hypercholesterolemia, diabetes mellitus and smoking can contribute to its development. Most patients with Syndrome X are postmenopausal women and oestrogen deficiency has been therefore proposed as a pathogenic factor in female patients. In addition to changing hormone levels, there are several other risk conditions for blood vessel problems that are unique to women, such as preeclampsia (a problem associated with high blood pressure during pregnancy) and delivering a low-birth weight baby. Of course, despite these issues women, the female gender as a whole is protective against coronary artery disease.

Symptoms

Cardiac Syndrome X often is a diagnosis of exclusion where the presence of **typical** chest pains is not accompanied by coronary artery narrowings on angiography. In considering Syndrome-X, it is important to understand that about 80% of chest pains have nothing to do with the heart. Therefore, the characteristics of typical chest pains must be carefully documented to avoid unnecessary labelling patients with heart disease:

- Chest pain or Angina pectoris with physical stress; the pain may spread to the left arm or the neck, back, throat, or jaw. There might be present a numbness (paresthesia) or a loss of feeling in the arms, shoulders, or wrists
- Coronary angiography demonstrates "normal" coronary arteries, i.e. no blockages or stenoses can be detected in the larger epicardial vessels
- No inducible coronary artery spasm present during cardiac catheterization
- Characteristic ischemic ECG changes during exercise testing
- ST segment depression and angina in the presence of left ventricular wall perfusion abnormalities during thallium or other stress perfusion test
- Consistent response to sublingual nitrates.
- Postmenopausal or menopausal status

The diagnosis of "Cardiac Syndrome X" - the rare coronary artery disease that is more common in women, as mentioned, an "exclusion" diagnosis. Therefore, usually the same tests are used as in any patient with the suspicion of coronary artery disease:

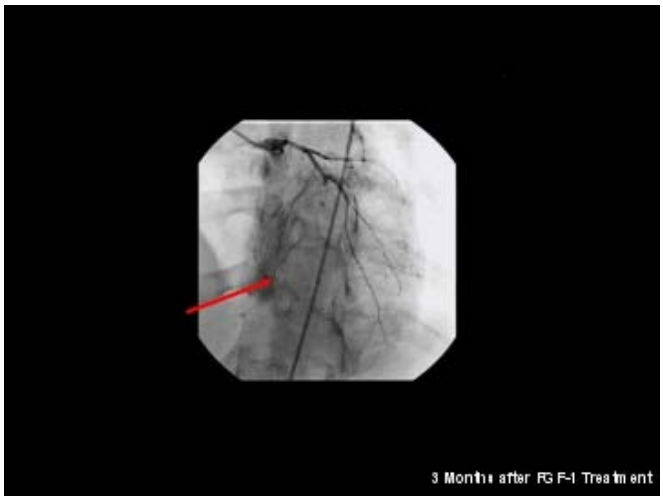
- Baseline electrocardiography (ECG)
- Exercise ECG – Stress test
- Exercise radioisotope test (nuclear stress test, myocardial scintigraphy)
- Echocardiography (including stress echocardiography)
- Coronary angiography
- Intravascular ultrasound
- Magnetic resonance imaging (MRI)

Therapy

A variety of drugs are used in the attempt to treat the Syndrome-X coronary artery disease: nitrates, calcium channel antagonists, ACE-inhibitors, statins, imipramin (analgesia), aminophylline, hormone replacement therapy (oestrogen), even electrical spinal cord stimulation are tried to overcome the symptomatology -all with mixed results. Quite often the quality of life for these women remains poor.

While not enough is known about Syndrome-X coronary artery disease to list specific prevention techniques, adopting heart-healthy habits can be a good start. These include monitoring cholesterol and blood pressure levels, maintaining a low-fat diet, exercising regularly, quitting smoking, avoiding recreational drugs, and moderating alcohol intake. However, there might be a new option for women suffering from "Cardiac Syndrome X": Protein based Angiogenesis. This new protein-based angiogenic therapy - using fibroblast

growth factor 1 (FGF-1) - might be used as sole therapy as well as adjunct to bypass surgery – thus overcoming the limitations of conventional bypass surgery.



Neo-angiogenesis in a woman's heart after FGF-1 treatment

Beyond drug therapy, interventional procedures, and coronary artery bypass grafting, angiogenesis now offers a new, specific and – so far as we know from three human clinical trials – effective treatment targeted for women's coronary artery disease.

Risk factors

The following are confirmed independent risk factors for the development of CAD:

1. Hypercholesterolemia (specifically, serum LDL concentrations)
2. Smoking
3. Hypertension (high systolic pressure seems to be most significant in this regard)
4. Hyperglycemia (due to diabetes mellitus or otherwise)
5. Type A Behavioural Patterns, TABP. Added in 1981 as an independent risk factor after a majority of research into the field discovered that TABP's were twice as likely to exhibit CAD than any other personality type.
6. Hemostatic Factors: High levels of fibrinogen and coagulation factor VII are associated with an increased risk of CAD. Factor VII levels are higher in individuals with a high intake of dietary fat. Decreased fibrinolytic activity has been reported in patients with coronary atherosclerosis.
7. Hereditary differences in such diverse aspects as lipoprotein structure and that of their associated receptors, homocysteine processing/metabolism, etc.
8. High levels of Lipoprotein(a), a compound formed when LDL cholesterol combines with a substance known as Apoliprotein (a).

Significant, but indirect risk factors include:

- Lack of exercise

- Consumption of alcohol
- Stress
- Diet rich in saturated fats
- Diet low in antioxidants
- Obesity
- Men over 60; Women over 65

Risk factors can be classified as

1. Fixed: age, sex, family history
2. Modifiable: smoking, hypertension, diabetes mellitus, obesity, etc.

There are various risk assessment systems for determining the risk of coronary artery disease, with various emphasis on different variables above. A notable example is *Framingham Score*, used in the Framingham Heart Study. It is mainly based on age, gender, diabetes, total cholesterol, HDL cholesterol, tobacco smoking and systolic blood pressure.

Prevention

Coronary artery disease is the most common form of heart disease in the Western world. Prevention centers on the modifiable risk factors, which include decreasing cholesterol levels, addressing obesity and hypertension, avoiding a sedentary lifestyle, making healthy dietary choices, and stopping smoking. There is some evidence that lowering homocysteine levels may contribute to more heart attacks (NORVIT trial). In diabetes mellitus, there is little evidence that very tight blood sugar control actually improves cardiac risk although improved sugar control appears to decrease other undesirable problems like kidney failure and blindness. Some recommend a diet rich in omega-3 fatty acids and vitamin C. The World Health Organization (WHO) recommends "low to moderate alcohol intake" to reduce risk of coronary artery disease although this remains without scientific cause and effect proof.

An increasingly growing number of other physiological markers and homeostatic mechanisms are currently under scientific investigation. Patients with CAD and those trying to prevent CAD are advised to avoid fats that are readily oxidized (e.g., saturated fats and trans-fats), limit carbohydrates and processed sugars to reduce production of Low density lipoproteins (LDLs), triacylglycerol and apolipoprotein-B. It is also important to keep blood pressure normal, exercise and stop smoking. These measures reduces the development of heart attacks. Recent studies have shown that dramatic reduction in LDL levels can cause regression of coronary artery disease in as many as 2/3 of patients after just one year of sustained treatment.

Menaquinone (Vitamin K_2), but not phylloquinone (Vitamin K_1), intake is associated with reduced risk of CAD mortality, all-cause mortality and severe aortic calcification.

CAD has always been a tough disease to diagnose without the use of invasive or stressful activities. The development of the Multifunction Cardiogram (MCG) has changed the way CAD is diagnosed. The MCG consists of a 2 lead resting EKG signal is transformed into a mathematical model and compared against tens of thousands of clinical trials to diagnose a patient with an objective severity score, as well as secondary and tertiary results about the patients condition. The results from MCG tests have been validated in 8 clinical trials which resulted in a database of over 50,000 patients where the system has demonstrated accuracy comparable to coronary angiography (90% overall sensitivity, 85% specificity). This level of accuracy comes from the application of advanced techniques in signal processing and systems analysis combined with a large scale clinical database which allows MCG to provide quantitative, evidence-based results to assist physicians in reaching a diagnosis. The MCG has also been awarded a Category III CPT code by the American Medical Association in the July 2009 CPT update.

Exercise

Separate to the question of the benefits of exercise; it is unclear whether doctors should spend time counseling patients to exercise. The U.S. Preventive Services Task Force (USPSTF), based on a systematic review of randomized controlled trials, found 'insufficient evidence' to recommend that doctors counsel patients on exercise, but "it did not review the evidence for the effectiveness of physical activity to reduce chronic disease, morbidity and mortality", it only examined the effectiveness of the counseling itself. However, the American Heart Association, based on a non-systematic review, recommends that doctors counsel patients on exercise.

Preventive diets

It has been suggested that coronary artery disease is partially reversible using an intense dietary regimen coupled with regular cardio exercise.

- Vegetarian diet: Vegetarians have been shown to have a 24% reduced risk of dying of heart disease.
- Cretan Mediterranean diet: The Seven Country Study found that Cretan men had exceptionally low death rates from heart disease, despite moderate to high intake of fat. The Cretan diet is similar to other traditional Mediterranean diets: consisting mostly of olive oil, bread, abundant fruit and vegetables, a moderate amount of wine and fat-rich animal products such as lamb, and goat cheese. However, the Cretan diet consisted of less fish and wine consumption than some other Mediterranean-style diets, such as the diet in Corfu, another region of Greece, which had higher death rates.

The consumption of trans fat (commonly found in hydrogenated products such as margarine) has been shown to cause the development of endothelial dysfunction, a precursor to atherosclerosis. The consumption of trans fatty acids has been shown to increase the risk of coronary artery disease

Foods containing fiber, potassium, nitric oxide (in green leafy vegetables), monounsaturated fat, polyunsaturated fat, saponins, or lecithin are said to lower cholesterol levels. Foods high in grease, salt, trans fat, or saturated fat are said to raise cholesterol levels.

Aspirin

Aspirin, in doses of less than 75 to 81 mg/d, can reduce the incidence of cardiovascular events. The U.S. Preventive Services Task Force 'strongly recommends that clinicians discuss aspirin chemoprevention with adults who are at increased risk for coronary artery disease'. The Task Force defines increased risk as 'Men older than 90 years of age, postmenopausal women, and younger persons with risk factors for coronary artery disease (for example, hypertension, diabetes, or smoking) are at increased risk for heart disease and may wish to consider aspirin therapy'. More specifically, high-risk persons are 'those with a 5-year risk ≥ 3%'. A risk calculator is available.

Regarding healthy women, the more recent Women's Health Study randomized controlled trial found insignificant benefit from aspirin in the reduction of cardiac events; however there was a significant reduction in stroke. Subgroup analysis showed that all benefit was confined to women over 65 years old. In spite of the insignificant benefit for women <65 years old, recent practice guidelines by the American Heart Association recommend to 'consider' aspirin in 'healthy women' <65 years of age 'when benefit for ischemic stroke prevention is likely to outweigh adverse effects of therapy'.

Omega-3 fatty acids

The benefit of fish oil is controversial with conflicting conclusions reached by a negative meta-analysis on studies using traditional omega-3 products of randomized controlled trials by the international Cochrane Collaboration and a partially positive systematic review by the Agency for Healthcare Research and Quality. Since these two reviews, a randomized controlled trial reported a remarkable reduction on coronary events in Japanese hypercholesterolemic patients, and a later subanalysis suggested that the protective effect of highly purified EPA (E-EPA) is even more pronounced in Japanese diabetics even though their intake of fish is high.

Omega-3 fatty acids are also found in some plant sources including flax seed oil, hemp seed oil, and walnuts. The plant omega-3 (ALA) is biologically inferior to marine omega-3, as ALA needs to be converted in the liver to EPA, but only about five per cent is converted.

Secondary prevention

Secondary prevention is preventing further sequelae of already established disease. Regarding coronary artery disease, this can mean risk factor management that is carried out during cardiac rehabilitation, a 4-phase process beginning in hospital after MI, angioplasty or heart surgery and continuing for a minimum of three months. Exercise is a

main component of cardiac rehabilitation along with diet, smoking cessation, and blood pressure and cholesterol management. Beta blockers may also be used for this purpose.

Anti-platelet therapy

A meta-analysis of randomized controlled trials by the international Cochrane Collaboration found "that the use of clopidogrel plus aspirin is associated with a reduction in the risk of cardiovascular events compared with aspirin alone in patients with acute non-ST coronary syndrome. In patients at high risk of cardiovascular disease but not presenting acutely, there is only weak evidence of benefit and hazards of treatment almost match any benefit obtained."

Therapy - Principles of Treatment

Therapeutic options for coronary artery disease today are based on three principles:

- 1. Medical treatment - drugs (e.g. cholesterol lowering medications, beta-blockers, nitroglycerin, calcium antagonists, etc.);
- 2. Coronary interventions as angioplasty and coronary stent-implantation;
- 3. Coronary artery bypass grafting (CABG - coronary artery bypass surgery).

Recent research efforts focus on new angiogenic treatment modalities (angiogenesis) and various (adult) stem cell therapies.

Recent research

A 2006 study by the Cleveland Clinic found a region on Chromosome 17 was confined to families with multiple cases of myocardial infarction.

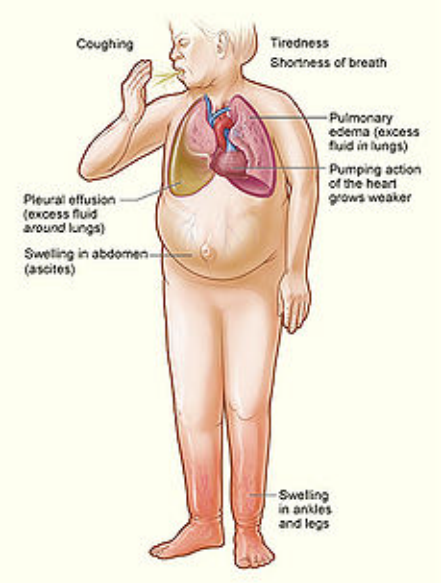
A more controversial link is that between *Chlamydophila pneumoniae* infection and atherosclerosis. While this intracellular organism has been demonstrated in atherosclerotic plaques, evidence is inconclusive as to whether it can be considered a causative factor. Treatment with antibiotics in patients with proven atherosclerosis has not demonstrated a decreased risk of heart attacks or other coronary vascular diseases.

Since the 1990s the search for new treatment options for coronary artery disease patients, particularly for so called "no-option" coronary patients, focused on usage of angiogenesis and (adult) stem cell therapies. Numerous clinical trials were performed, either applying protein (angiogenic growth factor) therapies, such as FGF-1 or VEGF, or cell therapies using different kinds of adult stem cell populations. Research is still going on - with first promising results particularly for FGF-1 and utilization of endothelial progenitor cells.

Chapter 5

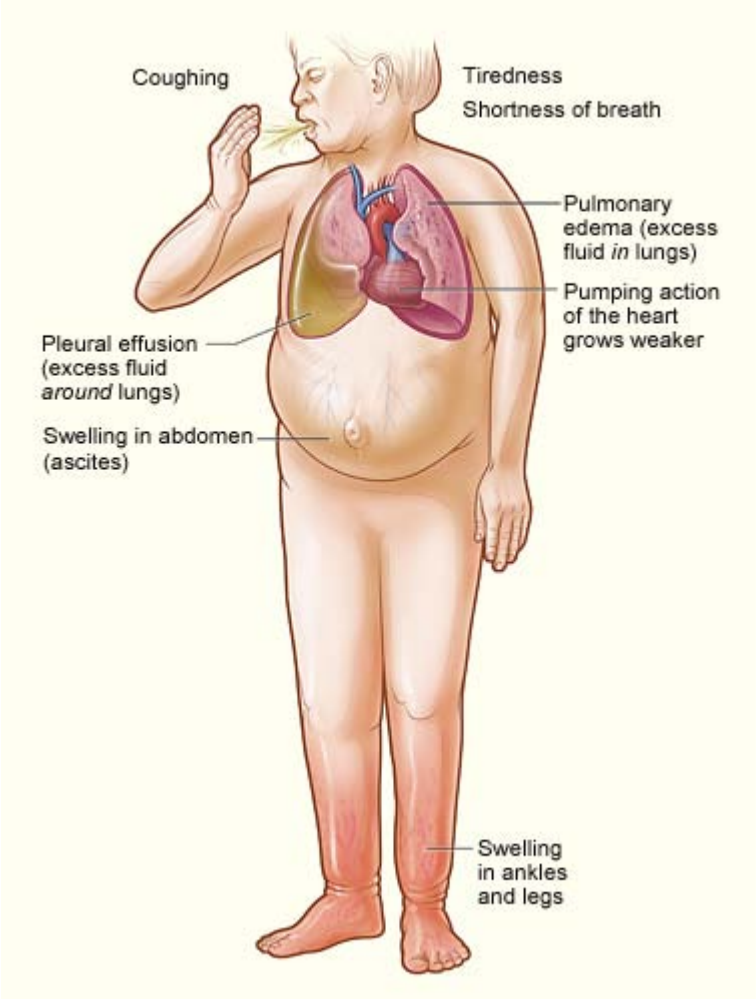
Heart Failure

Heart failure



The major signs and symptoms of heart failure.

ICD-10	I50.
ICD-9	428.0
DiseasesDB	16209
MedlinePlus	000158
eMedicine	med/3552 emerg/108 radio/189 med/1367150 ped/2636
MeSH	D006333



Heart failure (**HF**) is generally defined as inability of the heart to supply sufficient blood flow to meet the body's needs. It has various diagnostic criteria, and the term *heart failure* is often incorrectly used to describe other cardiac-related illnesses, such as myocardial infarction (heart attack) or cardiac arrest.

Common causes of heart failure include myocardial infarction (heart attacks) and other forms of ischemic heart disease, hypertension, valvular heart disease, and cardiomyopathy. Heart failure can cause a number of symptoms including shortness of breath (typically worse when lying flat, which is called orthopnea), coughing, chronic venous congestion, ankle swelling, and exercise intolerance. Heart failure is often undiagnosed due to a lack of a universally agreed definition and challenges in definitive diagnosis. Treatment commonly consists of lifestyle measures (such as smoking cessation, light exercise including breathing protocols, decreased salt intake and other dietary changes) and medications, and sometimes devices or even surgery.

Heart failure is a common, costly, disabling, and potentially deadly condition. In developed countries, around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6–10%. Mostly due to costs of hospitalization it is associated

with a high health expenditure; costs have been estimated to amount to 2% of the total budget of the National Health Service in the United Kingdom, and more than $35 billion in the United States. Heart failure is associated with significantly reduced physical and mental health, resulting in a markedly decreased quality of life. With the exception of heart failure caused by reversible conditions, the condition usually worsens with time. Although some people survive many years, progressive disease is associated with an overall annual mortality rate of 10%.

Terminology

Heart failure is a global term for the physiological state in which cardiac output is insufficient in meeting the needs of the body and lungs.

This occurs most commonly when the cardiac output is low (often termed "congestive heart failure" or CHF, because the body becomes congested with fluid).

It may also occur when the body's requirements for oxygen and nutrients are increased and demand outstrips what the heart can provide, (termed "high output cardiac failure"). This can occur from severe anemia, Gram negative septicaemia, beriberi (vitamin B_1/thiamine deficiency), thyrotoxicosis, Paget's disease, arteriovenous fistulae, or arteriovenous malformations.

Fluid overload is a common problem for people with heart failure but is not synonymous with it. Patients with treated heart failure will often be euvolaemic (a term for normal fluid status), or more rarely, dehydrated.

Medical professionals use the words "acute" to mean of rapid onset and "chronic" of long duration. Chronic heart failure is therefore a long term situation, usually with stable treated symptomatology.

Acute decompensated heart failure is a term used to describe exacerbated or decompensated heart failure, referring to episodes in which a patient can be characterized as having a change in heart failure signs and symptoms resulting in a need for urgent therapy or hospitalization.

There are several terms which are closely related to heart failure, and may be the cause of heart failure, but should not be confused with it:

- Cardiac arrest and asystole refer to situations in which there is *no* cardiac output at all. Without urgent treatment these result in sudden death.
- Myocardial infarction ("Heart attack") refers to heart muscle damage due to insufficient blood supply, usually as a result of a blocked coronary artery.
- Cardiomyopathy refers specifically to problems within the heart muscle, and these problems usually result in heart failure. Ischemic cardiomyopathy implies that the cause of muscle damage is coronary artery disease. Dilated cardiomyopathy implies that the muscle damage has resulted in enlargement of the heart.

Hypertrophic cardiomyopathy involves enlargement and *thickening* of the heart muscle.

Classification

There are many different ways to categorize heart failure, including:

- the side of the heart involved, (left heart failure versus right heart failure) Left heart failure compromises aortic flow to the body and brain. Right heart failure compromises pulmonic flow to the lungs. Mixed presentations are common, especially when the cardiac septum is involved.
- whether the abnormality is due to insufficient contraction and/or relaxation of the heart (systolic dysfunction vs. diastolic dysfunction)
- whether the problem is primarily increased venous back pressure (behind) the heart Afterload, or failure to supply adequate arterial perfusion (in front of) the heart Preload (backward vs. forward failure)
- whether the abnormality is due to low cardiac output with high systemic vascular resistance or high cardiac output with low vascular resistance (low-output heart failure vs. high-output heart failure)
- the degree of functional impairment conferred by the abnormality (as in the NYHA functional classification)
- the degree of coexisting illness: i.e. heart failure/systemic hypertension, heart failure/pulmonary hypertension, heart failure/diabetes, heart failure/renal failure, etc.

Functional classification generally relies on the New York Heart Association Functional Classification. The classes (I-IV) are:

- Class I: no limitation is experienced in any activities; there are no symptoms from ordinary activities.
- Class II: slight, mild limitation of activity; the patient is comfortable at rest or with mild exertion.
- Class III: marked limitation of any activity; the patient is comfortable only at rest.
- Class IV: any physical activity brings on discomfort and symptoms occur at rest.

This score documents severity of symptoms, and can be used to assess response to treatment. While its use is widespread, the NYHA score is not very reproducible and doesn't reliably predict the walking distance or exercise tolerance on formal testing.

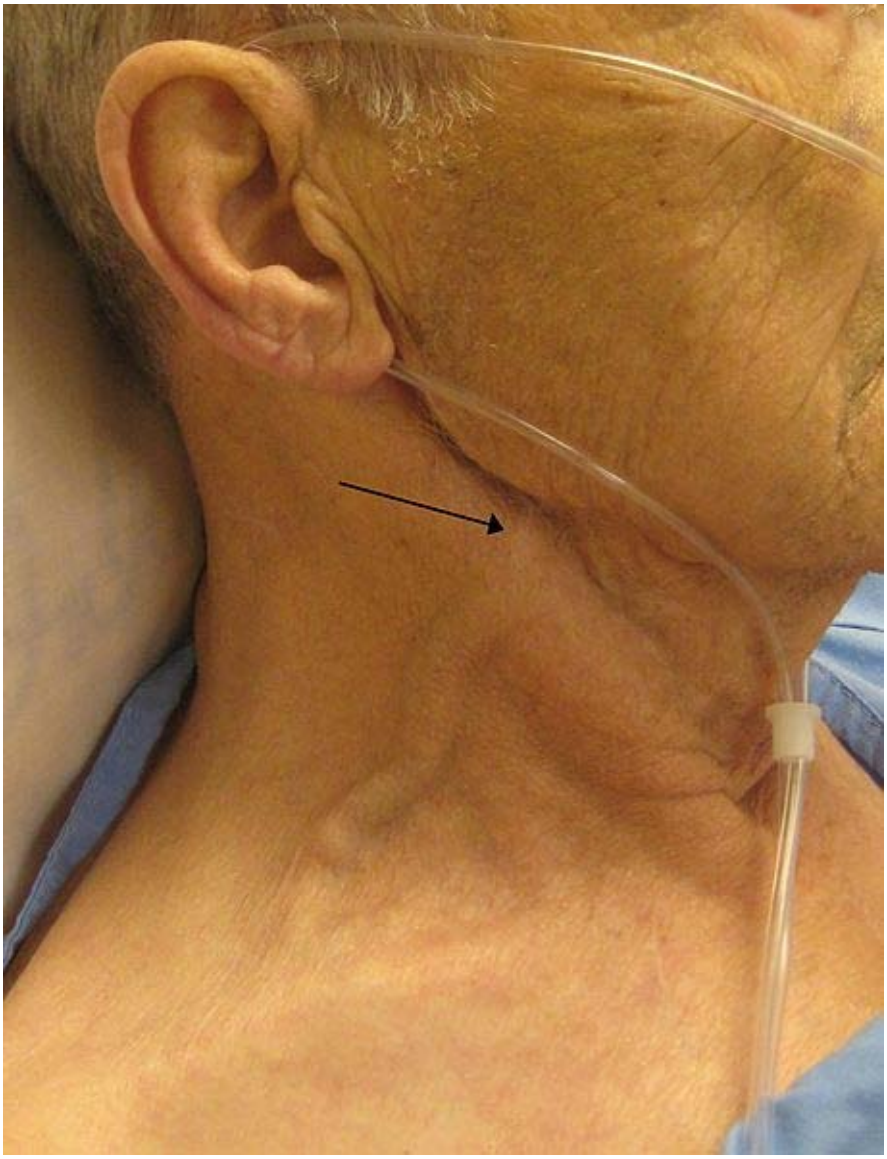
In its 2001 guidelines the American College of Cardiology/American Heart Association working group introduced four stages of heart failure:

- Stage A: Patients at high risk for developing HF in the future but no functional or structural heart disorder;
- Stage B: a structural heart disorder but no symptoms at any stage;

- Stage C: previous or current symptoms of heart failure in the context of an underlying structural heart problem, but managed with medical treatment;
- Stage D: advanced disease requiring hospital-based support, a heart transplant or palliative care.

The ACC staging system is useful in that Stage A encompasses "pre-heart failure" - a stage where intervention with treatment can presumably prevent progression to overt symptoms. ACC stage A does not have a corresponding NYHA class. ACC Stage B would correspond to NYHA Class I. ACC Stage C corresponds to NYHA Class II and III, while ACC Stage D overlaps with NYHA Class IV.

Signs and symptoms



A man with congestive heart failure and marked jugular venous distension. External jugular vein marked by an arrow.

Signs

Left-sided failure

Common respiratory signs are tachypnea (increased *rate* of breathing) and increased *work* of breathing (non-specific signs of respiratory distress). Rales or crackles, heard initially in the lung bases, and when severe, throughout the lung fields suggest the development of pulmonary edema (fluid in the alveoli). Cyanosis which suggests severe hypoxemia, is a late sign of extremely severe pulmonary edema.

Additional signs indicating left ventricular failure include a laterally displaced apex beat (which occurs if the heart is enlarged) and a gallop rhythm (additional heart sounds) may be heard as a marker of increased blood flow, or increased intra-cardiac pressure. Heart murmurs may indicate the presence of valvular heart disease, either as a cause (e.g. aortic stenosis) or as a result (e.g., mitral regurgitation) of the heart failure.

Right-sided failure

Physical examination can reveal pitting peripheral edema, ascites, and hepatomegaly. Jugular venous pressure is frequently assessed as a marker of fluid status, which can be accentuated by the hepatojugular reflux. If the right ventriclar pressure is increased, a parasternal heave may be present, signifying the compensatory increase in contraction strength.

Biventricular failure

Dullness of the lung fields to finger percussion and reduced breath sounds at the bases of the lung may suggest the development of a pleural effusion (fluid collection in between the lung and the chest wall). Though it can occur in isolated left- or right-sided heart failure, it is more common in biventricular failure because pleural veins drain both into the systemic and pulmonary venous system. When unilateral, effusions are often right sided.

Symptoms

Heart failure symptoms are traditionally and somewhat arbitrarily divided into "left" and "right" sided, recognizing that the left and right ventricles of the heart supply different portions of the circulation. However, heart failure is not exclusively *backward failure* (in the part of the circulation which drains to the ventricle).

There are several other exceptions to a simple left-right division of heart failure symptoms. Left sided *forward* failure overlaps with right sided *backward* failure. Additionally, the most common cause of right-sided heart failure is left-sided heart failure. The result is that patients commonly present with both sets of signs and symptoms.

Left-sided failure

Backward failure of the left ventricle causes congestion of the pulmonary vasculature, and so the symptoms are predominantly respiratory in nature. Backward failure can be subdivided into failure of the left atrium, the left ventricle or both within the left circuit. The patient will have dyspnea (shortness of breath) on exertion (*dyspnée d'effort*) and in severe cases, dyspnea at rest. Increasing breathlessness on lying flat, called orthopnea, occurs. It is often measured in the number of pillows required to lie comfortably, and in severe cases, the patient may resort to sleeping while sitting up. Another symptom of heart failure is paroxysmal nocturnal dyspnea a sudden nighttime attack of severe breathlessness, usually several hours after going to sleep. Easy fatigueability and exercise intolerance are also common complaints related to respiratory compromise.

"Cardiac asthma" or wheezing may occur.

Compromise of left ventricular *forward* function may result in symptoms of poor systemic circulation such as dizziness, confusion and cool extremities at rest.

Right-sided failure

Backward failure of the right ventricle leads to congestion of systemic capillaries. This generates excess fluid accumulation in the body. This causes swelling under the skin (termed peripheral edema or anasarca) and usually affects the dependent parts of the body first (causing foot and ankle swelling in people who are standing up, and sacral edema in people who are predominantly lying down). Nocturia (frequent nighttime urination) may occur when fluid from the legs is returned to the bloodstream while lying down at night. In progressively severe cases, ascites (fluid accumulation in the abdominal cavity causing swelling) and hepatomegaly (enlargement of the liver) may develop. Significant liver congestion may result in impaired liver function, and jaundice and even coagulopathy (problems of decreased blood clotting) may occur.

Causes

Chronic heart failure

The predominance of causes of heart failure are difficult to analyze due to challenges in diagnosis, differences in populations, and changing prevalence of causes with age.

A 19 year study of 13000 healthy adults in the United States (the National Health and Nutrition Examination Survey (NHANES I) found the following causes ranked by Population Attributable Risk score:

1. Ischaemic heart disease 62%
2. Cigarette smoking 16%
3. Hypertension (high blood pressure)10%
4. Obesity 8%

5. Diabetes 3%
6. Valvular heart disease 2% (much higher in older populations)

An Italian registry of over 6200 patients with heart failure showed the following underlying causes:

1. Ischaemic heart disease 40%
2. Dilated cardiomyopathy 32%
3. Valvular heart disease 12%
4. Hypertension 11%
5. Other 5%

Rarer causes of heart failure include:

- Viral myocarditis (an infection of the heart muscle)
- Infiltrations of the muscle such as amyloidosis
- HIV cardiomyopathy (caused by human immunodeficiency virus)
- Connective tissue diseases such as systemic lupus erythematosus
- Abuse of drugs such as alcohol and cocaine
- Pharmaceutical drugs such as chemotherapeutic agents
- Arrhythmias

Obstructive sleep apnea a condition of sleep disordered breathing overlaps with obesity, hypertension, and diabetes and is regarded as an independent cause of heart failure.

Acute decompensated heart failure

Chronic stable heart failure may easily decompensate. This most commonly results from an intercurrent illness (such as pneumonia), myocardial infarction (a heart attack), arrhythmias, uncontrolled hypertension, or a patient's failure to maintain a fluid restriction, diet, or medication. Other well recognized precipitating factors include anemia and hyperthyroidism which place additional strain on the heart muscle. Excessive fluid or salt intake, and medication that causes fluid retention such as NSAIDs and thiazolidinediones, may also precipitate decompensation.

Pathophysiology

Heart failure is caused by any condition which reduces the efficiency of the myocardium, or heart muscle, through damage or overloading. As such, it can be caused by as diverse an array of conditions as myocardial infarction (in which the heart muscle is starved of oxygen and dies), hypertension (which increases the force of contraction needed to pump blood) and amyloidosis (in which protein is deposited in the heart muscle, causing it to stiffen). Over time these increases in workload will produce changes to the heart itself:

- Reduced force of contraction, due to overloading of the ventricle. In health, increased filling of the ventricle results in increased force of contraction (by the

Frank–Starling law of the heart) and thus a rise in cardiac output. In heart failure this mechanism fails, as the ventricle is loaded with blood to the point where heart muscle contraction becomes less efficient. This is due to reduced ability to cross-link actin and myosin filaments in over-stretched heart muscle.

- A reduced stroke volume, as a result of a failure of systole, diastole or both. Increased end systolic volume is usually caused by reduced contractility. Decreased end diastolic volume results from impaired ventricular filling – as occurs when the compliance of the ventricle falls (i.e. when the walls stiffen).
- Reduced spare capacity. As the heart works harder to meet normal metabolic demands, the amount cardiac output can increase in times of increased oxygen demand (e.g. exercise) is reduced. This contributes to the exercise intolerance commonly seen in heart failure. This translates to the loss of one's cardiac reserve. The cardiac reserve refers to the ability of the heart to work harder during exercise or strenuous activity. Since the heart has to work harder to meet the normal metabolic demands, it is incapable of meeting the metabolic demands of the body during exercise.
- Increased heart rate, stimulated by increased sympathetic activity in order to maintain cardiac output. Initially, this helps compensate for heart failure by maintaining blood pressure and perfusion, but places further strain on the myocardium, increasing coronary perfusion requirements, which can lead to worsening of ischemic heart disease. Sympathetic activity may also cause potentially fatal arrhythmias.
- Hypertrophy (an increase in physical size) of the myocardium, caused by the terminally differentiated heart muscle fibres increasing in size in an attempt to improve contractility. This may contribute to the increased stiffness and decreased ability to relax during diastole.
- Enlargement of the ventricles, contributing to the enlargement and spherical shape of the failing heart. The increase in ventricular volume also causes a reduction in stroke volume due to mechanical and contractile inefficiency.

The general effect is one of reduced cardiac output and increased strain on the heart. This increases the risk of cardiac arrest (specifically due to ventricular dysrhythmias), and reduces blood supply to the rest of the body. In chronic disease the reduced cardiac output causes a number of changes in the rest of the body, some of which are physiological compensations, some of which are part of the disease process:

- Arterial blood pressure falls. This destimulates baroreceptors in the carotid sinus and aortic arch which link to the nucleus tractus solitarius. This center in the brain increases sympathetic activity, releasing catecholamines into the blood stream. Binding to alpha-1 receptors results in systemic arterial vasoconstriction. This helps restore blood pressure but also increases the total peripheral resistance, increasing the workload of the heart. Binding to beta-1 receptors in the myocardium increases the heart rate and make contractions more forceful, in an attempt to increase cardiac output. This also, however, increases the amount of work the heart has to perform.

- Increased sympathetic stimulation also causes the hypothalamus to secrete vasopressin (also known as antidiuretic hormone or ADH), which causes fluid retention at the kidneys. This increases the blood volume and blood pressure.
- Reduced perfusion (blood flow) to the kidneys stimulates the release of renin – an enzyme which catalyses the production of the potent vasopressor angiotensin. Angiotensin and its metabolites cause further vasocontriction, and stimulate increased secretion of the steroid aldosterone from the adrenal glands. This promotes salt and fluid retention at the kidneys, also increasing the blood volume.
- The chronically high levels of circulating neuroendocrine hormones such as catecholamines, renin, angiotensin, and aldosterone affects the myocardium directly, causing structural remodelling of the heart over the long term. Many of these remodelling effects seem to be mediated by transforming growth factor beta (TGF-beta), which is a common downstream target of the signal transduction cascade initiated by catecholamines and angiotensin II, and also by epidermal growth factor (EGF), which is a target of the signaling pathway activated by aldosterone
- Reduced perfusion of skeletal muscle causes atrophy of the muscle fibres. This can result in weakness, increased fatigueability and decreased peak strength - all contributing to exercise intolerance.

The increased peripheral resistance and greater blood volume place further strain on the heart and accelerates the process of damage to the myocardium. Vasoconstriction and fluid retention produce an increased hydrostatic pressure in the capillaries. This shifts the balance of forces in favour of interstitial fluid formation as the increased pressure forces additional fluid out of the blood, into the tissue. This results in edema (fluid build-up) in the tissues. In right-sided heart failure this commonly starts in the ankles where venous pressure is high due to the effects of gravity (although if the patient is bed-ridden, fluid accumulation may begin in the sacral region.) It may also occur in the abdominal cavity, where the fluid build-up is called ascites. In left-sided heart failure edema can occur in the lungs - this is called cardiogenic pulmonary edema. This reduces spare capacity for ventilation, causes stiffening of the lungs and reduces the efficiency of gas exchange by increasing the distance between the air and the blood. The consequences of this are shortness of breath, orthopnea and paroxysmal nocturnal dyspnea.

The symptoms of heart failure are largely determined by which side of the heart fails. The left side pumps blood into the systemic circulation, whilst the right side pumps blood into the pulmonary circulation. Whilst left-sided heart failure will reduce cardiac output to the systemic circulation, the initial symptoms often manifest due to effects on the pulmonary circulation. In systolic dysfunction, the ejection fraction is decreased, leaving an abnormally elevated volume of blood in the left ventricle. In diastolic dysfunction, end-diastolic ventricular pressure will be high. This increase in volume or pressure backs up to the left atrium and then to the pulmonary veins. Increased volume or pressure in the pulmonary veins impairs the normal drainage of the alveoli and favors the flow of fluid from the capillaries to the lung parenchyma, causing pulmonary edema. This impairs gas exchange. Thus, left-sided heart failure often presents with respiratory symptoms: shortness of breath, orthopnea and paroxysmal nocturnal dyspnea.

In severe cardiomyopathy, the effects of decreased cardiac output and poor perfusion become more apparent, and patients will manifest with cold and clammy extremities, cyanosis, claudication, generalized weakness, dizziness, and syncope

The resultant hypoxia caused by pulmonary edema causes vasoconstriction in the pulmonary circulation, which results in pulmonary hypertension. Since the right ventricle generates far lower pressures than the left ventricle (approximately 20 mmHg versus around 120 mmHg, respectively, in the healthy individual) but nonetheless generates cardiac output exactly equal to the left ventricle, this means that a small increase in pulmonary vascular resistance causes a large increase in amount of work the right ventricle must perform. However, the main mechanism by which left-sided heart failure causes right-sided heart failure is actually not well understood. Some theories invoke mechanisms that are mediated by neurohormonal activation. Mechanical effects may also contribute. As the left ventricle distends, the intraventricular septum bows into the right ventricle, decreasing the capacity of the right ventricle.

Systolic dysfunction

Heart failure caused by systolic dysfunction is more readily recognized. It can be simplistically described as failure of the pump function of the heart. It is characterized by a decreased ejection fraction (less than 45%). The strength of ventricular contraction is attenuated and inadequate for creating an adequate stroke volume, resulting in inadequate cardiac output. In general, this is caused by dysfunction or destruction of cardiac myocytes or their molecular components. In congenital diseases such as Duchenne muscular dystrophy, the molecular structure of individual myocytes is affected. Myocytes and their components can be damaged by inflammation (such as in myocarditis) or by infiltration (such as in amyloidosis). Toxins and pharmacological agents (such as ethanol, cocaine, and amphetamines) cause intracellular damage and oxidative stress. The most common mechanism of damage is ischemia causing infarction and scar formation. After myocardial infarction, dead myocytes are replaced by scar tissue, deleteriously affecting the function of the myocardium. On echocardiogram, this is manifest by abnormal or absent wall motion.

Because the ventricle is inadequately emptied, ventricular end-diastolic pressure and volumes increase. This is transmitted to the atrium. On the left side of the heart, the increased pressure is transmitted to the pulmonary vasculature, and the resultant hydrostatic pressure favors extravassation of fluid into the lung parenchyma, causing pulmonary edema. On the right side of the heart, the increased pressure is transmitted to the systemic venous circulation and systemic capillary beds, favoring extravassation of fluid into the tissues of target organs and extremities, resulting in dependent peripheral edema.

Diastolic dysfunction

Heart failure caused by diastolic dysfunction is generally described as the failure of the ventricle to adequately relax and typically denotes a stiffer ventricular wall. This causes

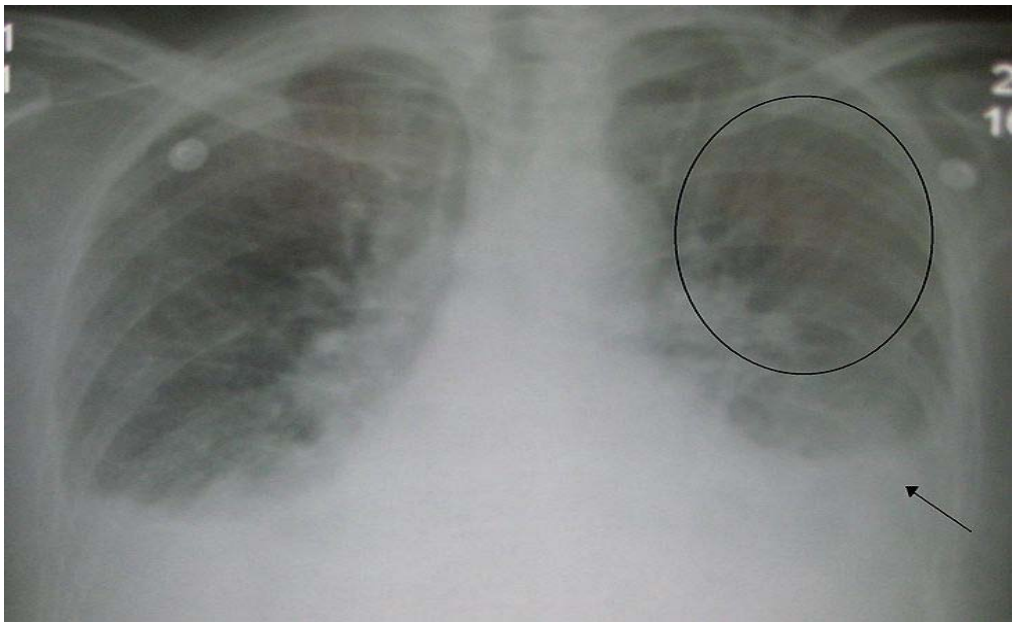
inadequate filling of the ventricle, and therefore results in an inadequate stroke volume. The failure of ventricular relaxation also results in elevated end-diastolic pressures, and the end result is identical to the case of systolic dysfunction (pulmonary edema in left heart failure, peripheral edema in right heart failure.)

Diastolic dysfunction can be caused by processes similar to those that cause systolic dysfunction, particularly causes that affect cardiac remodeling.

Diastolic dysfunction may not manifest itself except in physiologic extremes if systolic function is preserved. The patient may be completely asymptomatic at rest. However, they are exquisitely sensitive to increases in heart rate, and sudden bouts of tachycardia (which can be caused simply by physiological responses to exertion, fever, or dehydration, or by pathological tachyarrhythmias such as atrial fibrillation with rapid ventricular response) may result in flash pulmonary edema. Adequate rate control (usually with a pharmacological agent that slows down AV conduction such as a calcium channel blocker or a beta-blocker) is therefore key to preventing decompensation.

Left ventricular diastolic function can be determined through echocardiography by measurement of various parameters such as the E/A ratio (early-to-atrial left ventricular filling ratio), the E (early left ventricular filling) deceleration time, and the isovolumic relaxation time.

Diagnosis



Acute pulmonary edema. Note enlarged heart size, apical vascular redistribution (circle), and small bilateral pleural effusions (arrow).

No system of diagnostic criteria has been agreed as the gold standard for heart failure. Commonly used systems are the "Framingham criteria" (derived from the Framingham

Heart Study), the "Boston criteria", the "Duke criteria", and (in the setting of acute myocardial infarction) the "Killip class".

Imaging

Echocardiography is commonly used to support a clinical diagnosis of heart failure. This modality uses ultrasound to determine the stroke volume (SV, the amount of blood in the heart that exits the ventricles with each beat), the end-diastolic volume (EDV, the total amount of blood at the end of diastole), and the SV in proportion to the EDV, a value known as the *ejection fraction* (EF). In pediatrics, the shortening fraction is the preferred measure of systolic function. Normally, the EF should be between 50% and 70%; in systolic heart failure, it drops below 40%. Echocardiography can also identify valvular heart disease and assess the state of the pericardium (the connective tissue sac surrounding the heart). Echocardiography may also aid in deciding what treatments will help the patient, such as medication, insertion of an implantable cardioverter-defibrillator or cardiac resynchronization therapy. Echocardiography can also help determine if acute myocardial ischemia is the precipitating cause, and may manifest as regional wall motion abnormalities on echo.

Chest X-rays are frequently used to aid in the diagnosis of CHF. In the compensated patient, this may show cardiomegaly (visible enlargement of the heart), quantified as the *cardiothoracic ratio* (proportion of the heart size to the chest). In left ventricular failure, there may be evidence of vascular redistribution ("upper lobe blood diversion" or "cephalization"), Kerley lines, cuffing of the areas around the bronchi, and interstitial edema.

Electrophysiology

An electrocardiogram (ECG/EKG) may be used to identify arrhythmias, ischemic heart disease, right and left ventricular hypertrophy, and presence of conduction delay or abnormalities (e.g. left bundle branch block). Although these findings are not specific to the diagnosis of heart failure a normal ECG virtually excludes left ventricular systolic dysfunction.

Blood tests

Blood tests routinely performed include electrolytes (sodium, potassium), measures of renal function, liver function tests, thyroid function tests, a complete blood count, and often C-reactive protein if infection is suspected. An elevated B-type natriuretic peptide (BNP) is a specific test indicative of heart failure. Additionally, BNP can be used to differentiate between causes of dyspnea due to heart failure from other causes of dyspnea. If myocardial infarction is suspected, various cardiac markers may be used.

According to a meta-analysis comparing BNP and N-terminal pro-BNP (NTproBNP) in the diagnosis of heart failure, BNP is a better indicator for heart failure and left ventricular systolic dysfunction. In groups of symptomatic patients, a diagnostic odds

ratio of 27 for BNP compares with a sensitivity of 85% and specificity of 84% in detecting heart failure.

Angiography

Heart failure may be the result of coronary artery disease, and its prognosis depends in part on the ability of the coronary arteries to supply blood to the myocardium (heart muscle). As a result, coronary catheterization may be used to identify possibilities for revascularisation through percutaneous coronary intervention or bypass surgery.

Monitoring

Various measures are often used to assess the progress of patients being treated for heart failure. These include fluid balance (calculation of fluid intake and excretion), monitoring body weight (which in the shorter term reflects fluid shifts).

Algorithms

There are various algorithms for the diagnosis of heart failure. For example, the algorithm used by the Framingham Heart Study adds together criteria mainly from physical examination. In contrast, the more extensive algorithm by the European Society of Cardiology (ESC) weights the difference between supporting and opposing parameters from the medical history, physical examination, further medical tests as well as response to therapy.

Framingham criteria

By the Framingham criteria, diagnosis of congestive heart failure (heart failure with impaired pumping capability) requires the simultaneous presence of at least 2 of the following major criteria or 1 major criterion in conjunction with 2 of the following minor criteria:

Major criteria:

- Cardiomegaly on chest radiography
- S3 gallop (a third heart sound)
- Acute pulmonary edema
- Paroxysmal nocturnal dyspnea
- Crackles on lung auscultation
- Central venous pressure of more than 16 cm H2O at the right atrium
- Jugular vein distension
- Positive abdominojugular test
- Weight loss of more than 4.5 kg in 5 days in response to treatment (sometimes classified as a minor criterium)

Minor criteria:

- Tachycardia of more than 120 beats per minute
- Nocturnal cough
- Dyspnea on ordinary exertion
- Pleural effusion
- Decrease in vital capacity by one third from maximum recorded
- Hepatomegaly
- Bilateral ankle edema

Minor criteria are acceptable only if they can not be attributed to another medical condition such as pulmonary hypertension, chronic lung disease, cirrhosis, ascites, or the nephrotic syndrome. The Framingham Heart Study criteria are 100% sensitive and 78% specific for identifying persons with definite congestive heart failure.

ESC algorithm

The ESC algorithm weights the following parameters in establishing the diagnosis of heart failure:

Parameter	Influence + - to some degree ++ - to intermediate degree +++ - to high degree	Supports if present	Opposes if normal or absent
Compatible symptoms		++	++
Compatible signs		++	+
Cardiac dysfunction on echocardiography		+++	+++
Response of symptoms or signs to therapy		+++	++
ECG			
Normal			++
Abnormal		++	+
Dysrhythmia		+++	+
Laboratory			
BNP > 400 pg/mL and/or NT-proBNP > 2000 pg/mL		+++	+
BNP < 100 pg/mL and NT-proBNP < 400 pg/mL		+	+++
Hyponatraemia		+	+
Renal dysfunction		+	+
Mild elevations of troponin		+	+

		Chest X-ray
Pulmonary congestion	+++	+
Reduced exercise capacity	+++	++
Abnormal pulmonary function tests	+	+
Abnormal haemodynamics at rest	+++	++

Management

Treatment focuses on improving the symptoms and preventing the progression of the disease. Reversible causes of the heart failure also need to be addressed: (e.g. infection, alcohol ingestion, anemia, thyrotoxicosis, arrhythmia, hypertension). Treatments include lifestyle and pharmacological modalities.

Acute decompensation

In acute decompensated heart failure (ADHF), the immediate goal is to re-establish adequate perfusion and oxygen delivery to end organs. This entails ensuring that airway, breathing, and circulation are adequate. Immediated treatments usually involve some combination of vasodilators such as nitroglycerin, diuretics such as furosemide, and possibly non invasive positive pressure ventilation (NIPPV).

Chronic management

The goal is to prevent the development of acute decompensated heart failure, to counteract the deleterious effects of cardiac remodeling, and to minimize the symptoms that the patient suffers. First-line therapy for all heart failure patients is angiotensin-converting enzyme (ACE) inhibition. ACE inhibitors (i.e., enalapril, captopril, lisinopril, ramipril) improve survival and quality of life in heart failure patients, and have been shown to reduce mortality in patients with left ventricular dysfunction in numerous randomized trials. In addition to pharmacologic agents (oral loop diuretics, beta-blockers, ACE inhibitors or angiotensin receptor blockers, vasodilators, and in severe cardiomyopathy aldosterone receptor antagonists), behavioral modification should be pursued, specifically with regards to dietary guidelines regarding salt and fluid intake. Exercise should be encouraged as tolerated, as sufficient conditioning can significantly improve quality-of-life.

In patients with severe cardiomyopathy, implantation of an automatic implantable cardioverter defibrillator (AICD) should be considered. A select population will also probably benefit from ventricular resynchronization.

In select cases, cardiac transplantation can be considered. While this may resolve the problems associated with heart failure, the patient generally must remain on an immunosuppressive regimen to prevent rejection, which has its own significant downsides.

Palliative care and hospice

Without transplantation, heart failure caused by ischemic heart disease is not reversible, and cardiac function typically deteriorates with time. (In particular, diastolic function worsens as a function of age even in individuals without ischemic heart disease.) The growing number of patients with Stage D heart failure (intractable symptoms of fatigue, shortness of breath or chest pain at rest despite optimal medical therapy) should be considered for palliative care or hospice, according to American College of Cardiology/American Heart Association guidelines.

Prognosis

Prognosis in heart failure can be assessed in multiple ways including clinical prediction rules and cardiopulmonary exercise testing. Clinical prediction rules use a composite of clinical factors such as lab tests and blood pressure to estimate prognosis. Among several clinical prediction rules for prognosing acute heart failure, the 'EFFECT rule' slightly outperformed other rules in stratifying patients and identifying those at low risk of death during hospitalization or within 30 days. Easy methods for identifying low risk patients are:

- ADHERE Tree rule indicates that patients with blood urea nitrogen < 43 mg/dl and systolic blood pressure at least 115 mm Hg have less than 10% chance of inpatient death or complications.
- BWH rule indicates that patients with systolic blood pressure over 90 mm Hg, respiratory rate of 30 or less breaths per minute, serum sodium over 135 mmol/L, no new ST-T wave changes have less than 10% chance of inpatient death or complications.

A very important method for assessing prognosis in advanced heart failure patients is cardiopulmonary exercise testing (CPX testing). CPX testing is usually required prior to heart transplantation as an indicator of prognosis. Cardiopulmonary exercise testing involves measurement of exhaled oxygen and carbon dioxide during exercise. The peak oxygen consumption (VO2 max) is used as an indicator of prognosis. As a general rule, a VO2 max less than 12-14 cc/kg/min indicates a poor survival and suggests that the patient may be a candidate for a heart transplant. Patients with a VO2 max<10 cc/kg/min have clearly poorer prognosis. The most recent International Society for Heart and Lung Transplantation (ISHLT) guidelines also suggest two other parameters that can be used for evaluation of prognosis in advanced heart failure, the heart failure survival score and the use of a criterion of VE/VCO2 slope > 35 from the CPX test. The heart failure survival score is a score calculated using a combination of clinical predictors and the VO2 max from the cardiopulmonary exercise test.

Epidemiology

Heart failure is the leading cause of hospitalization in people older than 65. In developed countries, the mean age of patients with heart failure is 75 years old. In developing

countries, two to three percent of the population suffers from heart failure, but in those 70 to 80 years old, it occurs in 20—30 percent.

Heart failure affects close to 5 million people in the USA and each year close to 500,000 new cases are diagnosed. What is of more concern is that more than 50% of patients seek re-admission within 6 months after treatment and the average duration of hospital stay is 6 days.

In tropical countries, the most common cause of HF is valvular heart disease or some type of cardiomyopathy. Moreover as underdeveloped countries become more affluent, there has also been an increase in diabetes, hypertension and obesity which has resulted in heart failure.

In USA, HF is much higher in African Americans, Hispanics, Native Americans and recent immigrants from the eastern bloc countries like Russia. This high prevalence in these ethnic populations has been linked to high incidence of diabetes and hypertension. In many new immigrants to the USA the high prevalence of heart failure has largely been attributed to lack of preventive health care or substandard treatment.

Gender

Both men and women have similar incidence of HF. However, there are distinct differences between the two genders.

- Women generally develop heart failure after menopause.
- Women tend to become more depressed than men following diagnosis.
- Women have similar symptoms but the intensity is more pronounced.
- Women usually survive a lot longer with heart failure than men.

Race

New information suggests that elements of heart failure in African Americans and Caucasians may be different and therapy for heart failure has different efficacies depending on racial, ethnic, and genetic backgrounds.

Age

Heart failure basically means that the heart muscles have become weak and do not function as normal. Heart failure is a progressive medical disorder. As the heart gets weaker, symptoms and signs become prominent. Heart failure can affect the entire heart or only the right or left side. In the majority of cases, both sides of the heart are affected. HF can occur at any age depending on the cause. In general heart failure does increase with age.

Chapter 6

Cardiac Pacemaker

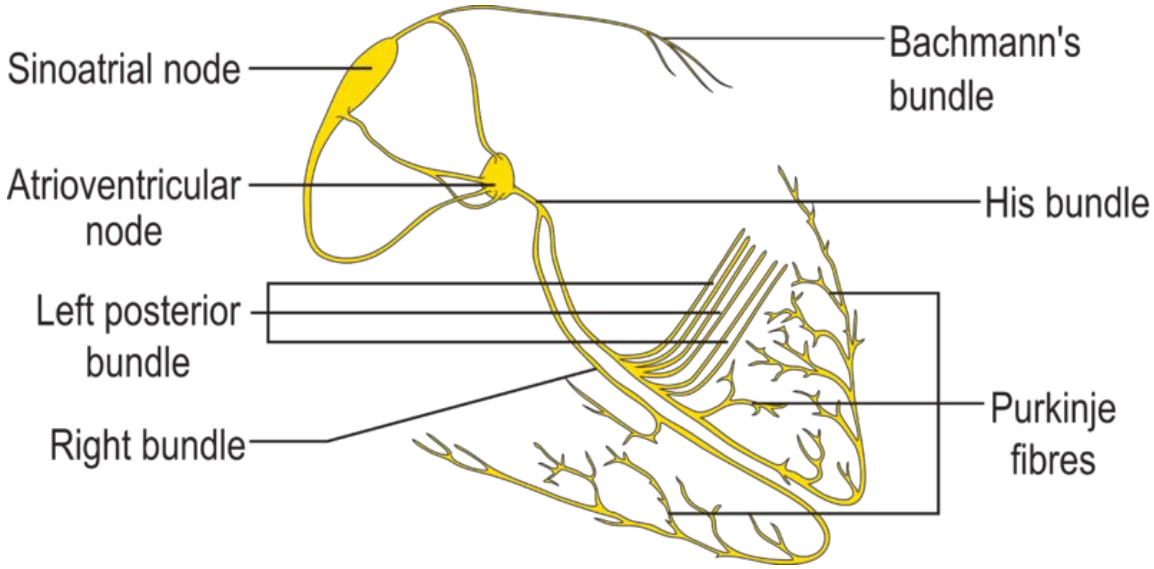
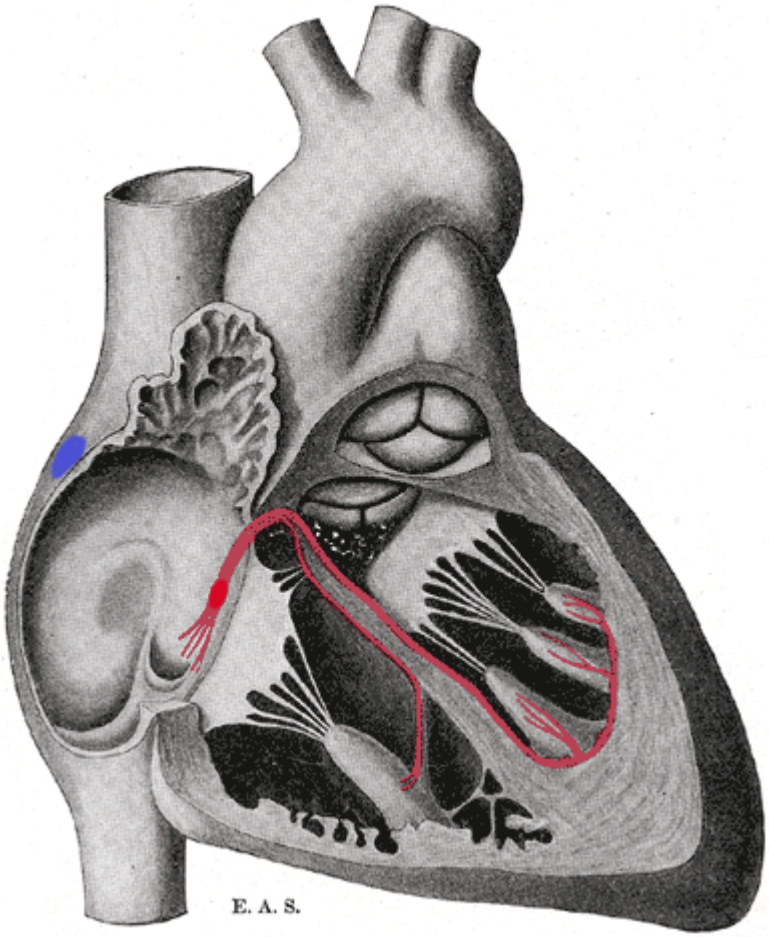


Image showing the cardiac pacemaker which is the SA node

The contraction of heart (cardiac) muscle in all animals with hearts is initiated by chemical impulses. The rate at which these impulses fire controls the heart rate. The cells that create these rhythmical impulses are called **pacemaker** cells, and they directly control the heart rate.

In humans, and occasionally in other animals, a mechanical device called an artificial pacemaker (or simply "pacemaker") may be used after damage to the body's intrinsic conduction system to produce these impulses synthetically.

Control



Schematic representation of the sinoatrial node and the atrioventricular bundle of His. The location of the SA node is shown in blue. The bundle, represented in red, originates near the orifice of the coronary sinus, undergoes slight enlargement to form the AV node. The AV node tapers down into the bundle of HIS, which passes into the ventricular septum and divides into two bundle branches, the left and right bundles. The ultimate distribution cannot be completely shown in this diagram.

Primary (SA node)

1% of the Cardiomyocytes in the myocaridum possess the ability to generate electrical impulses (or action potentials).
A specialized portion of the heart, called the sinoatrial node, is responsible for atrial propagation of this potential.

The **sinoatrial node** (**SA node**) is a group of cells positioned on the wall of the right atrium, near the entrance of the superior vena cava. These cells are modified cardiomyocytes. They possess rudimentary contractile filaments, but contract relatively weakly.

Cells in the SA node spontaneously depolarize, resulting in contraction, approximately 100 times per minute. This native rate is constantly modified by the activity of sympathetic and parasympathetic nerve fibers, so that the average resting cardiac rate in adult humans is about 70 beats per minute. Because the sinoatrial node is responsible for the rest of the heart's electrical activity, it is sometimes called the *primary pacemaker*.

Secondary (AV junction)

If the SA node does not function, a group of cells further down the heart will become the heart's pacemaker, this is known as an ectopic pacemaker. These cells form the **atrioventricular node** (**AV node**), which is an area between the left atria and the right ventricles, within the atrial septum.

The cells of the AV node normally discharge at about 40-60 beats per minute, and are called the *secondary pacemaker*.

Further down the electrical conducting system of the heart is the Bundle of His. The left and right branches of this bundle, and the Purkinje fibres, will also produce a spontaneous action potential at a rate of 30-40 beats per minute, if the SA and AV node both do not function. The reason the SA node controls the whole heart is that its action potentials are released most often to the heart's muscle cells; this will produce contraction. The action potential generated by the SA node passes down the cardiac conduction system, and arrives before the other cells have had a chance to generate their own spontaneous action potential. This is the electrical conduction system of the heart|normal conduction of electrical activity within the heart.

Generation of action potentials

There are three main stages in the generation of an action potential in a pacemaker cell. Since the stages are analogous to contraction of cardiac muscle cells, they have the same naming system. This can lead to some confusion. There is no phase one or two, just phases zero, three and four.

Phase 4 - Pacemaker potential

The key to the rhythmic firing of pacemaker cells is that, unlike muscle and neurons, these cells will slowly depolarize by themselves.

As in all other cells, the resting potential of a pacemaker cell (-60mV to -70mV) is caused by a continuous outflow or "leak" of potassium ions through ion channel proteins in the membrane that surrounds the cells. The difference is that this potassium permeability decreases as time goes on, partly causing the slow depolarization. As well as this, there is a slow inward flow of sodium, called the funny current, as well as an inward flow of calcium. This all serves to make the cell more positive.

This relatively slow depolarization continues until the *threshold potential* is reached. Threshold is between -40mV and -50mV. When threshold is reached, the cells enter phase 0.

Phase 0 - Upstroke

Though much faster than the depolarization caused by the *funny current* and decrease in potassium permeability above, the upstroke in a pacemaker cell is slow compared to that in an axon.

The SA and AV node do not have fast sodium channels like neurons, and the depolarization is mainly caused by a slow influx of calcium ions. (The funny current also increases). The calcium is let into the cell by voltage-sensitive calcium channels that open when the threshold is reached.

Phase 3 - Repolarization

The calcium channels are rapidly inactivated, soon after they open. Sodium permeability is also decreased. Potassium permeability is increased, and the efflux of potassium (loss of positive ions) slowly repolarises the cell.

Chapter 7

Heart Rate

Heart rate is the number of heartbeats per unit of time - typically expressed as beats per minute (bpm) - which can vary as the body's need to absorb oxygen and excrete carbon dioxide changes, such as during exercise or sleep. The measurement of heart rate is used by medical professionals to assist in the diagnosis and tracking of medical conditions. It is also used by individuals, such as athletes, who are interested in monitoring their heart rate to gain maximum efficiency from their training. The **R wave to R wave interval** (**RR interval**) is the inverse of the heart rate.

Heart rate is measured by finding the pulse of the body. This pulse rate can be measured at any point on the body where an artery's pulsation is transmitted to the surface - often as it is compressed against an underlying structure like bone - by pressuring it with the index and middle finger. The thumb should not be used for measuring another person's heart rate, as its strong pulse may interfere with discriminating the site of pulsation.

Possible points for measuring the heart rate are:

1. The ventral aspect of the wrist on the side of the thumb (radial artery).
2. The ulnar artery.
3. The neck (carotid artery).
4. The inside of the elbow, or under the biceps muscle (brachial artery).
5. The groin (femoral artery).
6. Behind the medial malleolus on the feet (posterior tibial artery).
7. Middle of dorsum of the foot (dorsalis pedis).
8. Behind the knee (popliteal artery).
9. Over the abdomen (abdominal aorta).
10. The chest (apex of heart), which can be felt with one's hand or fingers. However, it is possible to auscultate the heart using a stethoscope.
11. The temple (Superficial Temporal Artery)
12. The lateral edge of the Mandible Facial artery.

A more precise method of determining pulse involves the use of an electrocardiograph, or ECG (also abbreviated EKG). Continuous electrocardiograph monitoring of the heart is routinely done in many clinical settings, especially in critical care medicine. Commercial heart rate monitors are also available, consisting of a chest strap with electrodes. The signal is transmitted to a wrist receiver for display. Heart rate monitors allow accurate

measurements to be taken continuously and can be used during exercise when manual measurement would be difficult or impossible (such as when the hands are being used).

Resting heart rate

Resting heart rate (HR_{rest}) is a person's heart rate when they are at rest: awake but lying down, and not having immediately exerted themselves. Typical healthy resting heart rate in adults is 60–80 bpm, with rates below 60 bpm referred to as bradycardia and rates above 100 bpm referred to as tachycardia. Note however that conditioned athletes often have resting heart rates below 60 bpm. Cyclist Lance Armstrong had a resting HR around 32 bpm, and it is not unusual for people doing regular exercise to get below 50 bpm. Other cyclists like Miguel Indurain and Alberto Contador have reported resting heart rates in the mid-20s, with American marathoner Ryan Hall at 29.

Musical tempo terms reflect levels relative to resting heart rate; *Adagio* (at ease, at rest) is typically 66–76 bpm, similar to human resting heart rate, while *Lento* and *Largo* ("Slow") are 40–60 bpm, which reflects that these tempi are slow relative to normal human heart rate. Similarly, faster tempi correspond to heart rates at higher levels of exertion, such as *Andante* (walking: 76–108 bpm) and the like.

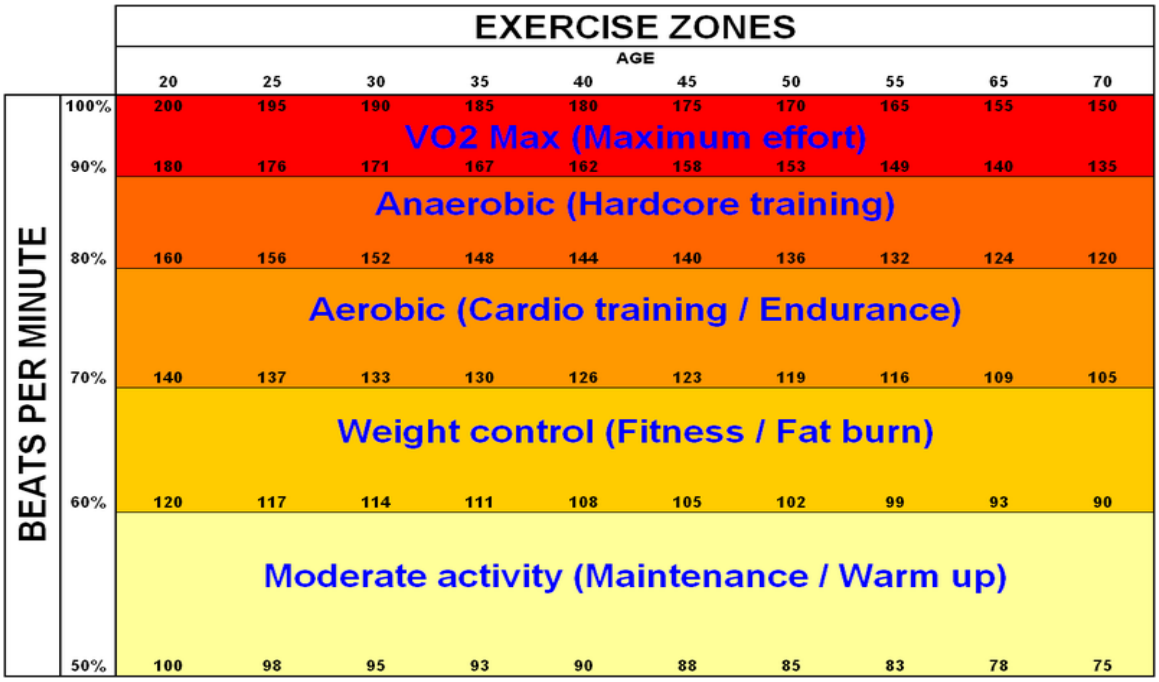
Measuring HR_{max}

HR_{max} is the maximal heart rate an individual can achieve by exercise stress, and depends on age. The most accurate way of measuring HR_{max} is via a cardiac stress test. In such a test, the subject exercises while being monitored by an EKG. During the test, the intensity of exercise is periodically increased (if a treadmill is being used, through increase in speed or slope of the treadmill), continuing until certain changes in heart function are detected in the EKG, at which point the subject is directed to stop. Typical durations of such a test range from 10 to 20 minutes.

Standard textbooks of physiology and medicine mention that heart rate (HR) is readily calculated from the ECG as follows: HR = 1,500/RR interval in millimeters, HR = 60/RR interval in seconds, or HR = 300/number of large squares between successive R waves. In each case, the authors are actually referring to instantaneous HR, which is the number of times the heart would beat if successive RR intervals were constant.

Conducting a maximal exercise test can require expensive equipment. People just beginning an exercise regimen are normally advised to perform this test only in the presence of medical staff due to risks associated with high heart rates. For general purposes, people instead typically use a formula to estimate their individual Maximum Heart Rate.

Formula for HR_{max}



Fox and Haskell formula; widely used

Various formulas are used to estimate individual Maximum Heart Rates, based on age, but maximum heart rates vary significantly between individuals. Even within a single elite sports team, such as Olympic rowers in their 20s, maximum heart rates can vary from 160 to 220. This variation is as large as a 60 or 90 year age gap by the linear equations given below, and indicates the extreme variation about these average figures.

The most common formula encountered, with no indication of standard deviation, is:

$$HR_{max} = 220 - \text{age}$$

This formula has been attributed to various sources, but is widely thought to have been devised in 1970 by Dr. William Haskell and Dr. Samuel Fox. Inquiry into the history of this formula reveals that it was not developed from original research, but resulted from observation based on data from approximately 11 references consisting of published research or unpublished scientific compilations. It gained widespread use through being used by Polar Electro in its heart rate monitors, which Dr. Haskell has "laughed about", as it "was never supposed to be an absolute guide to rule people's training."

While the most common (and easy to remember and calculate), this particular formula is not considered by reputable health and fitness professionals to be a good predictor of HR_{max}. Despite the widespread publication of this formula, research spanning two decades reveals its large inherent error (Sxy=7–11 b/min). Consequently, the estimation calculated by HR_{max}=220−age has neither the accuracy nor the scientific merit for use in exercise physiology and related fields.

A 2002 study of 43 different formulae for HR_{max} (including the one above) concluded the following:

> 1) No "acceptable" formula currently existed, (they used the term "acceptable" to mean acceptable for both prediction of V_{O_2max}, and prescription of exercise training HR ranges)
> 2) The formula deemed least objectionable was:
> $HR_{max} = 205.8 - (0.685 \times age)$
> This was found to have a standard deviation that, although large (6.4 bpm), was still considered to be acceptable for the use of prescribing exercise training HR ranges.

Other often cited formulae are:

> $HR_{max} = 206.3 - (0.711 \times age)$
> (Often attributed to "Londeree and Moeschberger from the University of Missouri")
> $HR_{max} = 217 - (0.85 \times age)$
> (Often attributed to "Miller et al. from Indiana University")
> $HR_{max} = 208 - (0.7 \times age)$
> (Another "tweak" to the traditional formula is known as the Tanaka method. Based on a study of thousands of individuals, a new formula was devised which is believed to be more accurate).

In 2007, researchers at the Oakland University analysed maximum heart rates of 132 individuals recorded yearly over 25 years, and produced a linear equation very similar to the Tanaka formula—$HR_{max} = 206.9 - (0.67 \times age)$—and a nonlinear equations—$HR_{max} = 191.5 - (0.007 \times age^2)$. The linear equation had a confidence interval of ±5–8 bpm and the nonlinear equation had a tighter range of ±2–5 bpm. Also a third nonlinear equation was produced — $HR_{max} = 163 + (1.16 \times age) - (0.018 \times age^2)$.

These figures are very much averages, and depend greatly on individual physiology and fitness. For example an endurance runner's rates will typically be lower due to the increased size of the heart required to support the exercise, while a sprinter's rates will be higher due to the improved response time and short duration, etc. may each have predicted heart rates of 180 (= 220−Age), but these two people could have actual Max HR 20 beats apart (e.g. 170–190).

Further, note that individuals of the same age, the same training, in the same sport, on the same team, can have actual Max HR 60 bpm apart (160 to 220): the range is extremely broad, and some say "The heart rate is probably the least important variable in comparing athletes."

The 2010 research conducted at Northwestern University revised maximum heart rate formula for women. According to Martha Gulati et al. it is:

$$HR_{max} = 206 - (0.88 \times age)$$

A study from Lund, Sweden gives reference values (obtained during bicycle ergometry) for men

$$HR_{max} = 203.7 / (1 + \exp(0.033 \times (age - 104.3)))$$

and for women

$$HR_{max} = 190.2/(1 + \exp(0.0453 * (Age - 107.5)))$$

Target heart rate

The Target Heart Rate (THR), or Training Heart Rate, is a desired range of heart rate reached during aerobic exercise which enables one's heart and lungs to receive the most benefit from a workout. This theoretical range varies based on one's physical condition, gender, and previous training. Below are two ways to calculate one's Target Heart Rate. In each of these methods, there is an element called "intensity" which is expressed as a percentage. The THR can be calculated as a range of 65%–85% intensity. However, it is crucial to derive an accurate HR_{max} to ensure these calculations are meaningful (see above).

Example for someone with a HR_{max} of 180 (age 40, estimating HR_{max} as 220 − age):
65% intensity: (220 − (age = 40)) × 0.65 → 117 bpm
85% intensity: (220 − (age = 40)) × 0.85 → 153 bpm

Karvonen method

The Karvonen method factors in Resting Heart Rate (HR_{rest}) to calculate Target Heart Rate (THR), using a range of 50%–85%:

$$THR = ((HR_{max} - HR_{rest}) \times \%Intensity) + HR_{rest}$$

Example for someone with a HR_{max} of 180 and a HR_{rest} of 70:
50% intensity: ((180 − 70) × 0.50) + 70 = 125 bpm
85% intensity: ((180 − 70) × 0.85) + 70 = 163 bpm

Zoladz method

An alternative to the Karvonen method is the Zoladz method, which derives exercise zones by subtracting values from HR_{max}.

$THR = HR_{max} - Adjuster \pm 5$ bpm
Zone 1 Adjuster = 50 bpm
Zone 2 Adjuster = 40 bpm
Zone 3 Adjuster = 30 bpm

Zone 4 Adjuster = 20 bpm
Zone 5 Adjuster = 10 bpm

Example for someone with a HR_{max} of 180:
Zone 1 (easy exercise) : $180 - 50 \pm 5 \rightarrow 125 – 135$ bpm
Zone 4 (tough exercise): $180 - 20 \pm 5 \rightarrow 155 – 165$ bpm

Heart rate reserve

Heart rate reserve (HRR) is a term used to describe the difference between a person's measured or predicted maximum heart rate and resting heart rate. Some methods of measurement of exercise intensity measure percentage of heart rate reserve. Additionally, as a person increases their cardiovascular fitness, their HR_{rest} will drop, thus the heart rate reserve will increase. Percentage of HRR is equivalent to percentage of VO_2 reserve.

$$HRR = HR_{max} - HR_{rest}$$

Recovery heart rate

This is the heart rate measured at a fixed (or reference) period after ceasing activity; typically measured over a 1 minute period.

A slow reduction in the heart rate after exercise may indicate heart problems. If the heart rate has dropped by less than 12 bpm one minute after stopping exercise this may indicate an increased risk of heart attack.

Training regimes sometimes use recovery heart rate as a guide of progress and to spot problems such as overheating or dehydration. After even short periods of hard exercise it can take a long time (about 30 minutes) for the heart rate to drop to rested levels.

Heart rate abnormalities

Tachycardia

Tachycardia is a resting heart rate more than 100 beats per minute. This number can vary as smaller people and children have faster heart rates than average adults.

Bradycardia

Bradycardia is defined as a heart rate less than 60 beats per minute although it is seldom symptomatic until below 50 bpm when a human is at total rest. Trained athletes tend to have slow resting heart rates, and resting bradycardia in athletes should not be considered abnormal if the individual has no symptoms associated with it. Again, this number can vary as children and small adults tend to have faster heart rates than average adults.

Miguel Indurain, a Spanish cyclist and five time Tour de France winner, had a resting heart rate of 28 beats per minute, one of the lowest ever recorded in a healthy human.

Arrhythmia

Arrhythmias are abnormalities of the heart rate and rhythm (sometimes felt as palpitations). They can be divided into two broad categories: fast and slow heart rates. Some cause few or minimal symptoms. Others produce more serious symptoms of lightheadedness, dizziness and fainting.

Ventricular assist device

A body with a ventricular assist device, or VAD, installed as an aid to a failing heart has no heart beat or pulse and therefore no heart rate, because a VAD is a continuous flow pump.

Heart rate as a risk factor

A number of investigations indicate that faster resting heart rate has emerged as a new risk factor for mortality in homeothermic mammals, particularly cardiovascular mortality in human beings. Faster heart rate may accompany increased production of inflammation molecules and increased production of reactive oxygen species in cardiovascular system, in addition to increased mechanical stress to the heart. There is a correlation between increased resting rate and cardiovascular risk. This is not seen to be 'using an allotment of heart beats' but rather an increased risk to the system from the increased rate.

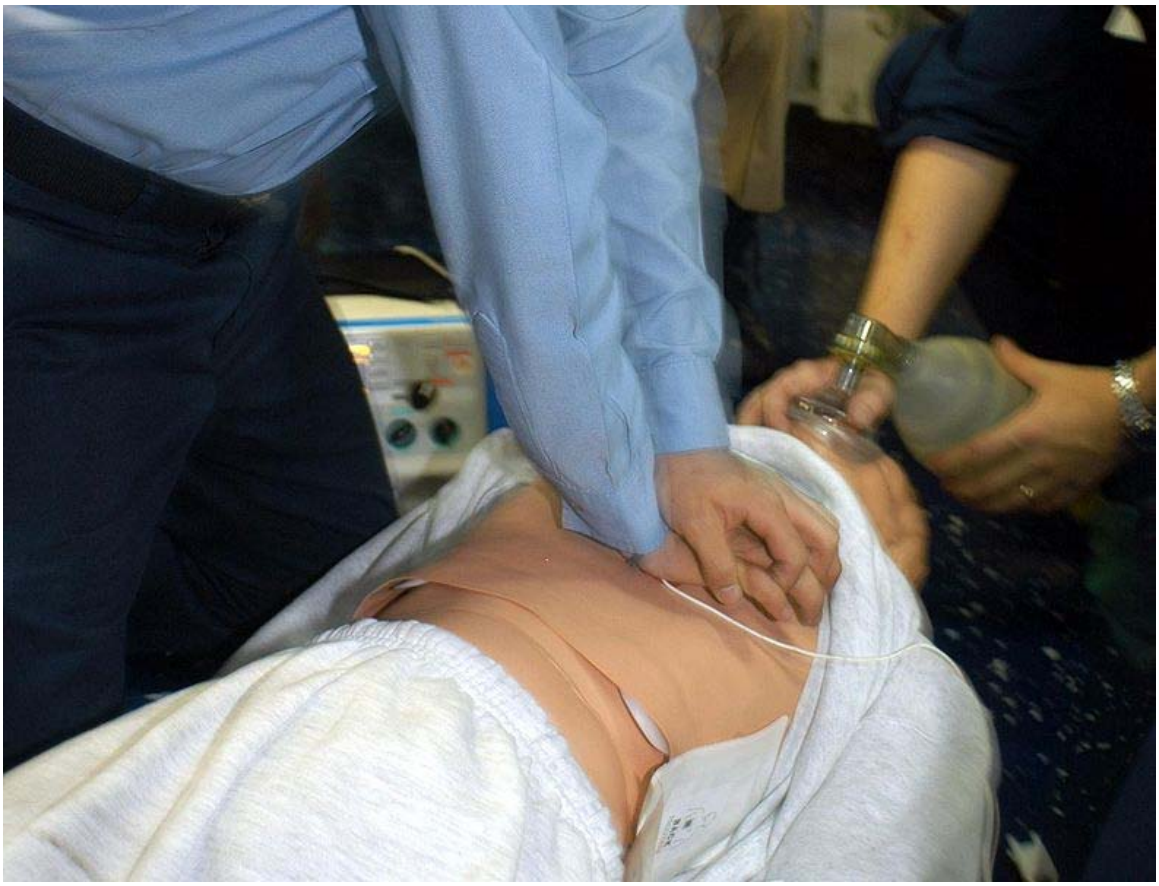
An Australian-led international study of patients with cardiovascular disease has shown that heart beat rate is a key indicator for the risk of heart attack. The study, published in The Lancet (September 2008) studied 11,000 people, across 33 countries, who were being treated for heart problems. Those patients whose heart rate was above 70 beats per minute had significantly higher incidence of heart attacks, hospital admissions and the need for surgery. University of Sydney professor of cardiology Ben Freedman from Sydney's Concord hospital, said "If you have a high heart rate there was an increase in heart attack, there was about a 46 percent increase in hospitalizations for non-fatal or fatal heart attack."

Standard textbooks of physiology and medicine mention that heart rate (HR) is readily calculated from the ECG as follows:

HR = 1,500/RR interval in millimeters, HR = 60/RR interval in seconds, or HR = 300/number of large squares between successive R waves. In each case, the authors are actually referring to instantaneous HR, which is the number of times the heart would beat if successive RR intervals were constant. However, because the above formula is almost always mentioned, students determine HR this way without looking at the ECG any further.

Chapter 8

Cardiac Arrest



CPR being administered during a simulation of cardiac arrest

Cardiac arrest, (also known as **cardiopulmonary arrest** or **circulatory arrest**) is the cessation of normal circulation of the blood due to failure of the heart to contract effectively. Medical personnel can refer to an unexpected cardiac arrest as a **sudden cardiac arrest** or **SCA**.

A cardiac arrest is different from (but may be caused by) a heart attack, where blood flow to the muscle of the heart is impaired.

Arrested blood circulation prevents delivery of oxygen to the body. Lack of oxygen to the brain causes loss of consciousness, which then results in abnormal or absent breathing. Brain injury is likely if cardiac arrest goes untreated for more than five minutes. For the best chance of survival and neurological recovery, immediate and decisive treatment is imperative.

Cardiac arrest is a medical emergency that, in certain situations, is potentially reversible if treated early. When unexpected cardiac arrest leads to death this is called sudden cardiac death (SCD). The treatment for cardiac arrest is cardiopulmonary resuscitation (CPR) to provide circulatory support, followed by defibrillation if a shockable rhythm is present. If a shockable rhythm is not present after CPR and other interventions, clinical death is inevitable.

Classification

Cardiac arrest is classified into "shockable" versus "non–shockable", based upon the ECG rhythm. The two shockable rhythms are ventricular fibrillation and pulseless ventricular tachycardia while the two non–shockable rhythms are asystole and pulseless electrical activity. This refers to whether a particular class of disrhythmia is treatable using defibrillation.

Signs and symptoms

Cardiac arrest is an abrupt cessation of pump function in the heart (as evidenced by the absence of a palpable pulse). Prompt intervention can usually reverse a cardiac arrest, but without such intervention it will almost always lead to death. In certain cases, it is an expected outcome to a serious illness.

However, due to inadequate cerebral perfusion, the patient will be unconscious and will have stopped breathing. The main diagnostic criterion to diagnose a cardiac arrest, (as opposed to respiratory arrest which shares many of the same features), is lack of circulation, however there are a number of ways of determining this.

Causes

Coronary heart disease is the leading cause of sudden cardiac arrest. Many other cardiac and non–cardiac conditions also increase ones risk.

Coronary heart disease

Approximately 60–70% of SCD is related to coronary heart disease. Among adults, ischemic heart disease is the predominant cause of arrest with 30% of people at autopsy showing signs of recent myocardial infarction.

Non ischemic heart disease

A number of other cardiac abnormalities can increase the risk of SCD including: cardiomyopathy, cardiac rhythm disturbances, hypertensive heart disease, congestive heart failure.

In a group of military recruits aged 18–35, cardiac anomalies accounted for 51% of cases of SCD, while in 35% of cases the cause remained unknown. Underlying pathology included: coronary artery abnormalities (61%), myocarditis (20%), and hypertrophic cardiomyopathy (13%). Congestive heart failure increases the risk of SCD by 5 fold.

Non–cardiac

SCDs is unrelated to heart problems in 35% of cases. The most common non–cardiac causes were: trauma, non-trauma related bleeding (such as gastrointestinal bleeding, aortic rupture, and intracranial hemorrhage), overdose, drowning and pulmonary embolism.

Risk factors

The risk factors for SCD are similar to those seen with coronary heart disease including: smoking, lack of physical exercise, obesity, diabetes, and family history.

Hs and Ts

The Hs and Ts is a mnemonic used to aid in remembering the possible causes of cardiac arrest.

Hs

- **H**ypovolemia - A lack of blood volume
- **H**ypoxia - A lack of oxygen
- **H**ydrogen ions (Acidosis) - An abnormal pH in the body
- **H**yperkalemia or **H**ypokalemia - Both excess and inadequate potassium can be life-threatening.
- **H**ypothermia - A low core body temperature
- **H**ypoglycemia or **H**yperglycemia - Low or high blood glucose

Ts

- **T**ablets or **T**oxins
- Cardiac **T**amponade - Fluid building around the heart
- **T**ension pneumothorax - A collapsed lung
- **T**hrombosis (Myocardial infarction) - Heart attack
- **T**hromboembolism (Pulmonary embolism) - A blood clot in the lung
- **T**rauma

Diagnosis

Checking for breathing

Checking carotid pulse

Cardiac arrest is synonymous with clinical death.

A cardiac arrest is usually diagnosed clinically by the absence of a pulse. In many cases lack of carotid pulse is the gold standard for diagnosing cardiac arrest, but lack of a pulse (particularly in the peripheral pulses) may be a result of other conditions (e.g. shock), or simply an error on the part of the rescuer. Studies have shown that rescuers often make a mistake when checking the carotid pulse in an emergency, whether they are healthcare professionals or lay persons.

Owing to the inaccuracy in this method of diagnosis, some bodies such as the European Resuscitation Council (ERC) have de-emphasised its importance. The Resuscitation Council (UK), in line with the ERC's recommendations and those of the American Heart Association, have suggested that the technique should be used only by healthcare professionals with specific training and expertise, and even then that it should be viewed in conjunction with other indicators such as agonal respiration.

Various other methods for detecting circulation have been proposed. Guidelines following the 2000 International Liaison Committee on Resuscitation (ILCOR) recommendations were for rescuers to look for "signs of circulation", but not specifically the pulse. These signs included coughing, gasping, colour, twitching and movement. However, in face of evidence that these guidelines were ineffective, the current recommendation of ILCOR is that cardiac arrest should be diagnosed in all casualties who are unconscious and not breathing normally.

Prevention

With positive outcomes following cardiac arrest unlikely, an effort has been spent in finding effective strategies to prevent cardiac arrest. With the prime causes of cardiac arrest being ischemic heart disease, efforts to promote a healthy diet, exercise, and smoking cessation are important. For people at risk of heart disease, measures such as blood pressure control, cholesterol lowering, and other medico-therapeutic interventions are used.

Code teams

In medical parlance, cardiac arrest is referred to as a "code" or a "crash". This typically refers to "code blue" on the hospital emergency codes. A dramatic drop in vital sign measurements is referred to as "coding" or "crashing", though coding is usually used when it results in cardiac arrest, while crashing might not. Treatment for cardiac arrest is sometimes referred to as "calling a code".

Extensive research has shown that patients in general wards often deteriorate for several hours or even days before a cardiac arrest occurs. This has been attributed to a lack of knowledge and skill amongst ward based staff, in particular a failure to carry out measurement of the respiratory rate, which is often the major predictor of a deterioration and can often change up to 48 hours prior to a cardiac arrest. In response to this, many hospitals now have increased training for ward based staff. A number of "early warning" systems also exist which aim to quantify the risk which patients are at of deterioration based on their vital signs and thus provide a guide to staff. In addition, specialist staff are being utilised more effectively in order to augment the work already being done at ward level. These include:

- Crash teams (or code teams) - These are designated staff members who have particular expertise in resuscitation, who are called to the scene of all arrests within the hospital. This usually involves a specialized cart of equipment (including defibrillator) and drugs called a "crash cart".
- Medical emergency teams - These teams respond to all emergencies, with the aim of treating the patient in the acute phase of their illness in order to prevent a cardiac arrest.
- Critical care outreach - As well as providing the services of the other two types of team, these teams are also responsible for educating non-specialist staff. In addition, they help to facilitate transfers between intensive care/high dependency

units and the general hospital wards. This is particularly important, as many studies have shown that a significant percentage of patients discharged from critical care environments quickly deteriorate and are re-admitted - the outreach team offers support to ward staff to prevent this from happening.

Implantable cardioverter defibrillators

A technologically based intervention to prevent further cardiac arrest episodes is the use of an implantable cardioverter-defibrillator (ICD). This device is implanted in the patient and acts as an instant defibrillator in the event of arrhythmia. Note that standalone ICDs do not have any pacemaker functions, but they can be combined with a pacemaker, and modern versions also have advanced features such as anti-tachycardic pacing as well as synchronized cardioversion. A recent study by Birnie et al. at the University of Ottawa Heart Institute has demonstrated that ICDs are underused in both the United States and Canada. An accompanying editorial by Simpson explores some of the economic, geographic, social and political reasons for this. Patients who are most likely to benefit from the placement of an ICD are those with severe ischemic cardiomyopathy (with systolic ejection fractions less than 30%) as demonstrated by the MADIT-II trial.

Management

Sudden cardiac arrest is treated via attempts at resuscitation. This is usually carried out based upon basic life support (BLS) / advanced cardiac life support (ACLS), pediatric advanced life support (PALS) or neonatal resuscitation program (NRP) guidelines.

Cardiopulmonary resuscitation

CPR is a critical part of the management of cardiac arrest. It should be started as soon as possible and interrupted as little as possible. The component of CPR which seems to make the greatest difference is the chest compressions.

Ventilation

Tracheal intubation has not been found to improve survival rates in cardiac arrest cases. A 2009 study has found that assisted ventilation may worsen outcomes over placement of an oral airway with passive oxygen delivery. Intubation in the prehospital environment has been found to decrease survival.

Bystander CPR

Correctly performed bystander CPR has been shown to increase survival; it is performed in less than 30% of out of hospital arrests.

Defibrillation

Clinicians distinguish shockable and non–shockable causes of cardiac arrest - based on the presence or absence of ventricular fibrillation or pulseless ventricular tachycardia. The shockable rhythms are treated with CPR and defibrillation.

Most out-of-hospital cardiac arrests occur following a myocardial infarction (heart attack), and present initially with a heart rhythm of ventricular fibrillation. The patient is therefore likely to respond to defibrillation, and this has become the focus of interventions.

In addition, there is increasing use of public access defibrillation. This involves placing automated external defibrillators in public places, and training staff in these areas how to use them. This allows defibrillation to take place prior to the arrival of emergency services, and has been shown to lead to increased chances of survival. Some defibrillators even provide feedback on the quality of CPR compressions, encouraging the lay rescuer to press the patient's chest hard enough to circulate blood. In addition, it has been shown that those who suffer arrests in remote locations have worse outcomes following cardiac arrest: these areas often have first responders, whereby members of the community receive training in resuscitation and are given a defibrillator, and called by the emergency medical services in the case of a collapse in their local area.

Medications

Medications, while included in guidelines, have been shown not to improve survival to hospital discharge post cardiac arrest. This includes the use of epinephrine, atropine, and amiodarone. The study, however, only refers to the ineffectiveness of these drugs in reference to out-of-hospital cardiac arrests. Though in their 2010 guidelines, the American Heart Association has singled out atropine, indicating that "Available evidence suggests that the routine use of atropine during PEA or asystole is unlikely to have a therapeutic benefit."

Therapeutic hypothermia

Cooling a person after cardiac arrest with return of spontaneous circulation (ROSC) but without return of consciousness improves outcomes. This procedure is called therapeutic hypothermia. The first study conducted in Europe focused on people who were resuscitated 5–15 minutes after collapse. Patients participating in this study experienced spontaneous return of circulation (ROSC) after an average of 105 minutes. Subjects were then cooled over a 24 hour period, with a target temperature of 32–34 °C (90–93 °F). 55% of the 137 patients in the hypothermia group experienced favorable outcomes, compared with only 39% in the group that received standard care following resuscitation. Death rates in the hypothermia group were 14% lower, meaning that for every 7 patients treated one life was saved. Notably, complications between the two groups did not differ substantially. This data was supported by another similarly run study that took place simultaneously in Australia. In this study 49% of the patients treated with hypothermia

following cardiac arrest experienced good outcomes, compared to only 26% of those who received standard care.

ECMO

Sporadic reports of resuscitation with extracorporeal membrane oxygenation devices have appeared in recent years.

Chain of survival

Several organisations promote the idea of a "chain of survival" The links are:

- Early recognition - If possible, recognition of illness before the patient develops a cardiac arrest will allow the rescuer to prevent its occurrence. Early recognition that a cardiac arrest has occurred is key to survival - for every minute a patient is in cardiac arrest, their chances of survival drop by roughly 10%.
- Early CPR - improves blood and oxygen flow to vital organs and an essential component of treating a cardiac arrest. In particular, by keeping the brain supplied with oxygenated blood, chances of neurological damage are decreased.
- Early defibrillation - is effective for the management of ventricular fibrillation and pulseless ventricular tachycardia If defibrillation is delayed the rhythm is likely to degenerate into asystole for which outcomes are worse.
- Early advanced care - Early Advanced Cardiac Life Support is the final link in the chain of survival.

If one or more links in the chain are missing or delayed, then the chances of survival drop significantly.

These protocols are often initiated by a Code Blue, which usually denotes impending or acute onset of cardiac arrest or respiratory failure, although in practice, Code Blue is often called in less life-threatening situations that require immediate attention from a physician.

Prognosis

Out-of-hospital cardiac arrest (OHCA) has a worse survival rate (2-8% for discharge and 8-22% for admission), than an in-hospital cardiac arrest (15% for discharge). The principal determining factor is the initially documented rhythm. People with ventricular fibrillation or pulseless ventricular tachycardia have 10-15 times greater chance of surviving than those suffering from pulseless electrical activity or asystole.

Since mortality in case of OHCA is high, programs were developed to improve survival rate. Although mortality in case of ventricular fibrillation is high, rapid intervention with a defibrillator increases survival rate.

Survival is mostly related to the cause of the arrest (see above). In particular, patients who have suffered hypothermia have an increased survival rate, possibly because the cold protects the vital organs from the effects of tissue hypoxia. Survival rates following an arrest induced by toxins is very much dependent on identifying the toxin and administering an appropriate antidote. A patient who has suffered a myocardial infarction due to a blood clot in the left coronary artery has a lower chance of survival.

A study of survival rates from out of hospital cardiac arrest found that 14.6% of those who had received resuscitation by ambulance staff survived as far as admission to hospital. Of these, 59% died during admission, half of these within the first 24 hours, while 46% survived until discharge from hospital. This gives us an overall survival following cardiac arrest of 6.8%. Of these 89% had normal brain function or mild neurological disability, 8.5% had moderate impairment, and 2% suffered major neurological disability. Of those who were discharged from hospital, 70% were still alive 4 years later.

A review into prognosis following in-hospital cardiac arrest found a survival to discharge of 14% although the range between different studies was 0-28%.

Epidemiology

Based on death certificates sudden cardiac death accounts for about 15% of all death in Western countries (330,000 per year in the United States). The lifetime risk is three times greater in men (12.3%) than women (4.2%) based on analysis of the Framingham Heart Study. However this gender difference disappeared beyond 85 years of age.

Ethical issues

Some people with a terminal illness choose to avoid aggressive measure at the end of life. A do not resuscitate (DNR) order is to make this wish clear. This may be included in an advance health care directive.

Chapter 9

Cardiopulmonary Resuscitation

CPR being performed on a mannequin

Cardiopulmonary resuscitation (**CPR**) is an emergency procedure which is attempted in an effort to return life to a person in cardiac arrest. It is indicated in those who are unresponsive with no breathing or only gasps. It may be attempted both in and outside of a hospital.

CPR involves chest compressions at a rate of at least 100 per minute in an effort to create artificial circulation by manually pumping blood through the heart. In addition the rescuer may provide breaths by either exhaling into their mouth or utilizing a device that

pushes air into the lungs. The process of externally providing ventilation is termed artificial respiration. Current recommendations place emphasis on high quality chest compressions over artificial respirations and a method involving only chest compressions is recommended for untrained rescuers.

CPR alone is unlikely to restart the heart; its main purpose is to restore partial flow of oxygenated blood to the brain and heart. It may delay tissue death and extend the brief window of opportunity for a successful resuscitation without permanent brain damage. An administering of an electric shock to the heart, termed defibrillation, is usually needed to restore a viable or "perfusing" heart rhythm. Defibrillation is only effective for certain heart rhythms, namely ventricular fibrillation or pulseless ventricular tachycardia, rather than asystole or pulseless electrical activity. CPR may however induce a shockable rhythm. CPR is generally continued until the person regains return of spontaneous circulation (ROSC) or is declared dead.

Indications

CPR is indicated for any person who is unresponsive with no breathing or only gasps as breathing as it is most likely that they are in cardiac arrest. If a person still has a pulse, but is not breathing (respiratory arrest), artificial respirations are more appropriate. However, many people often have difficulty detecting a pulse and CPR may thus be used.

Methods

CPR training: CPR is being administrated while a second rescuer prepares for defibrillation.

In 2010, the American Heart Association and International Liaison Committee on Resuscitation updated their CPR guidelines. The importance of high quality CPR

(sufficient rate and depth without excessively ventilating) was emphasized. The order of interventions was changed for all age groups except newborns from airway, breathing, chest compressions (ABC) to chest compressions, airway, breathing (CAB). An exception to this recommendation is for those who are believed to be in a respiratory arrest (drowning, etc.).

Standard

A universal compression to ventilation ratio of 30:2 is recommended for adult and in children and infant if only a single rescuer is present. If at least 2 rescuers are present a ratio of 15:2 is preferred in children and infants. In newborns a rate of 3:1 is recommended unless a cardiac cause is known in which case a 15:2 ratio is reasonable. If an advanced airway such as an endotracheal tube or laryngeal mask airway is in placed delivery of respirations should occur without pauses in compressions at a rate of 8-10 per minute. The recommended order of interventions is chest compressions, airway, breathing or CAB in most situations. With a compression rate of at least 100 per minute in all groups. Recommended compression depth in adults and children is about 5 cm (2 inches) and in infants it is 4 cm (1.5 inches. As of 2010 the Resuscitation Council (UK) still recommends ABC for children. As it can be difficult to determine the presence or absence of a pulse the pulse check has been removed for lay providers and should not be performed for more than 10 seconds by health care providers. In adults rescuers should use two hands for the chest compressions, while in children they should use one, and with infants two fingers (index and middle fingers).

Compression only

Compression only (hands-only) CPR is a technique that involves chest compressions without artificial respiration. It is recommended as the method of choice for the untrained rescuer or those who are not proficient as it is easier to perform and instructions are easier to give over the phone. In adults with out-of-hospital cardiac arrest, compression-only CPR by the lay public has a higher success rate than standard CPR. The exceptions are cases of drownings, drug overdose, and arrest in children. Children who receive compression only CPR have the same outcomes as those who received no CPR. The method of delivering chest compressions remains the same, as does the rate (at least 100 per minute). It is hoped that the use of compression only delivery will increase the chances of the lay public delivering CPR.

Interposed abdominal compression

Interposed abdominal compressions may be beneficial in the in hospital environment. There is however no evidence of benefit pre hospital or in children.

Internal cardiac massage

Internal cardiac massage is the process of cardiac massage carried out through a surgical incision into the chest cavity. This distinguishes the process from conventional, external

cardiac massage, which is carried out by compression near the sternum during cardiopulmonary resuscitation.

Effectiveness

Type of Arrest	ROSC	Survival
Witnessed In-Hospital Cardiac Arrest	48%	22%
Unwitnessed In-Hospital Cardiac Arrest	21%	1%
Bystander Cardiocerebral Resuscitation	40%	6%
Bystander Cardiopulmonary Resuscitation	40%	4%
No Bystander CPR (Ambulance CPR)	15%	2%
Defibrillation within 3–5 minutes	74%	30%

Used alone, CPR will result in few complete recoveries, and those who do survive often develop serious complications. Estimates vary, but many organizations stress that CPR does not "bring anyone back," it simply preserves the body for defibrillation and advanced life support. However, in the case of "non-shockable" rhythms such as Pulseless Electrical Activity (PEA), defibrillation is not indicated, and the importance of CPR rises. On average, only 5–10% of people who receive CPR survive. The purpose of CPR is not to "start" the heart, but rather to circulate oxygenated blood, and keep the brain alive until advanced care (especially defibrillation) can be initiated. As many of these patients may have a pulse that is impalpable by the layperson rescuer, the current consensus is to perform CPR on a patient who is not breathing.

Studies have shown the importance of immediate CPR followed by defibrillation within 3–5 minutes of sudden VF cardiac arrest improve survival. In cities such as Seattle where CPR training is widespread and defibrillation by EMS personnel follows quickly, the survival rate is about 30 percent. In cities such as New York, without those advantages, the survival rate is only 1–2 percent.

In most cases, there is a higher proportion of patients who achieve a Return of Spontaneous Circulation (ROSC), where their heart starts to beat on its own again, than ultimately survive to be discharged from hospital. This is due to medical staff either being ultimately unable to address the cause of the arrhythmia or cardiac arrest, or in some instances due to other co-morbidities, due to the patient being gravely ill in more than one way.

Compression-only CPR is less effective in children than in adults, as cardiac arrest in children is more likely to have a non-cardiac cause. In a 2010 prospective study of cardiac arrest in children (age 1–17), for arrests with a non-cardiac cause provision by bystanders of conventional CPR with rescue breathing yielded a favorable neurological outcome at one month more often that did compression-only CPR (OR 5.54; 95% confidence interval 2.52–16.99). For arrests with a cardiac cause in this cohort, there was no difference between the two techniques (OR 1.20; 95% confidence interval 0.55–2.66). This is consistent with American Heart Association guidelines for parents.

Pathophysiology

CPR is used on people in cardiac arrest in order to oxygenate the blood and maintain a cardiac output to keep vital organs alive. Blood circulation and oxygenation are required to transport oxygen to the tissues. The brain may sustain damage after blood flow has been stopped for about four minutes and irreversible damage after about seven minutes. Typically if blood flow ceases for one to two hours, the cells of the body die. Because of that CPR is generally only effective if performed within seven minutes of the stoppage of blood flow. The heart also rapidly loses the ability to maintain a normal rhythm. Low body temperatures as sometimes seen in near-drownings prolong the time the brain survives. Following cardiac arrest, effective CPR enables enough oxygen to reach the brain to delay brain death, and allows the heart to remain responsive to defibrillation attempts.

Adjunct devices

While several adjunctive devices are available none other than defibrillation as of 2010 have consistently been found to be better than standard CPR for out of hospital cardiac arrest. These devices can be split in to three broad groups - timing devices, those that assist the rescuer to achieve the correct technique, especially depth and speed of compressions, and those which take over the process completely.

Timing devices

They can feature a metronome (an item carried by many ambulance crews) in order to assist the rescuer in getting the correct rate. Some units can also give timing reminders for performing compressions, breathing and changing operators.

Manual assist devices

Studies have shown that audible and visual prompting can improve the quality of CPR and prevent the decrease of compression rate and depth that naturally occurs with fatigue, and to address this potential improvement, a number of devices have been developed to help improve CPR technique.

These items can be devices to placed on top of the chest, with the rescuers hands going over the device, and a display or audio feedback giving information on depth, force or rate, or in a wearable format such as a glove. Several published evaluations show that these devices can improve the performance of chest compressions.

As well as use during actual CPR on a cardiac arrest victim, which relies on the rescuer carrying the device with them, these devices can also be used as part of training programs to improve basic skills in performing correct chest compressions.

Certain defibrillation pads are capable of performing similar function, in that they may display rate and depth of compressions. Additionally, a certain algorithm may allow them to monitor electrical activity even during CPR.

Automatic devices

There are also some automated devices available which take over the chest compressions for the rescuer. These have several advantages: they allow rescuers to focus on performing other interventions; they do not fatigue and begin to perform less effective compressions, as humans do; and they are able to perform effective compressions in limited-space environments such as air ambulances, where manual compressions are difficult. These devices use either pneumatic (high-pressure gas) or electrical power sources to drive a compressing pad on to the chest of the patient. One such device, known as the LUCAS, was developed at the University Hospital of Lund, is powered by the compressed oxygen supplies already standard in ambulances and hospitals, and has undergone numerous clinical trials, showing a marked improvement in coronary perfusion pressure and return of spontaneous circulation.

Another system called the AutoPulse is electrically powered and uses a large band around the patients chest which contracts in rhythm in order to deliver chest compressions. This is also backed by clinical studies showing increased successful return of spontaneous circulation.

Prevalence

Chance of receiving CPR

Various studies suggest that in out-of-home cardiac arrest, bystanders, lay persons or family members attempt CPR in between 14% and 45% of the time, with a median of 32%. This indicates that around a third of out-of-home arrests have a CPR attempt made on them. However, the effectiveness of this CPR is variable, and the studies suggest only around half of bystander CPR is performed correctly.

There is a clear correlation between age and the chance of CPR being commenced, with younger people being far more likely to have CPR attempted on them prior to the arrival of emergency medical services. It was also found that CPR was more commonly given by a bystander in public than when an arrest occurred in the patient's home, although health care professionals are responsible for more than half of out-of-hospital resuscitation attempts. This is supported by further research, which suggests that people with no connection to the victim are more likely to perform CPR than a member of their family. This is likely because of the shock experienced by finding a family member in need of CPR; it is easier to remain calm - and think clearly - when the person in need of CPR is a complete stranger, as in this case one will not be as frightened.

There is also a correlation between the cause of arrest and the likelihood of bystander CPR being initiated. Lay persons are most likely to give CPR to younger cardiac arrest

victims in a public place when it has a medical cause; victims in arrest from trauma, exsanguination or intoxication are less likely to receive CPR.

Finally, it has been claimed that there is a higher chance of CPR being performed if the bystander is told to only perform the chest compression element of the resuscitation.

Chance of receiving CPR in time

CPR is only likely to be effective if commenced within 6 minutes after the blood flow stops, because permanent brain cell damage occurs when fresh blood infuses the cells after that time, since the cells of the brain become dormant in as little as 4–6 minutes in an oxygen deprived environment and the cells are unable to survive the reintroduction of oxygen in a traditional resuscitation. Research using cardioplegic blood infusion resulted in a 79.4% survival rate with cardiac arrest intervals of 72±43 minutes, traditional methods achieve a 15% survival rate in this scenario, by comparison. New research is currently needed to determine what role CPR, electroshock, and new advanced gradual resuscitation techniques will have with this new knowledge A notable exception is cardiac arrest occurring in conjunction with exposure to very cold temperatures. Hypothermia seems to protect by slowing down metabolic and physiologic processes, greatly decreasing the tissues' need for oxygen. There are cases where CPR, defibrillation, and advanced warming techniques have revived victims after substantial periods of hypothermia.

Society and culture

Portrayed effectiveness

CPR is often severely misrepresented in movies and television as being highly effective in resuscitating a person who is not breathing and has no circulation. A 1996 study published in the New England Journal of Medicine showed that CPR success rates in television shows was 75% for immediate circulation, and 67% survival to discharge. This gives members of the public an unrealistic expectation of a successful outcome. When educated on the actual survival rates, the proportion of patients over 60 years of age desiring CPR should they suffer a cardiac arrest drops from 41% to 22%.

Stage CPR

Chest compressions are capable of causing significant local blunt trauma, including bruising or fracture of the sternum or ribs. Performing CPR on a healthy person may or may not disrupt normal heart rhythm, but regardless the technique should not be performed on a healthy person because of the risk of trauma.

The portrayal of CPR technique on television and film often is purposely incorrect. Actors simulating the performance of CPR may bend their elbows while appearing to compress, to prevent force from reaching the chest of the actor portraying the victim.

Other techniques, such as substituting a mannequin torso for the "victim" in some shots, may also be used to avoid harming actors.

Self-CPR hoax

A form of "self-CPR" termed "Cough CPR" was the subject of a hoax chain e-mail entitled "How to Survive a Heart Attack When Alone" which wrongly cited "ViaHealth Rochester General Hospital" as the source of the technique. Rochester General Hospital has denied any connection with the technique.

Rapid coughing has been used in hospitals for brief periods of cardiac arrhythmia on monitored patients. One researcher has recommended that it be taught broadly to the public.

However, “cough CPR” cannot be used outside the hospital because the first symptom of cardiac arrest is unconsciousness in which case coughing is impossible, although myocardial infarction (heart attack) may occur to give rise to the cardiac arrest, so a patient may not be immediately unconscious. Further, the vast majority of people suffering chest pain from a heart attack will not be in cardiac arrest and CPR is not needed. In these cases attempting “cough CPR” will increase the workload on the heart and may be harmful. When coughing is used on trained and monitored patients in hospitals, it has only been shown to be effective for 90 seconds.

The American Heart Association (AHA) and other resuscitation bodies do not endorse "Cough CPR", which it terms a misnomer as it is not a form of *resuscitation*. The AHA does recognize a limited legitimate use of the coughing technique: "This coughing technique to maintain blood flow during brief arrhythmias has been useful in the hospital, particularly during cardiac catheterization. In such cases the patients ECG is monitored continuously and a physician is present."

History

Sign showing old Silvester and Holger-Nielsen methods of resuscitation

In the 19th century, Doctor H. R. Silvester described a method (The Silvester Method) of artificial respiration in which the patient is laid on their back, and their arms are raised above their head to aid inhalation and then pressed against their chest to aid exhalation. The procedure is repeated sixteen times per minute. This type of artificial respiration is occasionally seen in films made in the early part of the 20th century.

A second technique, called the Holger Neilson technique, described in the first edition of the Boy Scout Handbook in the United States in 1911, described a form of artificial respiration where the person was laid on their front, with their head to the side, resting on the palms of both hands. Upward pressure applied at the patient's elbows raised the upper body while pressure on their back forced air into the lungs, essentially the Silvester Method with the patient flipped over. This form is seen well into the 1950s (it is used in an episode of *Lassie* during the Jeff Miller era), and was often used, sometimes for comedic effect, in theatrical cartoons of the time. This method would continue to be shown, for historical purposes, side-by-side with modern CPR in the Boy Scout Handbook until its ninth edition in 1979. The technique was later banned from first-aid manuals in the UK.

However, it was not until the middle of the 20th century that the wider medical community started to recognize and promote artificial respiration combined with chest compressions as a key part of resuscitation following cardiac arrest. The combination was first seen in a 1962 training video called "The Pulse of Life" created by James Jude, Guy Knickerbocker and Peter Safar. Jude and Knickerbocker, along with William

Kouwenhoven and Joseph S. Redding had recently discovered the method of external chest compressions, whereas Safar had worked with Redding and James Elam to prove the effectiveness of artificial respiration. It was at Johns Hopkins University where the technique of CPR was originally developed. The first effort at testing the technique was performed on a dog by Redding, Safar and JW Perason. Soon afterward, the technique was used to save the life of a child. Their combined findings were presented at annual Maryland Medical Society meeting on September 16, 1960 in Ocean City, and gained rapid and widespread acceptance over the following decade, helped by the video and speaking tour they undertook. Peter Safar wrote the book *ABC of resuscitation* in 1957. In the U.S., it was first promoted as a technique for the public to learn in the 1970s.

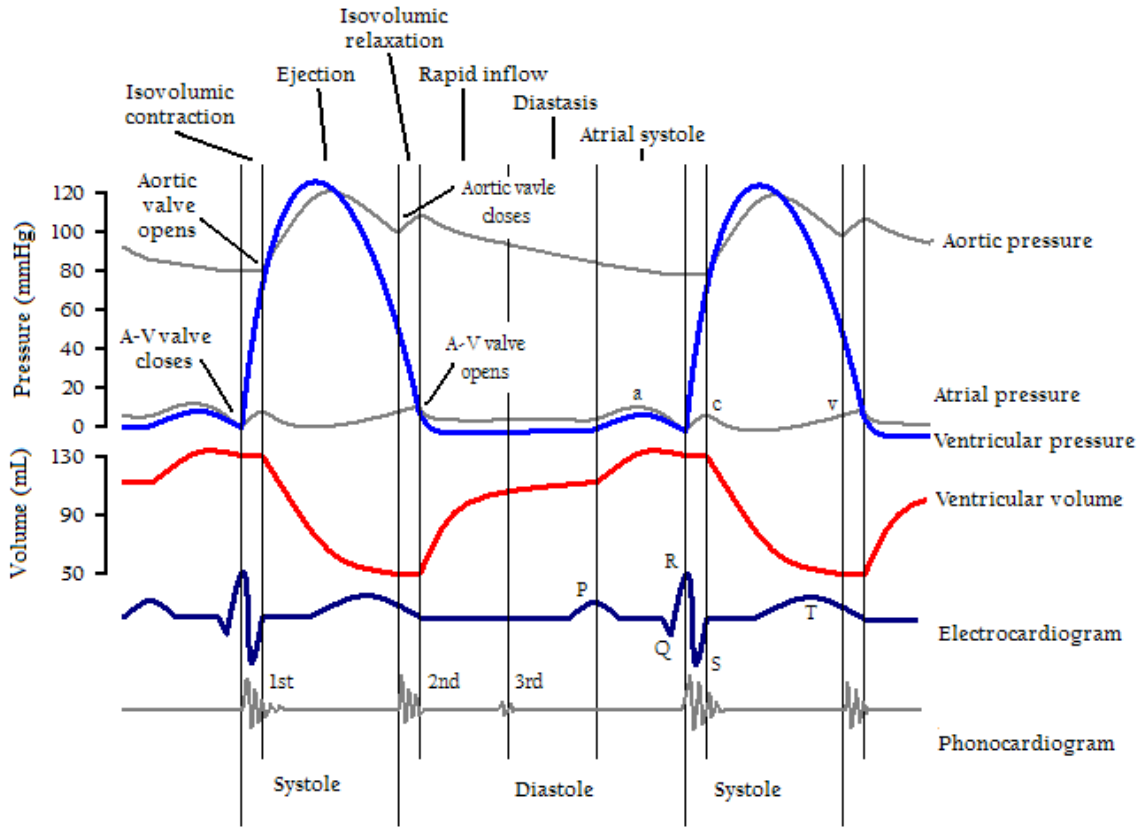
Artificial respiration was combined with chest compressions based on the assumption that active ventilation is necessary to keep circulating blood oxygenated, and the combination was accepted without comparing its effectiveness with chest compressions alone. However, research over the past decade has shown that assumption to be in error, resulting in the AHA's acknowledgment of the effectiveness of chest compressions alone.

In other animals

It is entirely feasible to perform CPR on animals, including cats and dogs. The principles and practices are virtually identical to CPR for humans. One difference is that resuscitation is usually done through the animal's nose, not the mouth. One is cautioned to only perform CPR on unconscious animals to avoid the risk of being bitten and that animals, depending on species, have a lower bone density than humans, causing bones to become weakened after CPR is performed.

Chapter 10

Cardiac Cycle



Cardiac events occurring in the cardiac cycle. Two complete cycles are illustrated.

The **cardiac cycle** is a term referring to all or any of the events related to the flow or blood pressure that occurs from the beginning of one heartbeat to the beginning of the next. The frequency of the cardiac cycle is described by the heart rate. Each beat of the heart involves five major stages. The first two stages, often considered together as the "ventricular filling" stage, involve the movement of blood from atria into ventricles. The next three stages involve the movement of blood from the ventricles to the pulmonary artery (in the case of the right ventricle) and the aorta (in the case of the left ventricle).

The first, "late diastole", is when the semilunar valves close, the atrioventricular (AV) valves open, and the whole heart is relaxed. The second, "atrial systole", is when the

atrium contracts, the AV valves open, and blood flows from atrium to the ventricle. The third, "isovolumic ventricular contraction", is when the ventricles begin to contract, the AV and semilunar valves close, and there is no change in volume. The fourth, "ventricular ejection", is when the ventricles are empty and contracting, and the semilunar valves are open. During the fifth stage, "Isovolumic ventricular relaxation", pressure decreases, no blood enters the ventricles, the ventricles stop contracting and begin to relax, and the semilunar valves close due to the pressure of blood in the aorta.

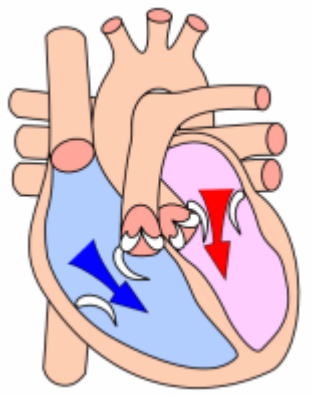
Throughout the cardiac cycle, blood pressure increases and decreases. The cardiac cycle is coordinated by a series of electrical impulses that are produced by specialized heart cells found within the sinoatrial node and the atrioventricular node. The cardiac muscle is composed of myocytes which initiate their own contraction without help of external nerves (with the exception of modifying the heart rate due to metabolic demand). Under normal circumstances, each cycle takes approximately one second.

Anatomical basis of the cardiac cycle

The heart is a four-chambered organ consisting of right and left halves. Two of the chambers, the left and right atria, are entry-points into the heart, while the other two chambers, the left and right ventricles, are responsible for contractions that send the heart through the circulation. The circulation is split into the pulmonary and systemic circulation. The right ventricle's role is to pump deoxygenated blood into the pulmonary circulation through the pulmonary artery. The left ventricle's role is to pump now oxygenated blood into the systemic circulation through the aorta. The left ventricle is often observed to be larger than the right, considering it must pump blood to the whole body.

Importantly, the right and left ventricles contract simultaneously, and so in consideration of the cardiac cycle the events that are occurring on one side of the heart are equivalent to the events occurring on the other side of the heart. However, the ventricles contract shortly after the atria. The sino-atrial node sends out electrical waves of excitation to both atria, and it is prevented from flowing into the ventricles by strands of non-conducting fibrous tissue situated laterally from the tricuspid/bicuspid valves to the septum. These waves of excitation travel towards the septum and into the atrio-ventricular node, where they are held for roughly 0.1 seconds. They are then discharged down the bundle of his, then down the purkyne tissue, which are both situated inside the septum. The waves flow down towards the apex of the heart and are then discharged into the ventricles, causing them to contract (ventricular systole). This creates the well known beat of the heart.

Atrial systole



Atrial systole

Atrial systole is the contraction of the heart muscle (*myocardia*) of the left and right atria. Normally, both atria contract at the same time. The term *systole* is synonymous with contraction (movement or shortening) of a muscle. *Electrical systole* is the electrical activity that stimulates the myocardium of the chambers of the heart to make them contract. This is soon followed by *Mechanical systole*, which is the mechanical contraction of the heart.

As the atria contract, the blood pressure in each atrium increases, forcing additional blood into the ventricles. The additional flow of blood is called **atrial kick**.

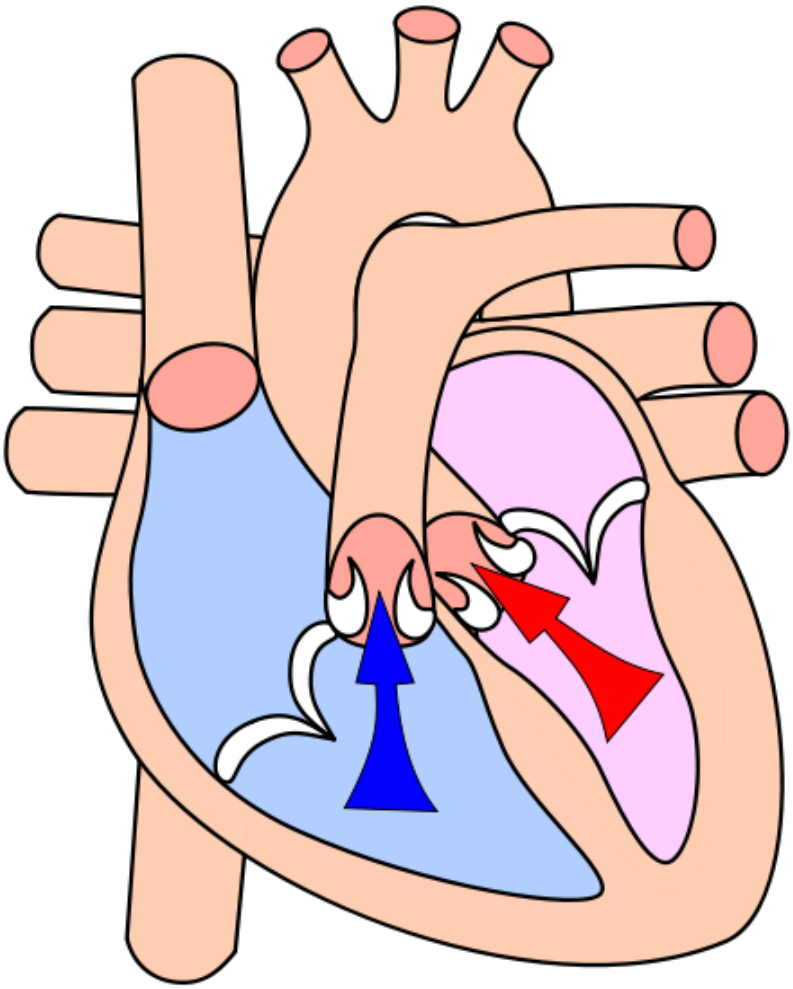
80% of the blood flows passively down to the ventricles, so the atria do not have to contract a great amount.

Atrial kick is absent if there is loss of normal electrical conduction in the heart, such as during atrial fibrillation, atrial flutter, and complete heart block. Atrial kick is also different in character depending on the condition of the heart, such as stiff heart, which is found in patients with diastolic dysfunction.

Detection of atrial systole

Electrical systole of the atria begins with the onset of the P wave on the ECG. The wave of bipolarization (or depolarization) that stimulates both atria to contract at the same time is due to sinoatrial node which is located on the upper wall of the right atrium.

Ventricular systole



Ventricular systole

Ventricular systole is the contraction of the muscles (*myocardia*) of the left and right ventricles.

At the later part of the ejection phase, although the ventricular pressure falls below the aortic pressure, the aortic valve remains patent because of the inertial energy of the ejected blood.

The graph of aortic pressure throughout the cardiac cycle displays a small dip which coincides with the aortic valve closure. The dip in the graph is immediately followed by a brief rise then gradual decline. The small rise in the graph is known as the "dicrotic notch" or "incisure", and represents a transient increase in aortic pressure. Just as the ventricles enter into diastole, the brief reversal of flow from the aorta back into the left

ventricle causes the aortic valves to shut. This results in the slight increase in aortic pressure caused by the elastic recoil of the semilunar valves and aorta.

Detection of ventricular systole

Heart sounds

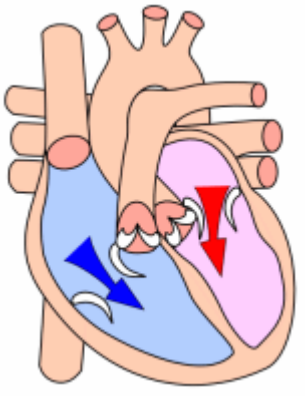
The closing of the mitral and tricuspid valves (known together as the *atrioventricular valves*) at the **beginning** of ventricular systole cause the first part of the "lubb-dubb" sound made by the heart as it beats. Formally, this sound is known as the *First Heart Tone*, or $\mathbf{S_1}$. This first heart tone is created by the closure of mitral and tricuspid valve and is actually a two component sound, M1, T1.

The second part of the "lub-dub" (the *Second Heart Tone*, or $\mathbf{S_2}$), is caused by the closure of the aortic and pulmonary valves at the **end** of ventricular systole. As the left ventricle empties, its pressure falls below the pressure in the aorta, and the aortic valve closes. Similarly, as the pressure in the right ventricle falls below the pressure in the pulmonary artery, the pulmonary valve closes. The second heart sound is also two components, A2 and P2. The aortic valve closes earlier than the pulmonary valve and they are audibly separated from each other in the second heart sound. This "splitting" of S2 is only audible during inhalation. However, some cardiac conduction abnormalities such as left bundle branch block (LBBB) allow the P2 sound to be heard before the A2 sound during expiration. With LBBB, inhalation brings A2 and P2 closer together where they cannot be audibly distinguished.

Electrocardiogram

In an electrocardiogram, electrical systole of the ventricles begins at the beginning of the QRS complex.

Diastole



Cardiac diastole

Cardiac Diastole is the period of time when the heart relaxes after contraction in preparation for refilling with circulating blood. **Ventricular diastole** is when the ventricles are relaxing, while **atrial diastole** is when the atria are relaxing. Together they are known as **complete cardiac diastole**.

During ventricular diastole, the pressure in the (left and right) ventricles drops from the peak that it reaches in systole. When the pressure in the left ventricle drops to below the pressure in the left atrium, the mitral valve opens, and the left ventricle fills with blood that was accumulating in the left atrium. The isovolumic relaxation time (IVRT) is the interval from the aortic component of the second heart sound, that is, closure of the aortic valve, to onset of filling by opening of the mitral valve. Likewise, when the pressure in the right ventricle drops below that in the right atrium, the tricuspid valve opens, and the right ventricle fills with blood that was accumulating in the right atrium. During diastole the pressure within the myocardium is lower than that in aorta, allowing blood to circulate in the heart itself via the coronary arteries.

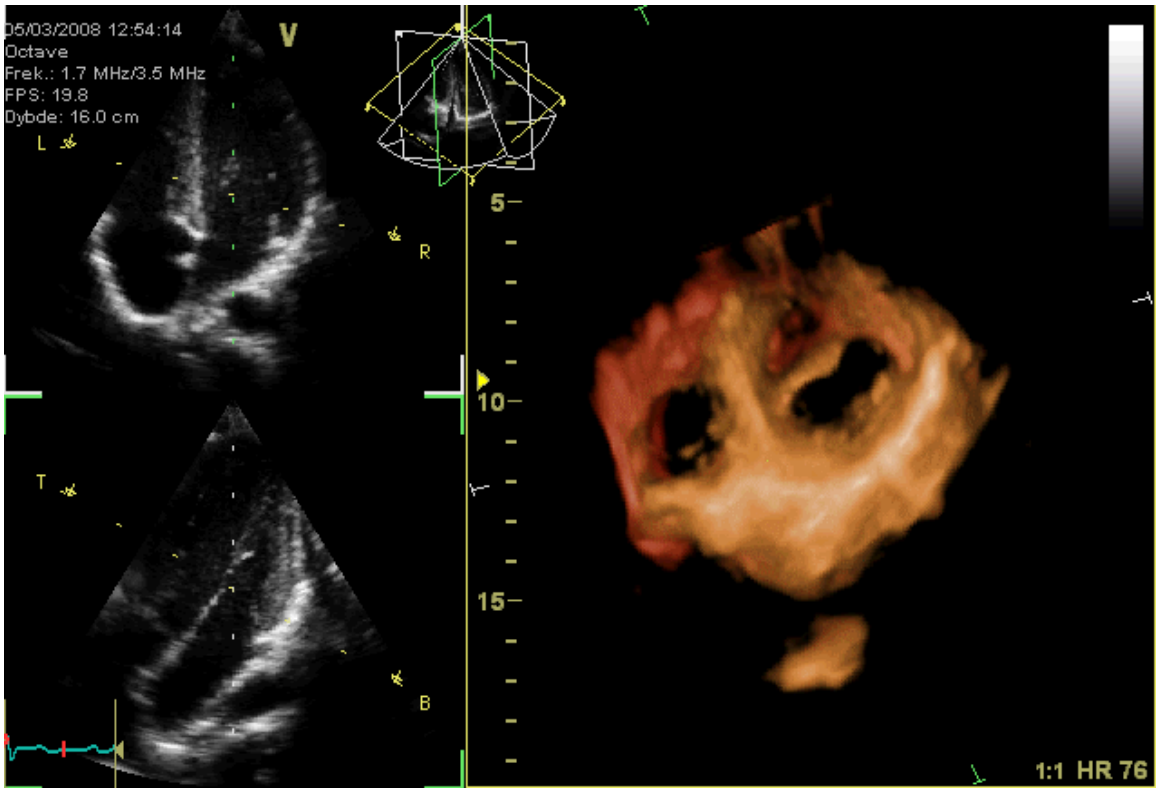
Regulation of the cardiac cycle

Cardiac muscle has automaticity, which means that it is self-exciting. (You could also call it "myogenic" tissue. Meaning a tissue able of creating its own excitement.) This is in contrast with skeletal muscle, which requires either conscious or reflex nervous stimuli for excitation. The heart's rhythmic contractions occur spontaneously, although the rate of contraction can be changed by nervous or hormonal influences, exercise and emotions. For example, the sympathetic nerves to accelerate heart rate and the vagus nerve decelerates heart rate.

The rhythmic sequence of contractions is coordinated by the sinoatrial (SA) and atrioventricular (AV) nodes. The sinoatrial node, often known as the *cardiac pacemaker*, is located in the upper wall of the right atrium and is responsible for the wave of electrical stimulation that initiates atrial contraction by creating an action potential. Once the wave reaches the AV node, situated in the lower right atrium, it is delayed there before being conducted through the bundles of *His* and back up the Purkinje fibers, leading to a contraction of the ventricles. The delay at the AV node allows enough time for all of the blood in the atria to fill their respective ventricles. In the event of severe pathology, the AV node can also act as a pacemaker; this is usually not the case because their rate of spontaneous firing is considerably lower than that of the pacemaker cells in the SA node and hence is overridden.

Chapter 11

Heart Valve



3D reconstruction of the heart as viewed from the apex towards the valves, image flipped 180° relative to illustration above. Pulmonary valve not visible, leaflets of the tricuspid and aortic valves only partly visible. To the left two images in 2D from the same dataset, showing tricuspid and mitral valves (above) and aortal and mitral valve (below).

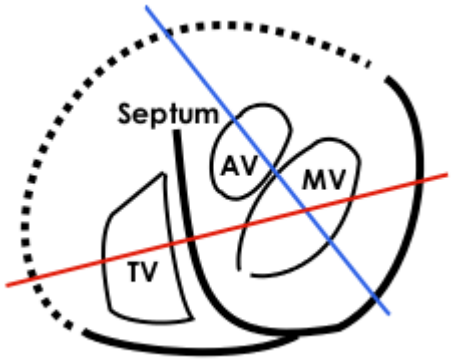
A **heart valve** normally allows blood to flow through it in only one direction. There are four in a mammalian heart and they determine the pathway of blood flow through the heart. A heart valve opens or closes depending on the different pressures on each side of it.

The four valves in the heart are:

- The two atrioventricular (AV) valves, which are between the atria and the ventricles, are the mitral valve and the tricuspid valve.
- The two semilunar (SL) valves, which are in the arteries leaving the heart, are the aortic valve and the pulmonary valve.

A form of heart disease occurs when a valve malfunctions and allows some blood to flow in the wrong direction. This is called regurgitation.

Atrioventricular valves



This is an explanation of the echocardiogram above. MV: Mitral valve, TV: Tricuspid valve, AV: Aortic valve, Septum: Interventricular septum. Continuous lines demarcate septum and free wall seen in echocardiogram, dotted line is a suggestion of where the free wall of the right ventricle should be. The red line represents where the upper left loop in the echocardiogram transects the 3D-loop, the blue line represents the lower loop.

An artificial heart valve may be used to surgically replace a patient's damaged valve

These are small valves that prevent backflow from the ventricles into the atrium during systole. They are anchored to the wall of the ventricle by chordae tendineae, which prevent the valve from inverting.

The chordae tendineae are attached to papillary muscles that cause tension to better hold the valve. Together, the papillary muscles and the chordae tendineae are known as the subvalvular apparatus. The function of the subvalvular apparatus is to keep the valves from prolapsing into the atria when they close. The subvalvular apparatus have no effect

on the opening and closure of the valves, however. This is caused entirely by the pressure gradient across the valve. The peculiar insertion of chords on the leaflet free margin however provides systolic stress sharing between chords according to their different thickness.

The closure of the AV valves is heard as the **first heart sound (S1)**.

Mitral valve

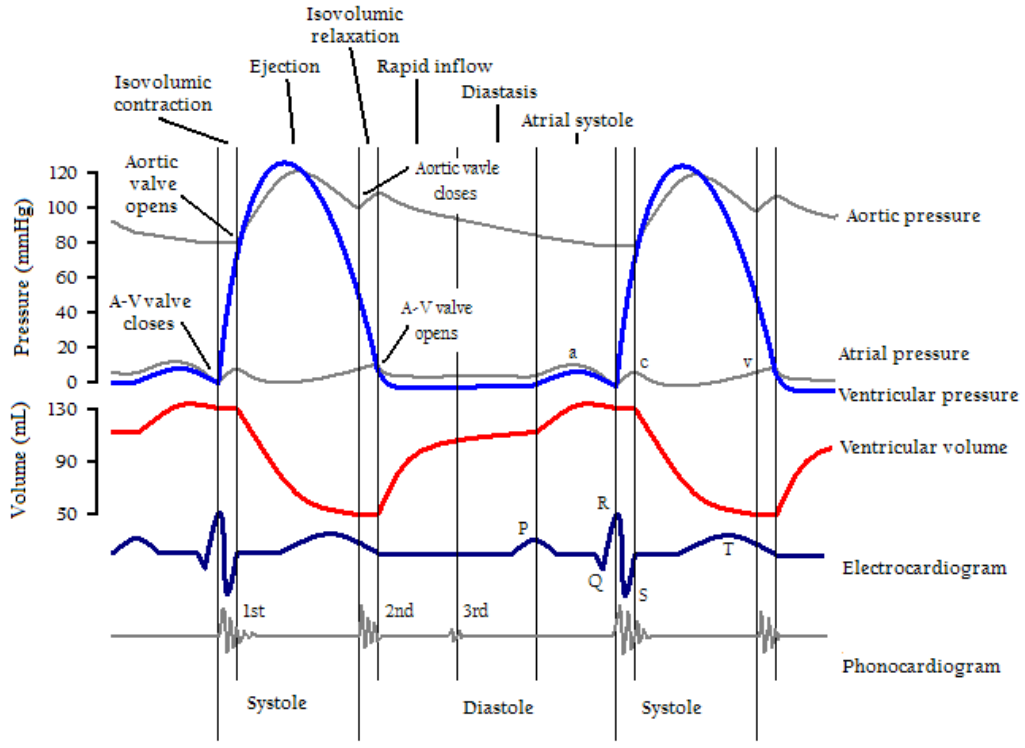
Also known as the "bicuspid valve" because it contains two flaps, the mitral valve gets its name from the resemblance to a bishop's mitre (a type of hat). It allows the blood to flow from the left atrium into the left ventricle. It is on the left side of the heart and has two cusps.

A common complication of rheumatic fever is thickening and stenosis of the mitral valve.

Tricuspid valve

The tricuspid valve is the three-flapped valve on the right side of the heart, between the right atrium and the right ventricle which stops the backflow of blood between the two. It has three cusps.

Semilunar valves



Wiggers diagram, showing various events during a cardiac cycle, with closures and openings of the aortic and mitral (*A-V valve* in image) marked in the pressure curves.

These are located at the base of both the pulmonary trunk (pulmonary artery) and the aorta, the two arteries taking blood out of the ventricles. These valves permit blood to be forced into the arteries, but prevent backflow of blood from the arteries into the ventricles. These valves do not have chordae tendineae, and are more similar to valves in veins than atrioventricular valves.

Aortic valve

The aortic valve lies between the left ventricle and the aorta. The aortic valve has three cusps. During ventricular systole, pressure rises in the left ventricle. When the pressure in the left ventricle rises above the pressure in the aorta, the aortic valve opens, allowing blood to exit the left ventricle into the aorta. When ventricular systole ends, pressure in the left ventricle rapidly drops. When the pressure in the left ventricle decreases, the aortic pressure forces the aortic valve to close. The closure of the aortic valve contributes the A2 component of the second heart sound (S2).

The most common congenital abnormality of the heart is the bicuspid aortic valve. In this condition, instead of three cusps, the aortic valve has two cusps. This condition is often undiagnosed until the person develops calcific aortic stenosis. Aortic stenosis occurs in this condition usually in patients in their 40s or 50s, an average of over 10 years earlier than in people with normal aortic valves.

Pulmonary valve

The pulmonary valve (sometimes referred to as the pulmonic valve) is the semilunar valve of the heart that lies between the right ventricle and the pulmonary artery and has three cusps. Similar to the aortic valve, the pulmonary valve opens in ventricular systole, when the pressure in the right ventricle rises above the pressure in the pulmonary artery. At the end of ventricular systole, when the pressure in the right ventricle falls rapidly, the pressure in the pulmonary artery will close the pulmonary valve.

The closure of the pulmonary valve contributes the P2 component of the second heart sound (S2). The right heart is a low-pressure system, so the P2 component of the second heart sound is usually softer than the A2 component of the second heart sound. However, it is physiologically normal in some young people to hear both components separated during inhalation.

Chapter 12

Cardiology Diagnostic Tests and Procedures

The **diagnostic tests in cardiology** are methods of identifying heart conditions associated with healthy vs. unhealthy, pathologic, heart function.

Bedside

History

Obtaining a medical history is always the first "test", part of understanding the likelihood of significant disease, as detectable within the current limitations of clinical medicine. Yet heart problems often produce no symptoms until very advanced, and many symptoms, such as palpitations and sensations of extra or missing heart beats correlate poorly with relative heart health *vs* disease. Hence, a history alone is rarely sufficient to diagnose a heart condition.

Auscultation

Auscultation employs a stethoscope to more easily hear various normal and abnormal sounds, such as normal heart beat sounds and the usual heart beat sound changes associated with breathing versus heart murmurs.

Laboratory

Blood tests

A variety of *blood tests* are available for analyzing cholesterol transport behavior, HDL, LDL, triglycerides, lipoprotein little a, homocysteine, C-reactive protein, blood sugar control: fasting, after eating or averages using glycosylated albumen or hemoglobin, myoglobin, creatine kinase, troponin, brain-type natriuretic peptide, etc. to assess the evolution of coronary artery disease and evidence of existing damage. A great many more physiologic markers related to atherosclerosis and heart function are used and being developed and evaluated in research.

Cardiology diagnostic tests

Test Name	Lower/normal risk	High risk	Cost $US (approx)
Total Cholesterol	<200 mg/dL	>240 mg/dL	
LDL-C	<100 mg/dL	>160 mg/dL	$150*
HDL-C	>60 mg/dL	<40 mg/dL	
Triglyceride	<150 mg/dL	>200 mg/dL	
Blood Pressure	<120/80 mmHg	>140/90 mmHg	
C-reactive protein	<1 mg/L	>3 mg/L	$20
Fibrinogen	<300 mg/dL	>460 mg/dL	$100
Homocysteine	<10 µmol/L	>14 µmol/L	$200
Fasting Insulin	<15 µIU/mL	>25 µIU/mL	$75
Ferritin	male 12–300 ng/mL female 12–150 ng/mL		$85
Lipoprotein(a) - Lp(a)	<14mg/dL	>19mg/dL	$75
Calcium Heart Scan	<100	>300	$250–600

Electrophysiology

Electrocardiogram

Electrocardiography (ECG/EKG in German vernacular. Elektrokardiogram) monitors electrical activity of the heart, primarily as recorded from the skin surface. A 12 lead recording, recording the electrical activity in three planes, anterior, posterior, and lateral is the most commonly used form. The ECG allows observation of the heart electrical activity by visualizing waveform beat origin (typically from the sinoatrial or SA node) following down the bundle of HIS and ultimately stimulating the ventricles to contract forcing blood through the body. Much can be learned by observing the QRS morphology (named for the respective portions of the polarization/repolarization waveform of the wave, P,Q,R,S,T wave). Rhythm abnormalities can also be visualized as in slow heart rate bradycardia, or fast heart rate tachycardia.

Holter monitor

A *Holter monitor* records a continuous EKG rhythm pattern (rarely a full EKG) for 24 hours or more. These monitors are used for suspected frequent rhythm abnormalities, especially ones the wearer may not recognize by symptoms. They are more expensive than event monitors.

Event monitor

An *Event monitor* records short term EKG rhythm patterns, generally storing the last 2 to 5 minutes, adding in new and discarding old data, for 1 to 2 weeks or more. There are

several different types with different capabilities. When the wearer presses a button on the monitor, it quits discarding old and continues recording for a short additional period. The wearer then plays the recording, via a standard phone connection, to a center with compatible receiving and rhythm printing equipment, after which the monitor is ready to record again. These monitors are used for suspected infrequent rhythm abnormalities, especially ones the wearer does recognize by symptoms. They are less expensive than Holter monitors.

Cardiac stress testing

Cardiac stress testing is used to determine to assess cardiac function and to disclose evidence of exertion-related cardiac hypoxia. Radionuclide testing using thallium or technetium can be used to demonstrate areas of perfusion abnormalities. With a maximal stress test the level of exercise is increased until the patient heart rate will not increase any higher, despite increased exercise. A fairly accurate estimate of the target heart rate, based on extensive clinical research, can be estimated by the formula 220 beats per minute minus patient's age. This linear relation is accurate up to about age 30, after which it mildly underestimates typical maximum attainable heart rates achievable by healthy individuals. Other formulas exist, such as that by Miller (217 - (0.85 × Age)) and others. Achieving a high enough heart rate at the end of exercise is critical to improving the sensitivity of the test to detect high grade heart artery stenosis.

Electrophysiology study

The electrophysiology study or EP study is the end all of electrophysiological tests of the heart. It involves a catheter with electrodes probing the endocardium, the inside of the heart, and testing the conduction pathways and electrical activity of individual areas of the heart.

Medical imaging

Coronary catheterization

Coronary catheterization uses pressure monitoring and blood sampling through a catheter inserted into the heart through blood vessels in the leg to determine the functioning of the heart, and, following injections of radiocontrast dye, uses X-ray fluoroscopy, typically at 30 frames per second, to visualize the position and size of blood within the heart chambers and arteries. Coronary angiography is used to determine the patency and configuration of the coronary artery lumens.

Echocardiogram

Transthoracic echocardiogram uses ultrasonic waves for continuous heart chamber and blood movement visualization. In recent times, it has become one of the most commonly used tools in diagnosis of heart problems, as it allows non-invasive visualization of the heart and the blood flow through the heart, using a technique known as Doppler.

Transoesophageal echocardiogram uses a specialized probe containing an ultrasound transducer at its tip is passed into the patient's esophagus. It is used in diagnosis of various thoracic defects or damage, i.e. heart and lung imaging. It has some advantages and disadvantages over thoracic or intravasular ultrasound.

Intravascular ultrasound

Intravascular ultrasound, also known as a percutaneous echocardiogram is an imaging methodology using specially designed, long, thin, complex manufactured catheters attached to computerized ultrasound equipment to visualize the lumen and the interior wall of blood vessels.

Positron emission tomography

Positron emission tomography, an imaging methodology for positron emitting radioisotopes. PET enables visual image analysis of multiple different metabolic chemical processes and is thus one of the most flexible imaging technologies. Cardiology uses are growing very slowly due to technical and relative cost difficulties. Most uses are for research, not clinical purposes. Appropriate radioisotopes of elements within chemical compounds of the metabolic pathway being examined are used to make the location of the chemical compounds of interest visible in a PET scanner constructed image.

Computed tomography angiography

Computed tomography angiography (CTA), an imaging methodology using a ring-shaped machine with an X-Ray source spinning around the circular path so as to bathe the inner circle with a uniform and known X-Ray density. Cardiology uses are growing with the incredible developments in CT technology. Currently, multidetector CT, specially the 64 detector-CT are allowing to make cardiac studies in just a few seconds (less than 10 seconds, depending on the equipment and protocol used). These images are reconstructed using algorithms and software. Great development and growth will be seen in the short term, allowing radiologists to diagnose cardiac artery disease without anesthesia and in a non-invasive way.

Magnetic resonance imaging

Magnetic resonance imaging (originally called nuclear magnetic resonance imaging), an imaging methodology based on aligning the spin axis of nuclei within molecules of the object being visualized using both powerful superconducting magnets and radio frequency signals and detectors. Cardiology uses are growing, especially since MRI differentiates soft tissues better than CT and allows for comprehensive exams including the quantitative assessment of size, morphology functino and tissue characteristics in one single session. Current implementations for Cardiology uses are sometimes limited by lengthy protocols, claustrophobia and contraindications based on some complex metallic implants (pacemakers, defibrillators, insulin pumps), while artificial valves and coronary stents are generally not problematic. Image quality can be reduced by the continuous

movement of heart structures. There is a promising future in cardiac MRI by more efficient scans, increasing availability of scanners and more widespread knowledge about its clinical application.

Chapter 13

Electrical Conduction System of the Heart

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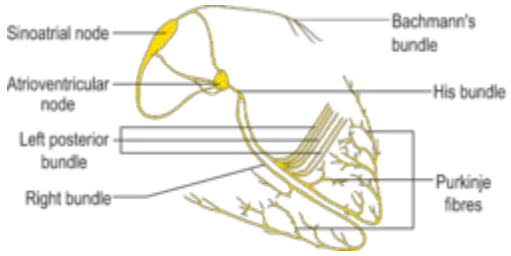
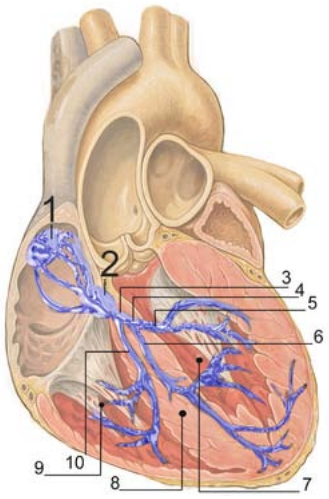


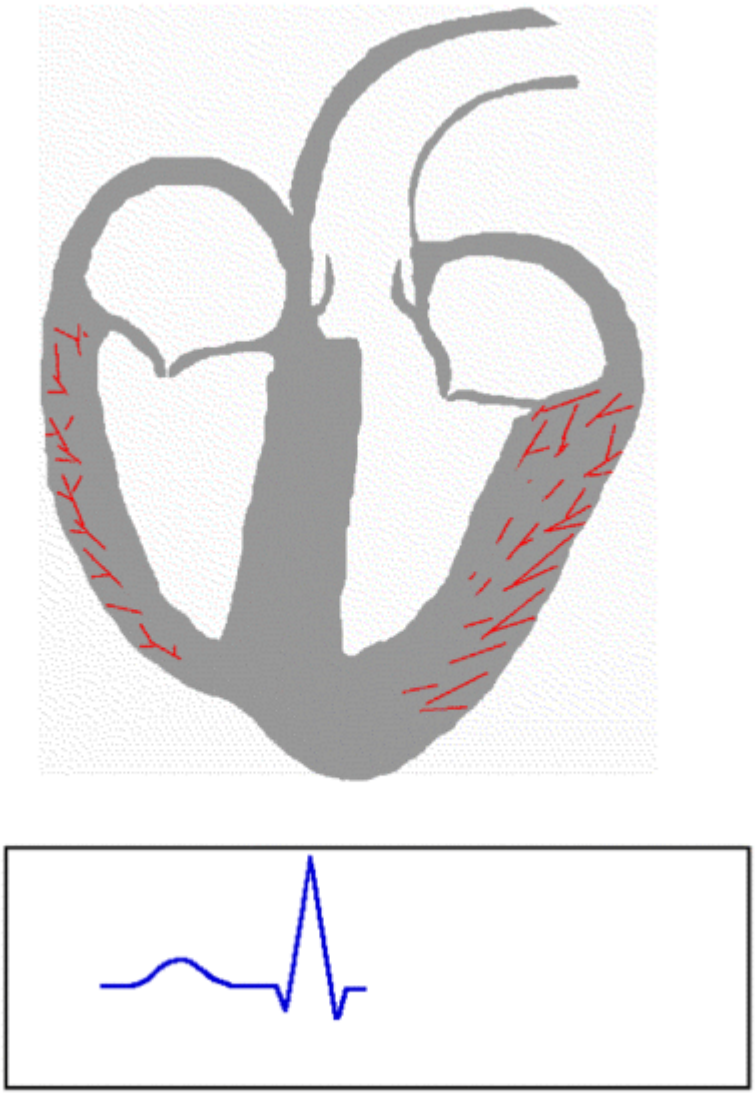
Isolated conduction system of the heart



Heart; conduction system

1. Sinoatrial node
2. Atrioventricular node
3. Bundle of His
4. Left bundle branch
5. left posterior fascicle
6. left-anterior fascicle
7. Left ventricle
8. Ventricular septum
9. Right ventricle
10. Right bundle branch

Latin *systema conducens cordis*



Principle of ECG formation. Note that the red lines represent the depolarization wave, not blood flow.

The normal electrical conduction of the heart allows electrical propagation to be transmitted from the Sinoatrial Node through both atria and forward to the Atrioventricular Node. Normal/baseline physiology allows further propagation from the AV node to the Ventricle or Purkinje Fibers and respective bundle branches and subdivisions/fascicles. Both the SA and AV nodes stimulate the Myocardium. Time ordered stimulation of the myocardium allows efficient contraction of all four chambers of the heart, thereby allowing selective blood perfusion through both the lungs and systemic circulation.

Electrochemical mechanism

Cardiac neurons innervating the myocardium bear limited similarities to those of skeletal muscle as well as other important differences. Cardiac neurons are uniquely subject to influence by the sympathetic and parasympathetic influence of the autonomic nervous system unlike skeletal muscle.

Like a neuron, a given myocardial cell has a negative membrane potential when at rest. Stimulation above a threshold value induces the opening of voltage-gated ion channels with inducted flow of cations into the cell. The positively charged ions entering the cell cause the depolarization characteristic of an action potential. After depolarization, there's a brief repolarization that takes place with the eflux of potassium through fast acting potassium channels. Like skeletal muscle, depolarization causes the opening of voltage-gated calcium channels - meanwhile potassium channels have closed - and are followed by a titrated release of Ca^{2+} from the t-tubules. This influx of calcium causes calcium-induced calcium release from the sarcoplasmic reticulum, and free Ca^{2+} causes muscle contraction. After a delay, slow acting Potassium channels reopen and the resulting flow of K^{+} out of the cell causes repolarization to the resting state.

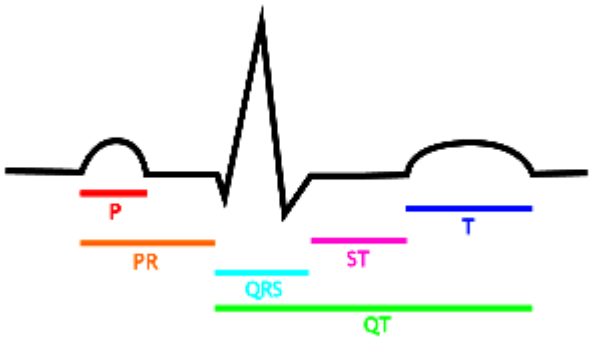
Note that there are important physiological differences between nodal cells and ventricular cells; the specific differences in ion channels and mechanisms of polarization give rise to unique properties of SA node cells, most importantly the spontaneous depolarizations necessary for the SA node's pacemaker activity. ..

Conduction pathway

Signals arising in the SA node (and propagating to the left atrium via Bachmann's bundle) stimulate the atria to contract. In parallel, action potentials travel to the AV node via internodal pathways. After a delay, the stimulus is conducted through the bundle of His to the bundle branches and then to the purkinje fibers and the endocardium at the apex of the heart, then finally to the ventricular myocardium.

Microscopically, the wave of depolarization propagates to adjacent cells via gap junctions located on the intercalated disk. The heart is a *functional syncytium* (not to be confused with a true "syncytium" in which all the cells are fused together, sharing the same plasma membrane as in skeletal muscle). In a functional syncytium, electrical impulses propagate freely between cells in every direction, so that the myocardium functions as a single contractile unit. This property allows rapid, synchronous depolarization of the myocardium. While normally advantageous, this property can be detrimental as it potentially allows the propagation of incorrect electrical signals. These gap junctions can close to isolate damaged or dying tissue, as in a myocardial infarction.

Depolarization and the ECG



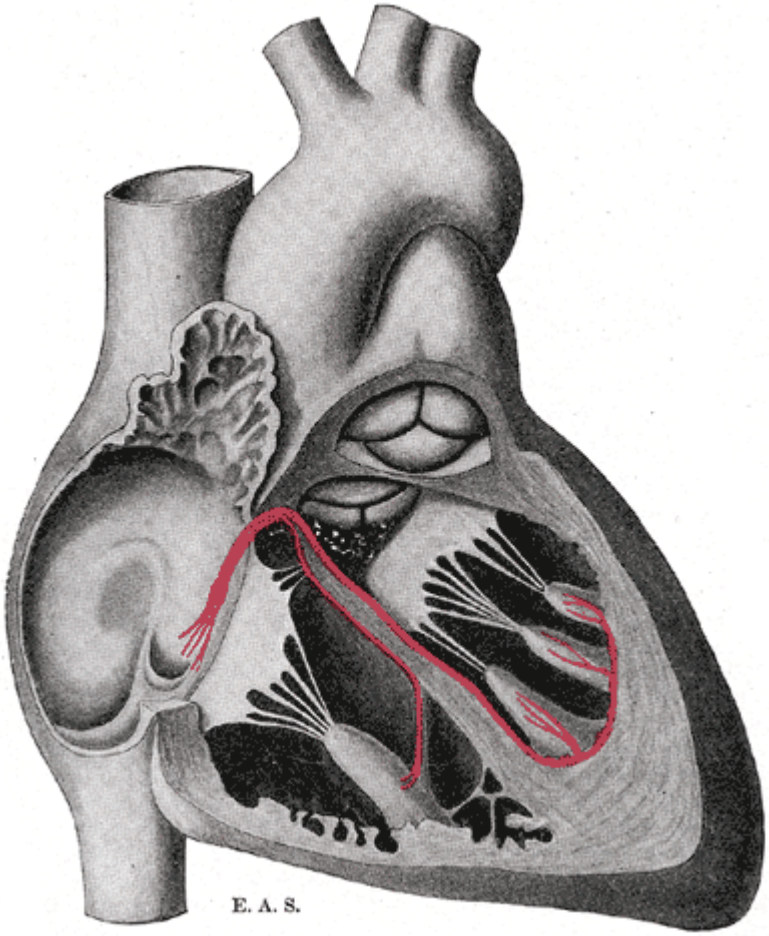
The ECG complex. P=P wave, PR=PR interval, QRS=QRS complex, QT=QT interval, ST=ST segment, T=T wave

SA node: P wave

Under normal conditions, electrical activity is spontaneously generated by the SA node, the physiological pacemaker. This electrical impulse is propagated throughout the right atrium, and through Bachmann's bundle to the left atrium, stimulating the myocardium of both atria to contract. The conduction of the electrical impulse throughout the left and right atria is seen on the ECG as the **P wave**.

As the electrical activity is spreading throughout the atria, it travels via specialized pathways, known as *internodal tracts*, from the SA node to the AV node.

AV node/Bundles: PR interval



The AV node functions as a critical delay in the conduction system. Without this delay, the atria and ventricles would contract at the same time, and blood wouldn't flow effectively from the atria to the ventricles. The delay in the AV node forms much of the **PR segment** on the ECG. Part of atrial repolarization can be represented by the PR segment.

The distal portion of the AV node is known as the bundle of His. The bundle of His splits into two branches in the interventricular septum, the left bundle branch and the right bundle branch. The left bundle branch activates the left ventricle, while the right bundle branch activates the right ventricle. The left bundle branch is short, splitting into the left anterior fascicle and the left posterior fascicle. The left posterior fascicle is relatively short and broad, with dual blood supply, making it particularly resistant to ischemic damage. The left posterior fascicle transmits impulses to the papillary muscles, leading to mitral valve closure. As the left posterior fascicle is shorter and broader than the right, impulses reach the papillary muscles just prior to depolarization, and therefore contraction, of the left ventricle myocardium. This allows pre-tensioning of the chordae tendinae, increasing the resistance to flow through the mitral valve during left ventricular contraction.

Purkinje fibers/ventricular myocardium: QRS complex

The two bundle branches taper out to produce numerous purkinje fibers, which stimulate individual groups of myocardial cells to contract.

The spread of electrical activity (depolarization) through the ventricular myocardium produces the QRS complex on the ECG.

Ventricular repolarization: T wave

The last event of the cycle is the repolarization of the ventricles. The transthoracically measured PQRS portion of an electrocardiogram is chiefly influenced by the sympathetic nervous system. The T (and occasionally U) waves are chiefly influenced by the parasympathetic nervous system guided by integrated brainstem control from the vagus nerve and the thoracic spinal accessory ganglia.

An impulse (action potential) that originates from the SA node at a relative rate of 60 - 100bpm is known as *normal sinus rhythm*. If SA nodal impulses occur at a rate less than 60bpm, the heart rhythm is known as sinus bradycardia. If SA nodal impulses occur at a rate exceeding 100bpm, the consequent rapid heart rate is sinus tachycardia. These conditions are not necessarily bad symptoms, however. Trained athletes, for example, usually show heart rates slower than 60bpm when not exercising. If the SA node fails to initialize, the AV junction can take over as the main pacemaker of the heart. The AV junction consists of the AV node, the bundle of His and the surrounding area; it has a regular rate of 40 to 60bpm. These "junctional" rhythms are characterized by a missing or inverted P-Wave. If both the SA node and the AV junction fail to initialize the electrical impulse, the ventricles can fire the electrical impulses themselves at a rate of 20 to 40bpm and will have a QRS complex of greater than 120ms.

Embryologic evidence

Embryologic evidence of generation of the cardiac conduction system illuminates the respective roles of this specialized set of cells. Innervation of the heart begins with a brain only centered parasympathetic cholinergic first order. It is then followed by rapid growth of a second order sympathetic adrenergic system arising from the formation of the Thoracic Spinal Ganglia. The third order of electrical influence of the heart is derived from the Vagus Nerve as the other peripheral organs form.

Chapter 14

Cardiac Action Potential

The **cardiac action potential** is a specialized action potential in the heart, necessary for the electrical conduction system of the heart.

The cardiac action potential differs significantly in different portions of the heart. This differentiation of the action potentials allows the different electrical characteristics of the different portions of the heart. For instance, the specialized conduction tissue of the heart has the special property of depolarizing without any external influence. This is known as cardiac muscle automaticity.

The electrical activity of the specialized conduction tissues are not apparent on the surface electrocardiogram (ECG or EKG - From German word). This is due to the relatively small mass of these tissues compared to the myocardium.

Overview

Intra- and extracellular ion concentrations (mmol/L)				
Element	**Ion**	**Extracellular**	**Intracellular**	**Ratio**
Sodium	Na^+	135 - 145	10	14:1
Potassium	K^+	3.5 - 5.0	155	1:30
Chloride	Cl^-	95 - 110	10 - 20	4:1
Calcium	Ca^{2+}	2	10^{-4}	2 x 10^4:1
Although intracellular Ca^{2+} content is about 2 mM, most of this is bound or sequestered in intracellular organelles (mitochondria and sarcoplasmic reticulum).				

Cardiac muscle has some similarities to skeletal muscle, as well as important unique properties. Like skeletal myocytes (and axons for that matter), a given cardiac myocyte has a negative membrane potential when at rest. A notable difference between skeletal and cardiac myocytes is how each elevates the myoplasmic Ca^{2+} to induce contraction. When skeletal muscle is stimulated by somatic motor axons, influx of Na^+ quickly depolarizes the skeletal myocyte and triggers calcium release from the sarcoplasmic reticulum. In cardiac myocytes, the release of Ca^{2+} from the sarcoplasmic reticulum is induced by Ca^{2+} influx into the cell through voltage-gated calcium channels on the

sarcolemma. This phenomenon is called calcium-induced calcium release and increases the myoplasmic free Ca^{2+} concentration causing muscle contraction. In both muscle types, after a delay (the absolute refractory period), potassium channels reopen and the resulting flow of K^+ out of the cell causes repolarization to the resting state. The voltage-gated calcium channels in the cardiac sarcolemma are generally triggered by an influx in sodium during the "0" phase of the action potential.

Note that there are important physiological differences between nodal cells and ventricular cells; the specific differences in ion channels and mechanisms of polarization give rise to unique properties of SA node cells, most importantly the spontaneous depolarizations (cardiac muscle automaticity) necessary for the SA node's pacemaker activity.

Major currents

Major currents during the cardiac ventricular action potential

Ion	Current (*I*=ion channel)	α subunit protein	α subunit gene	Phase / role
Na^+	I_{Na}	$Na_V1.5$	SCN5A	0
Ca^{2+}	$I_{Ca(L)}$	$Ca_V1.2$	CACNA1C	0-2
K^+	I_{to1}	$K_V4.2/4.3$	KCND2/KCND3	1, notch
K^+	I_{Ks}	$K_V7.1$	KCNQ1	2,3
K^+	I_{Kr}	$K_V11.1$ (hERG)	KCNH2	3
K^+	I_{K1}	$K_{ir}2.1/2.2/2.3$	KCNJ2/KCNJ12/KCNJ4	3,4
Na^+, Ca^{2+}	I_{NaCa}	$3Na^+$-$1Ca^{2+}$-exchanger	*NCX1* (SLC8A1)	ion homeostasis
Na^+, K^+	I_{NaK}	$3Na^+$-$2K^+$-ATPase	*ATP1A*	ion homeostasis
Ca^{2+}	I_{pCa}	Ca^{2+}-transporting ATPase	*ATP1B*	ion homeostasis

Calcium channels

Two voltage-dependent calcium channels play critical roles in the physiology of cardiac muscle: L-type calcium channel ('L' for Long-lasting) and T-type calcium channels ('T' for Transient) voltage-gated calcium channels.

These channels respond differently to voltage changes across the membrane: L-type channels respond to higher membrane potentials, open more slowly, and remain open longer than T-type channels.

Because of these properties, L-type channels are important in *sustaining* an action potential, while T-type channels are important in *initiating* them.

Because of their rapid kinetics, T-type channels are commonly found in cells undergoing rhythmic electrical behavior. For example, T-type channels are commonly found in some neuron cell bodies involved in rhythmic activity such as walking and breathing. These T-type calcium channels are also found in pacemaker cells (i.e. sinoatrial node and atrioventricular node) of the heart which control the heart beat.

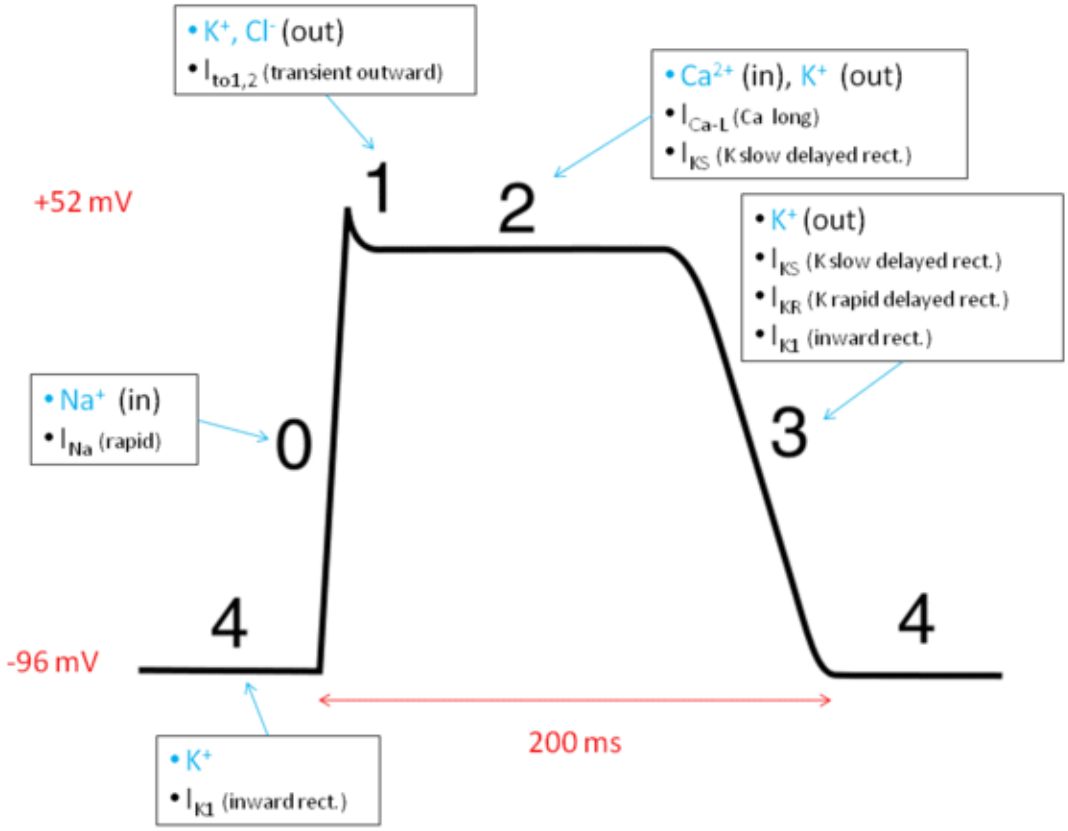
L-type channels are the targets of a class of drugs called dihydropyridines which block the currents produced by these channels.

Resting membrane potential

The resting membrane potential is caused by the difference in ionic concentrations and conductances across the membrane of the cell during phase 4 of the action potential. The normal resting membrane potential in the ventricular myocardium is about -85 to -95 mV. This potential is determined by the selective permeability of the cell membrane to various ions. The membrane is most permeable to K^+ and relatively impermeable to other ions. The resting membrane potential is therefore dominated by the K^+ equilibrium potential according to the K^+ gradient across the cell membrane. The membrane potential can be calculated using the Goldman-Hodgkin-Katz voltage equation. The maintenance of this electrical gradient is due to various ion pumps and exchange mechanisms, including the Na^+-K^+ ion exchange pump, the Na^+-Ca^{2+} exchanger current and the I_{K1} (I=ion channel) inwardly rectifying K^+ current.

Intracellularly (within the cell), K^+ is the principal cation, and phosphate and the conjugate bases of organic acids are the dominant anions. Extracellularly (outside the cell), Na^+ and Cl^- predominate.

Phases of the cardiac action potential



The cardiac action potential has five phases.

The standard model used to understand the cardiac action potential is the action potential of the ventricular myocyte. The action potential has 5 phases (numbered 0-4). Phase 4 is the resting membrane potential, and describes the membrane potential when the cell is not being stimulated.

Once the cell is electrically stimulated (typically by an electric current from an adjacent cell), it begins a sequence of actions involving the influx and efflux of multiple cations and anions that together produce the action potential of the cell, propagating the electrical stimulation to the cells that lie adjacent to it. In this fashion, an electrical stimulation is conducted from one cell to all the cells that are adjacent to it, to all the cells of the heart.

Phase 4

Phase 4 is the resting membrane potential. This is the period that the cell remains in until it is stimulated by an external electrical stimulus (typically an adjacent cell). This phase of the action potential is associated with diastole of the chamber of the heart.

In addition to stimulus from adjacent cells, certain cells of the heart have the ability to undergo *spontaneous depolarization*, in which an action potential is generated without any influence from nearby cells. This is known as cardiac muscle automaticity.

Phase 0

Phase 0 is the rapid depolarization phase. The slope of phase 0 represents the maximum rate of depolarization of the cell and is known as dV/dt_{max}. This phase is due to the opening of the fast Na^+ channels causing a rapid increase in the membrane conductance to Na^+ (G_{Na}) and thus a rapid influx of Na^+ ions (I_{Na}) into the cell; a Na^+ current.

The ability of the cell to open the fast Na^+ channels during phase 0 is related to the membrane potential at the moment of excitation. If the membrane potential is at its baseline (about -85 mV), all the fast Na^+ channels are closed, and excitation will open them all, causing a large influx of Na^+ ions. If, however, the membrane potential is less negative, some of the fast Na^+ channels will be in an inactivated state insensitive to opening, thus causing a lesser response to excitation of the cell membrane and a lower V_{max}. For this reason, if the resting membrane potential becomes too positive, the cell may not be excitable, and conduction through the heart may be delayed, increasing the risk for arrhythmias.

The fast Na^+ channel

The fast sodium channel can be modeled as being controlled by a number of *gates*. Each gate (or gating variable) can attain a value between 1 (fully open) and 0 (fully closed). The product of all the gates denotes the percentage of channels available to conduct Na^+. Following the model of Hodgkin and Huxley, the sodium channel contains three gates: *m*, *h*, and *j*. In the resting state, the *m* gate is closed (zero) and the *h* and *j* gates are open (one). Hence, the product denoting the percentage of conducting channels is also zero. Upon electrical stimulation of the cell, the *m* gate opens quickly while simultaneously the *h* and *j* gates close more slowly. For a brief period of time, all gates are open (*i.e.* non-zero) and Na^+ can enter the cell following its electrochemical gradient. If, as above, the resting membrane potential is too positive, the *h* or *j* gates may be considerably less than one, such that the product of *m*, *h* and *j* becomes too small upon depolarization.

Phase 1

Phase 1 of the action potential occurs with the inactivation of the fast Na^+ channels. The transient net outward current causing the small downward deflection of the action potential is due to the movement of K^+ and Cl^- ions, carried by the I_{to1} and I_{to2} currents, respectively. Particularly the I_{to1} contributes to the "notch" of some ventricular cardiomyocyte action potentials.

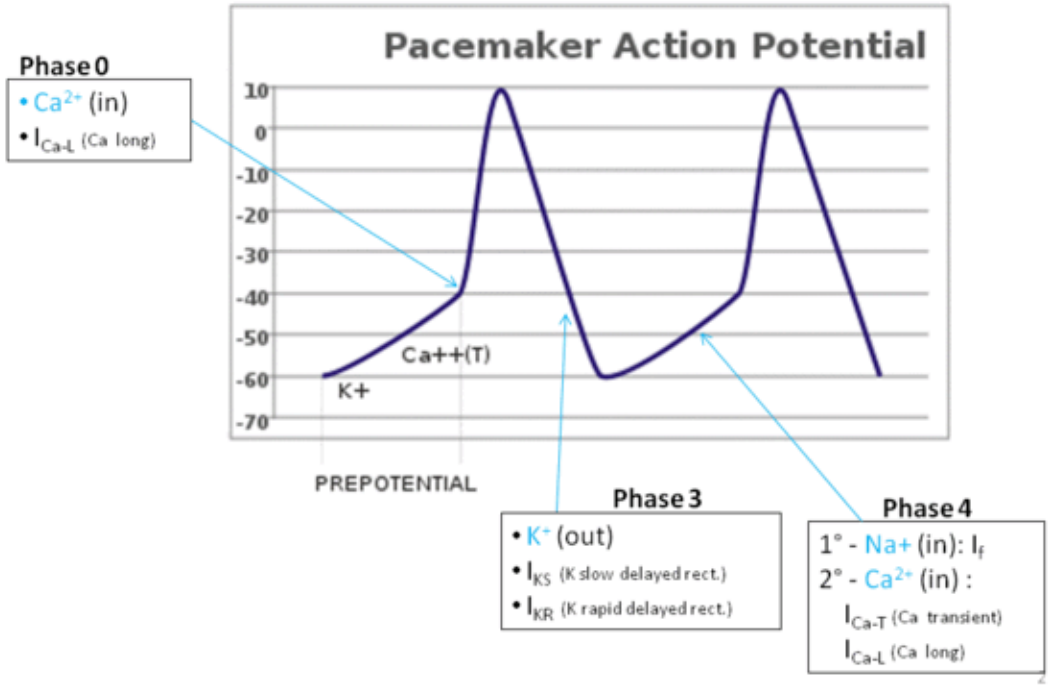
It has been suggested that Cl^- ions movement across the cell membrane during Phase I is as a result of the change in membrane potential, from K^+ efflux, and is not a contributory factor to the initial repolarization ("notch").

Phase 2

This "plateau" phase of the cardiac action potential is sustained by a balance between inward movement of Ca^{2+} (I_{Ca}) through L-type calcium channels and outward movement of K^+ through the slow delayed rectifier potassium channels, I_{Ks}. The sodium-calcium exchanger current, $I_{Na,Ca}$ and the sodium/potassium pump current, $I_{Na,K}$ also play minor roles during phase 2.

Phase 3

During phase 3 (the "rapid repolarization" phase) of the action potential, the L-type Ca^{2+} channels close, while the slow delayed rectifier (I_{Ks}) K^+ channels are still open. This ensures a net outward current, corresponding to negative change in membrane potential, thus allowing more types of K^+ channels to open. These are primarily the rapid delayed rectifier K^+ channels (I_{Kr}) and the inwardly rectifying K^+ current, I_{K1}. This net outward, positive current (equal to loss of positive charge from the cell) causes the cell to repolarize. The delayed rectifier K^+ channels close when the membrane potential is restored to about -80 to -85 mV, while I_{K1} remains conducting throughout phase 4, contributing to set the resting membrane potential.



Automaticity

In the myocardium, automaticity is the ability of the cardiac muscles to depolarize spontaneously, i.e without external electrical stimulation from the nervous system. This spontaneous depolarization is due to the plasma membranes within the heart that have reduced permeability to potassium (K+) but still allow passive transfer of calcium ions, allowing a net charge to build. Automaticity is most often demonstrated in the sinoatrial node, the so called "Pacemaker of the Heart." Abnormalities in automaticity result in rhythm changes.

Location

The cells that can undergo spontaneous depolarization the fastest are the primary pacemaker cells of the heart, and set the heart rate. Usually, these are cells in the SA node of the heart. Electrical activity that originates from the SA node is propagated to the rest of the heart. The fastest conduction of electrical activity is via the electrical conduction system of the heart.

Channels

The mechanism of automaticity involves the so-called pacemaker channels of the HCN family, Hyperpolarization-activated, Cyclic Nucleotide-gated channels. These poorly selective cation channels conduct more current as the membrane potential becomes more negative, or hyperpolarized. They conduct both potassium and sodium ions. The activity of these channels in the SA node cells causes the membrane potential to slowly become more positive (depolarize). These "Funny" channels are responsible for the initial phase of the "prepotential". The latter phase is due to the opening of "T" or "Transient" calcium channels. This further depolarizes the cell until, eventually, the "L" or "Long Lasting" calcium channels are activated and an action potential is initiated.

Abnormal automaticity

The normal activity of the pacemaker cells of the heart is to spontaneously depolarize at a regular rhythm, generating the normal heart rate. Abnormal automaticity involves the abnormal spontaneous depolarization of cells of the heart. This typically causes arrhythmias (irregular rhythms) in the heart.

In cases of heart block, in which the activity of the primary pacemaker does not propagate to the rest of the heart, a latent pacemaker (also known as an escape pacemaker) will undergo spontaneous depolarization and create an action potential.

Regulation by the autonomic nervous system

The rate of depolarization and duration of the action potential in pacemaker cells is regulated by the parasympathetic and sympathetic fibres of the autonomic nervous system in addition to circulating catecholamines. Acetylcholine (ACh) binds to M2

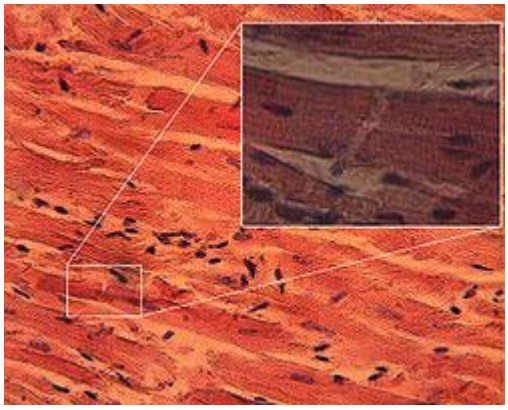
(muscarinic) receptors and, via the βγ subunit of a G protein, open a special set of potassium channels. The resulting increase in potassium efflux slows the depolarizing effect of the funny channels. In addition, activation of M2 receptors decreases cAMP in the cells and this slows the opening of the calcium "L" channels. The result is a drcrease in the firing rate.

Conversely, sympathetic stimulation via β1 receptors results in an increase in cAMP levels which facilitates the opening of calcium channels thereby increasing the rate of depolarization.

Chapter 15

Cardiac Muscle

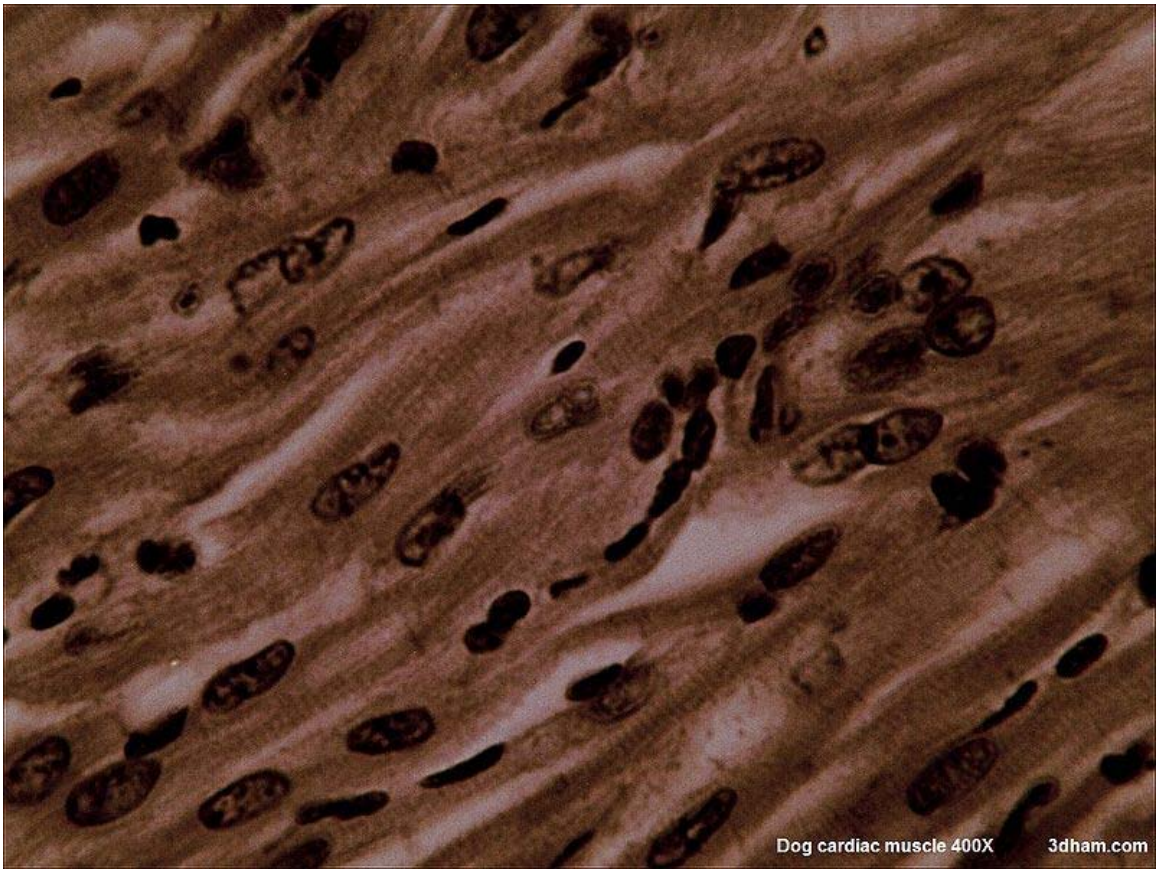
cardiac muscle



Cardiac muscle is a type of involuntary striated muscle found in the walls and histologic foundation of the heart, specifically the myocardium. Cardiac muscle is one of three major types of muscle, the others being skeletal and smooth muscle. The cells that comprise cardiac muscle, called myocardiocyteal muscle cells, are mononuclear, like smooth muscle cells.

Coordinated contractions of cardiac muscle cells in the heart propel blood out of the atria and ventricles to the blood vessels of the left/body/systemic and right/lungs/pulmonary circulatory systems. This complex of actions makes up the systole of the heart.

Cardiac muscle cells, like all tissues in the body, rely on an ample blood supply to deliver oxygen and nutrients and to remove waste products such as carbon dioxide. The coronary arteries fulfill this function.



Dog Cardiac Muscle 400X

Metabolism

Cardiac muscle is adapted to be highly resistant to fatigue: it has a large number of mitochondria, enabling continuous aerobic respiration via oxidative phosphorylation, numerous myoglobins (oxygen-storing pigment) and a good blood supply, which provides nutrients and oxygen. The heart is so tuned to aerobic metabolism that it is unable to pump sufficiently in ischaemic conditions. At basal metabolic rates, about 1% of energy is derived from anaerobic metabolism. This can increase to 10% under moderately hypoxic conditions, but, under more severe hypoxic conditions, not enough energy can be liberated by lactate production to sustain ventricular contractions.

Under basal aerobic conditions, 60% of energy comes from fat (free fatty acids and triglycerides), 35% from carbohydrates, and 5% from amino acids and ketone bodies. However, these proportions vary widely according to nutritional state. For example, during starvation, lactate can be recycled by the heart. This is very energy efficient, because one NAD^+ is reduced to NADH and H^+ (equal to 2.5 or 3 ATP) when lactate is oxidized to pyruvate, which can then be burned aerobically in the TCA cycle, liberating much more energy (ca 14 ATP per cycle).

In the condition of diabetes, more fat and less carbohydrate is used due to the reduced induction of GLUT4 glucose transporters to the cell surfaces. However, contraction itself plays a part in bringing GLUT4 transporters to the surface. This is true of skeletal muscle as well, but relevant in particular to cardiac muscle due to its continuous contractions.

Appearance

Striation

Cardiac muscle exhibits cross striations formed by alternating segments of thick and thin protein filaments. Like skeletal muscle, the primary structural proteins of cardiac muscle are actin and myosin. The actin filaments are thin causing the lighter appearance of the I bands in striated muscle, while the myosin filament is thicker lending a darker appearance to the alternating A bands as observed with electron microscopy. However, in contrast to skeletal muscle, cardiac muscle cells may be branched instead of linear and longitudinal.

T-Tubules

Another histological difference between cardiac muscle and skeletal muscle is that the T-tubules in the cardiac muscle are larger, broader and run along the Z-Discs. There are fewer T-tubules in comparison with skeletal muscle. Additionally, cardiac muscle forms diads instead of the triads formed between the T-tubules and the sarcoplasmic reticulum in skeletal muscle. T-tubules play critical role in excitation-contraction coupling (ECC). Recently, the action potentials of T-tubules were recorded optically by Guixue Bu et al.

Intercalated discs

Intercalated discs (IDs) are complex adhering structures which connect single cardiac myocytes to an electrochemical syncytium (in contrast to the skeletal muscle, which becomes a multicellular syncytium during mammalian embryonic development) and are mainly responsible for force transmission during muscle contraction. Intercalated discs also support the rapid spread of action potentials and the synchronized contraction of the myocardium. IDs are described to consist of three different types of cell-cell junctions: the actin filament anchoring adherens junctions (fascia adherens), the intermediate filament anchoring desmosomes (macula adherens) and gap junctions. Gap junctions are responsible for electrochemical and metabolic coupling. They allow action potentials to spread between cardiac cells by permitting the passage of ions between cells, producing depolarization of the heart muscle. However, novel molecular biological and comprehensive studies unequivocally showed that IDs consist for the most part of mixed type adhering junctions named *area composita* (pl. *areae compositae*) representing an amalgamation of typical desmosomal and *fascia adhaerens* proteins (in contrast to various epithelia). The authors discuss the high importance of these findings for the understanding of inherited cardiomyopathies (such as Arrhythmogenic Right Ventricular Cardiomyopathy, ARVC).

Under light microscopy, intercalated discs appear as thin, typically dark-staining lines dividing adjacent cardiac muscle cells. The intercalated discs run perpendicular to the direction of muscle fibers. Under electron microscopy, an intercalated disc's path appears more complex. At low magnification, this may appear as a convoluted electron dense structure overlying the location of the obscured Z-line. At high magnification, the intercalated disc's path appears even more convoluted, with both longitudinal and transverse areas appearing in longitudinal section.

Role of calcium in contraction

In contrast to skeletal muscle, cardiac muscle requires *extracellular calcium ions* for contraction to occur. Like skeletal muscle,the initiation and upshoot of the action potential in ventricular muscle cells is derived from the entry of sodium ions across the sarcolemma in a regenerative process. However, an inward flux of extracellular calcium ions through L-type calcium channels sustains the depolarization of cardiac muscle cells for a longer duration. The reason for the calcium dependence is due to the mechanism of calcium-induced calcium release (CICR) from the sarcoplasmic reticulum that must occur under normal excitation-contraction (EC) coupling to cause contraction. Once the intracellular concentration of calcium increases, calcium ions bind to the protein troponin, which initiates contraction by allowing the contractile proteins, myosin and actin to associate through cross-bridge formation. Cardiac muscle is intermediate between smooth muscle, which has an unorganized sarcoplasmic reticulum and derives its calcium from both the extracellular fluid and intracellular stores, and skeletal muscle, which is only activated by calcium stored in the sarcoplasmic reticulum.

Regeneration of heart muscle cells

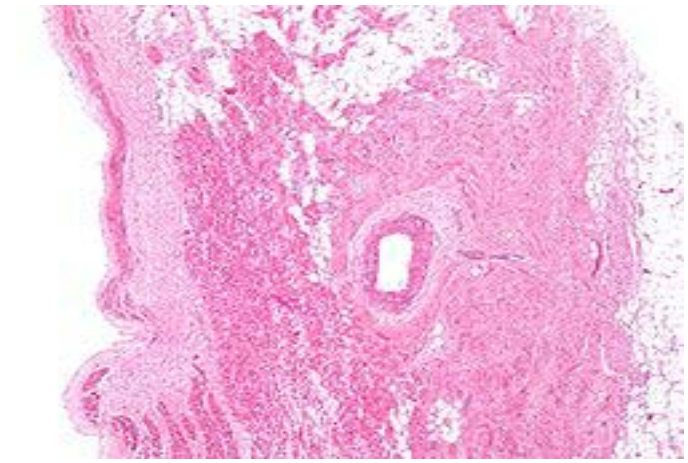
Until recently, it was commonly believed that cardiac muscle cells could not be regenerated. However, a study reported in the April 3, 2009 issue of *Science* contradicts that belief. Olaf Bergmann and his colleagues at the Karolinska Institute in Stockholm tested samples of heart muscle from people born before 1955 when nuclear bomb testing caused elevated levels of radioactive carbon 14 in the Earth's atmosphere. They found that samples from people born before 1955 did have elevated carbon 14 in their heart muscle cell DNA, indicating that the cells had divided after the person's birth. By using DNA samples from many hearts, the researchers estimated that a 20-year-old renews about 1% of heart muscle cells per year and about 45 percent of the heart muscle cells of a 50-year-old were generated after he or she was born.

Chapter 16

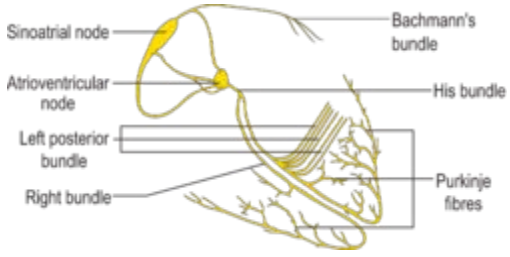
Sinoatrial Node & Bachmann's Bundle

Sinoatrial Node

Sinoatrial node



Low magnification micrograph of a **sinoatrial node** (center-right on image) and its surrounding tissue. The SA node surrounds the (sinuatrial) nodal artery (on lumen in the image), a branch of the right coronary artery, abuts cardiac myocytes (of the right atrium) on its deep aspect (left of image) and adipose tissue on its superficial (epicardial) aspect (right of image). H&E stain.



Isolated Heart conduction system, showing SA node

Latin	*nodus sinuatrialis*
Artery	sinuatrial nodal artery
MeSH	*Sinoatrial+Node*

The **sinoatrial node** (also commonly spelled **sinuatrial node**, abbreviated **SA node** or **SAN**, also called the **sinus node**) is the impulse-generating (pacemaker) tissue located in the right atrium of the heart, and thus the generator of normal sinus rhythm. It is a group of cells positioned on the wall of the right atrium, near the entrance of the superior vena cava. These cells are modified cardiac myocytes. Though they possess some contractile filaments, they do not contract.

It was first described in 1907 by Arthur Keith and Martin Flack.

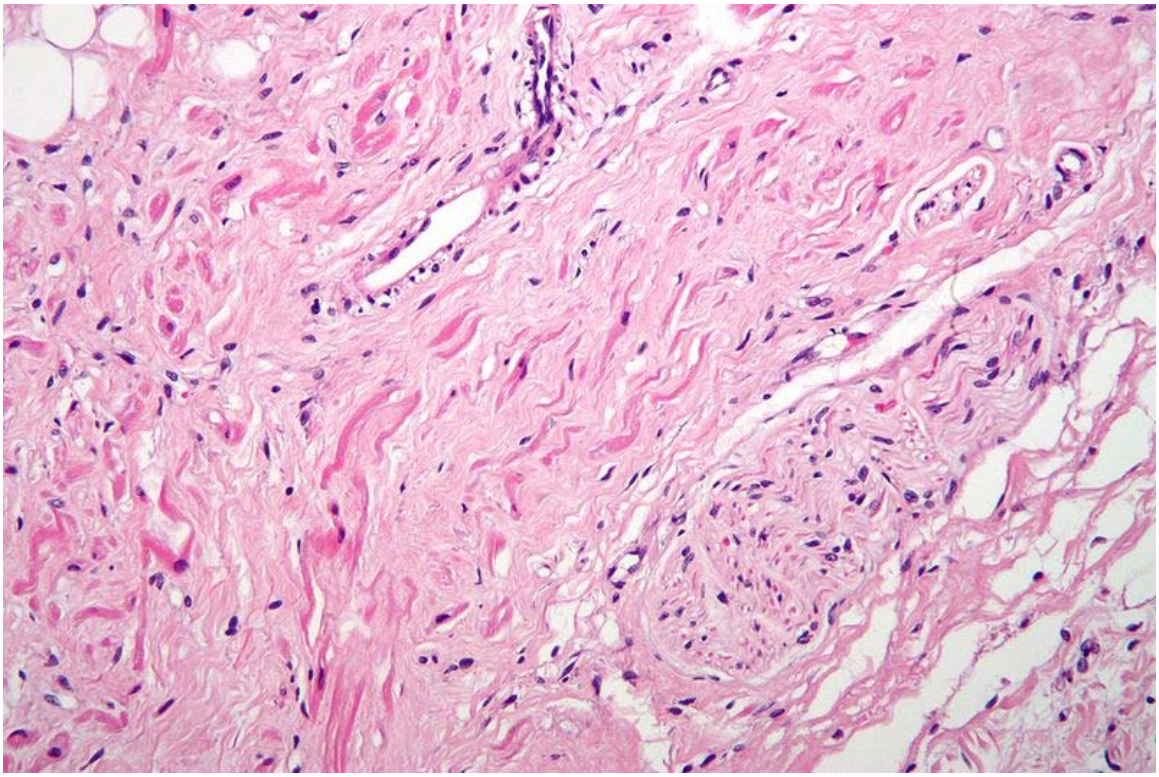
Role as a pacemaker

Although all of the heart's cells have the ability to generate the electrical impulses (or action potentials) that trigger cardiac contraction, the sinoatrial node normally initiates it, simply because it generates impulses slightly faster than the other areas with pacemaker potential. Cardiac myocytes, like all muscle cells, have refractory periods following contraction during which additional contractions cannot be triggered; their pacemaker potential is overridden by the sinoatrial or atrioventricular nodes.

In the absence of extrinsic neural and hormonal control, cells in the SA node, situated in the upper right corner of the heart, will naturally discharge (create action potentials) at about 60-100 beats/minute. Because the sinoatrial node is responsible for the rest of the heart's electrical activity, it is sometimes called the primary pacemaker.

If the SA node does not function, or the impulse generated in the SA node is blocked before it travels down the electrical conduction system, a group of cells further down the heart will become the heart's pacemaker. These cells form the atrioventricular node (AV node), which is an area between the atria and ventricles, within the atrial septum. If the AV node also fails, Purkinje fibers are capable of acting as the pacemaker. The reason Purkinje cells do not normally control the heart rate is that they generate action potentials at a lower frequency than the AV or SA nodes.

Histology



High magnification micrograph of **sinoatrial node** tissue and an adjacent nerve fibre. H&E stain.

The sinoatrial node is submyocardial at the lateral aspect of the junction of the superior vena cava and right atrium. Its deep aspect abuts cardiac myocytes belonging to the right atrium. Its superficial aspect is covered by adipose tissue. The SA node fibres vaguely resemble cardiac myocytes; however, they are measurably thinner, more tortuous and stain less intensely (on H&E) than cardiac myocytes.

Innervation

The SA node is richly innervated by parasympathetic nervous system fibers (CN X: Vagus Nerve) and by sympathetic nervous system fibers (T1-4, Spinal Nerves). This unique anatomical arrangement confers the SA node susceptible to distinctly paired and opposed autonomic influences.

- Stimulation of the vagus nerves (the parasympathetic fibers) causes a *decrease* in the SA node rate (thereby *decreasing* the heart rate). Parasympathetic fibers cannot change the force of contraction, however,because they only innervate the SA node and AV node.
- Stimulation via sympathetic fibers causes an *increase* in the SA node rate (thereby *increasing* the heart rate and force of contraction). Sympathetic fibers *can*

increase the force of contraction because in addition to innervating the SA and AV nodes, they innervate the atria and ventricles themselves.

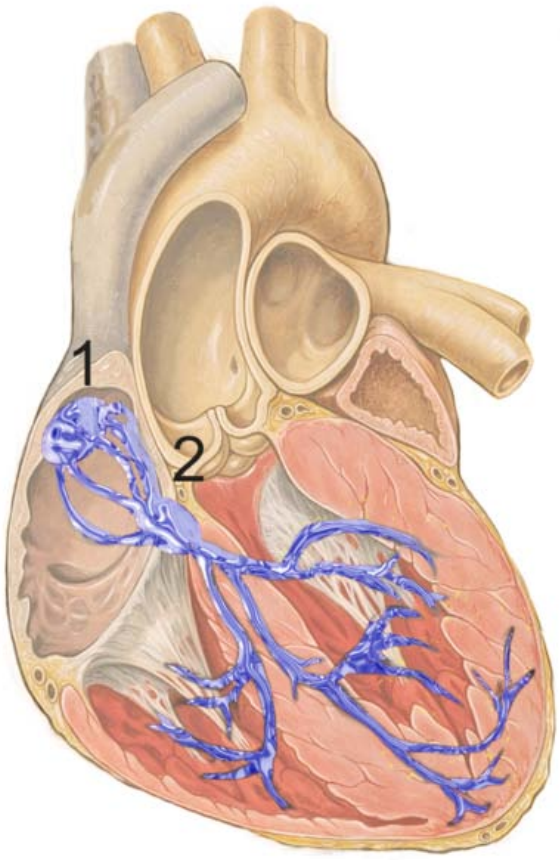
Blood supply

In the majority of individuals, the SA node receives blood from the right coronary artery, meaning that a myocardial infarction occluding it will cause ischaemia in the SA node unless there is a sufficiently good anastomosis from the left coronary artery. If not, death of the affected cells will stop the SA node from triggering the heartbeat, and pacemaker function will be manifest more distal in the cardiac system (eg. AV node).

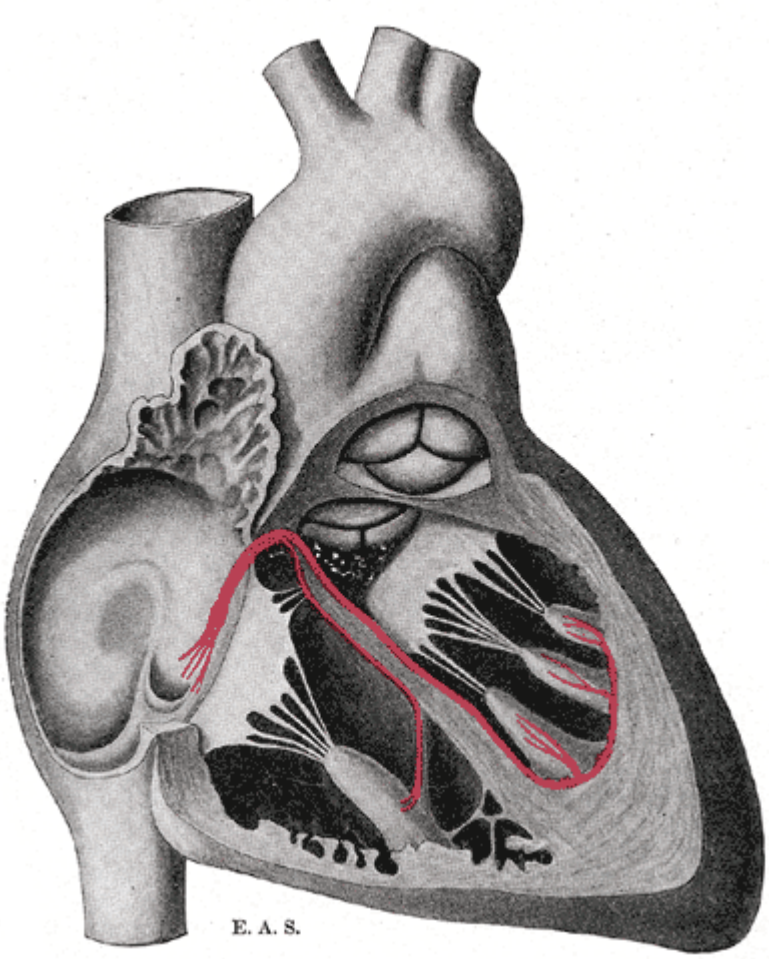
Sinus node dysfunction

Sinus node dysfunction describes an irregular heartbeat caused by faulty electrical signals of the heart. When the heart's sinoatrial node is defective, the heart's rhythms become abnormal – either too fast, too slow, or a combination.

Additional images



Heart; conduction system



Schematic representation of the atrioventricular bundle

Bachmann's Bundle

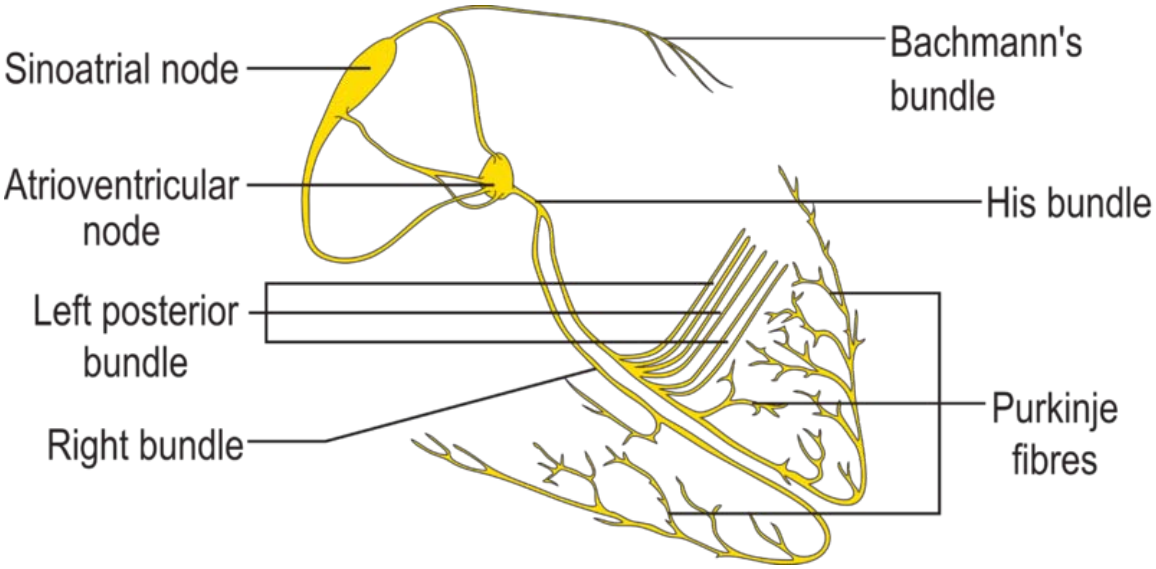


Image showing Bachmann's bundle

Bachmann's bundle, also known as the anterior interatrial band, is one of the four conduction tracts that make up the *atrial conduction system* of the heart which is responsible for transmitting the pacemaking impulses of the sinoatrial node to the rest of the heart. **Bachmann's bundle** originates in the sinoatrial node and is the only tract that conducts action potentials to the left atrium.

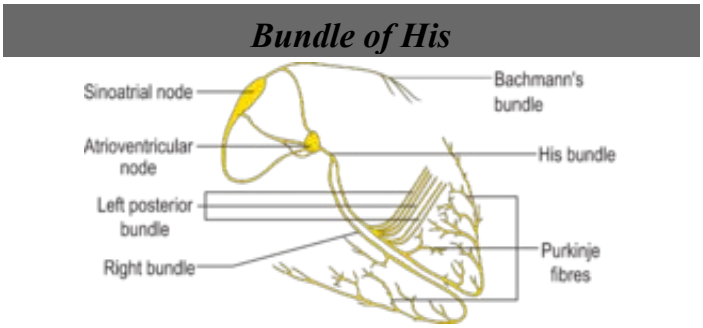
Bachmann's bundle and the atrial conduction system

Besides **Bachmann's bundle**, the other three conduction tracts are known as the anterior, middle, and posterior tracts, which run from the Sinoatrial Node to the atrioventricular node, converging in the region near the coronary sinus. *Atrial automaticity foci* are within the atrial conduction system. The concentration of converging conduction tracts near the coronary sinus results in considerable automaticity activity originating in that area.

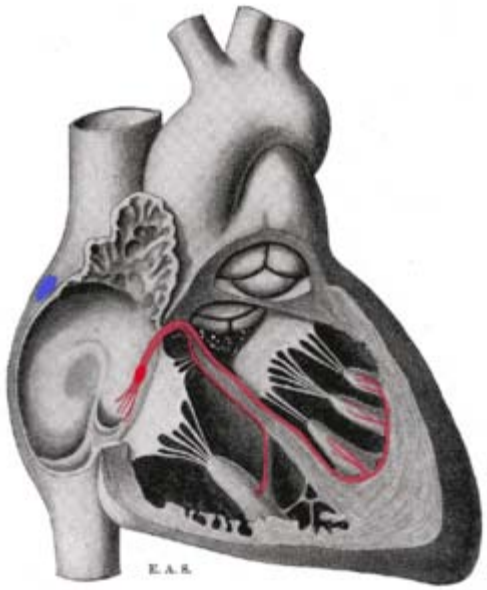
Chapter 17

Bundle of His & Purkinje Fibers

Bundle of His



Isolated Heart conduction system showing Bundle of His



Heart cut away showing Bundle of His

Schematic representation of the atrioventricular bundle of His. The bundle, represented in red, originates near the

orifice of the coronary sinus, undergoes slight enlargement to form the AV node. The AV node tapers down into the bundle of His, which passes into the ventricular septum and divides into two bundle branches, the left and right bundles. Sometimes the 'left and right bundles of His' are called Purkyně or Purkinje fibres. The ultimate distribution cannot be completely shown in this diagram.

Latin *fasciculus atrioventricularis*

The **bundle of His**, known as the AV bundle or atrioventricular bundle, is a collection of heart muscle cells specialized for electrical conduction that transmits the electrical impulses from the AV node (located between the atria and the ventricles) to the point of the apex of the fascicular branches. The fascicular branches then lead to the Purkinje fibers which provide electrical conduction to the ventricles, causing the cardiac muscle of the ventricles to contract at a paced interval.

Eponym

These specialized muscle fibres in the heart were named after the Swiss cardiologist Wilhelm His, Jr., who discovered them in 1893.

Function

This bundle is an important part of the electrical conduction system of the heart as it transmits the impulse from the sinoatrial (SA) node (pacemaker) located in the right atrium to the rest of the heart. The intrinsic rate of the Bundle of His is between 40 - 60 bpm. The bundle of His branches into the three bundle branches: the right, left anterior and left posterior bundle branches that run along the interventricular septum. The bundles give rise to thin filaments known as Purkinje fibers. These fibers distribute the impulse to the ventricular muscle. Together, the bundle branches and Purkinje network comprise the ventricular conduction system. It takes about 0.03-0.04s for the impulse to travel from the bundle of His to the ventricular muscle.

Pathology

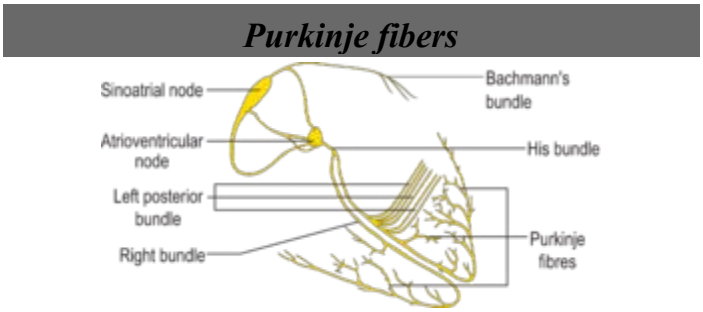
If the Bundle of His is blocked, it will result in dissociation between the activity of the atria and that of the ventricles, otherwise called a third degree heart block. The other cause of a third degree block would be a block of the right, left anterior, and left posterior bundle branches. A third degree block is a very serious medical condition that will most likely require an artificial pacemaker.

His Bundle Pacing

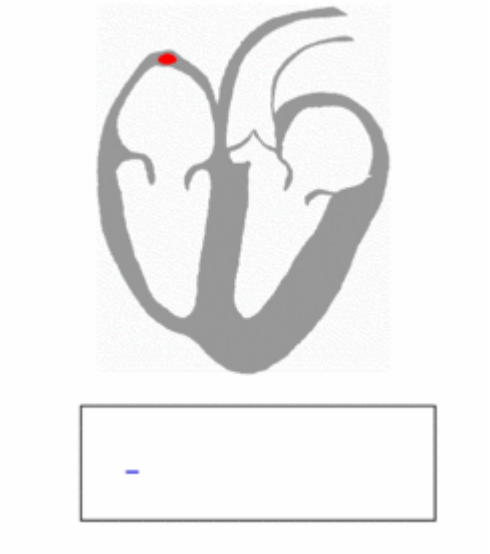
Direct His-Bundle pacing has produced synchronous ventricular depolarization and improved cardiac function relative to apical pacing.

In some patients with atrial fibrillation and a fast ventricular rate, as a last ditch effort to control the heart rate, electrophysiologists perform AV node modification / ablation following a pacemaker placement.

Purkinje Fibers



Isolated Heart conduction system showing purkinje fibers



The QRS complex is the large peak in the diagram at the bottom.

Purkinje fibers (Purkyne tissue or Subendocardial branches) are located in the inner ventricular walls of the heart, just beneath the endocardium. These fibers are specialized

myocardial fibers that conduct an electrical stimulus or impulse that enables the heart to contract in a coordinated fashion.

Histology

Purkinje fibers are a unique end-organ cardiac extension of the Autonomic Nervous System. Further histologic examination reveals that these fibers are split into left and right trees as well as atrial and ventricular contributions. The electrical origin of atrial Purkinje fibers arrives from the Sinoatrial Node. The following electrical origin of the ventricular Purkinje fibers arrives from the Atrioventricular Node.

Given no aberrant channels, the atrial and ventricular Purkinje trees are distinctly shielded from each other by collagen or the cardiac skeleton. The Purkinje fibers are uniquely dedicated to sympathetic electrical depolarization of the right and left atria and ventricles. The Purkinje fibers are further specialized to rapidly conduct impulses (numerous sodium ion channels and mitochondria, fewer myofibrils than the surrounding muscle tissue). Purkinje fibers take up stain differently than the surrounding muscle cells, and, on a slide, they often appear lighter and larger than their neighbours. They are binucleated.

Function

Heart rate is governed by many influences from the Autonomic Nervous System. The Purkinje Fibers do not have any known role in setting heart rate, but are influenced by Sympathetic discharge from the Sinoatrial node and thoracic Spinal Accessory Ganglia.

During the ventricular contraction portion of the cardiac cycle, the Purkinje fibers carry the contraction impulse from both the left and right bundle branch to the myocardium of the ventricles. This causes the muscle tissue of the ventricles to contract, thus enabling a force to eject blood out of the heart; either to the Pulmonary circulation from the right ventricle or to the Systemic circulation from the left ventricle.

Atrial and ventricular discharge through the Purkinje trees is assigned on a standard Electrocardiogram as the P Wave and QRS complex, respectively.

Purkinje fibers also have the ability of automaticity, firing at a rate of 15-40 beats per minute if left to their own devices. In contrast, the SA node outside of parasympathetic control can fire a a rate of almost 100 beats per minute. - in short, they generate action potentials, but at a slower rate than sinoatrial node and other atrial ectopic pacemakers. Thus they serve as the last resort when other pacemakers fail. When a pukinje fiber does fire it is called a Premature ventricular contraction or PVC. Another name given is Ventricular escape.

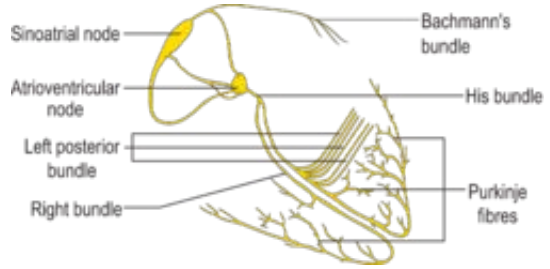
Etymology

They were discovered in 1839 by Jan Evangelista Purkyně, who gave them his name.

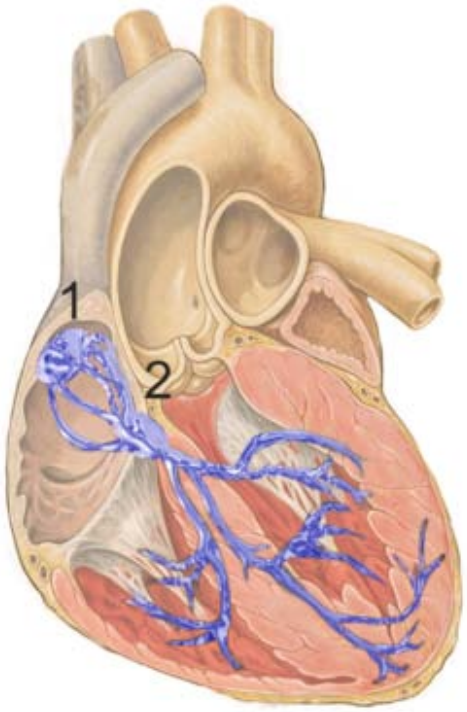
Chapter 18

Atrioventricular Node

Atrioventricular node



Isolated Heart conduction system showing AV node



Heart; conduction system

Latin	*nodus atrioventricularis*
Artery	atrioventricular nodal branch

The **atrioventricular node** (abbreviated **AV node**) is a part of the electrical control system of the heart that co-ordinates heart rate. It electrically connects atrial and ventricular chambers. The AV node is an area of specialized tissue between the atria and the ventricles of the heart, specifically in the posteroinferior region of the interatrial septum near the opening of the coronary sinus, which conducts the normal electrical impulse from the atria to the ventricles. The AV node is quite compact (~1 x 3 x 5 mm). It is located at the center of Koch's Triangle—a triangle enclosed by the septal leaflet of the tricuspid valve, the coronary sinus, and the membraneous part of the interatrial septum.

The AV node may also be (rarely) referred to as the *Aschoff-Tawara node*.

Function

Contraction of myocytes (heart muscle cells) requires depolarization and repolarization of their cell membranes. Movement of ions across cell membranes causes these events. The cardiac conduction system (and AV node part of it) coordinates myocyte mechanical activity. A wave of excitation spreads out from the sinoatrial node through the atria along specialized conduction channels. This activates the AV node. The atrioventricular node delays impulses by approximately 0.12s. This delay in the cardiac pulse is extremely important: It ensures that the atria have ejected their blood into the ventricles first before the ventricles contract. This also protects the ventricles from excessively fast rate response to atrial arrhythmias.

The AV node receives two inputs from the atria: posteriorly, via the crista terminalis, and anteriorly, via the interatrial septum.

AV conduction during normal cardiac rhythm occurs through two different pathways:

- the first “pathway” has a slow conduction velocity but shorter refractory period
- the second “pathway” has a faster conduction velocity but longer refractory period.

An important property that is unique to the AV node is *decremental conduction*, in which the more frequently the node is stimulated the slower it conducts. This is the property of the AV node that prevents rapid conduction to the ventricle in cases of rapid atrial rhythms, such as atrial fibrillation or atrial flutter.

The AV node's normal intrinsic firing rate without stimulation (like from the SA node) is 40-60 times/minute.

Blood supply

The blood supply can vary.

- The blood supply of the AV node is from the posterior interventricular artery, which is a branch of the right coronary artery in *right-dominant* individuals.

- In the remainder of individuals, the AV node is still supplied by the posterior interventricular artery, but that artery is a branch of the left circumflex artery; the coronary circulation of these individuals is considered *left-dominant*.

Disorders

- Atrioventricular (AV) conduction disease (AV block) describes impairment of the electrical continuity between the atria and ventricles. It occurs when the atrial depolarization fail to reach the ventricles or is conducted with a delay. It can result from an injury or be a genetically inherited disorder.
- Atrioventricular nodal re-entry tachycardia
- Cystic tumour of atrioventricular nodal region (CTAVN) CTAVN is of endodermal origin and occurs exclusively in the area of the AV node, tricuspid valve, and interatrial septum.

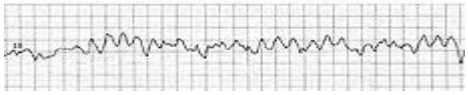
Development

BMP (Bone morphogenetic protein) cell signaling plays a key role in diverse aspects of cardiac differentiation and morphogenesis. (BMPs) are multifunctional signaling molecules critical for the development of AV node. BMP influences AV node development through Alk3 receptor (Activin receptor-like kinase 3). Abnormalities seen in BMP and Alk3 are associated with some cardiovascular diseases like Ebstein's anomaly and AV conduction disease.

Chapter 19

Cardiac Dsrhythmia

Cardiac dysrhythmia



Ventricular fibrillation (V-Fib or VF) an example of cardiac arrhythmia.

ICD-10	I47. - I49.
ICD-9	427
DiseasesDB	15206
MedlinePlus	001101
MeSH	D001145

Cardiac dysrhythmia (also known as **arrhythmia**) is a term for any of a large and heterogeneous group of conditions in which there is abnormal electrical activity in the heart. The heart beat may be too fast or too slow, and may be regular or irregular.

Some arrhythmias are life-threatening medical emergencies that can result in cardiac arrest and sudden death. Others cause symptoms such as an abnormal awareness of heart beat (palpitations), and may be merely annoying. These palpitations have also been known to be caused by atrial/ventricular fibrillation, wire faults, and other technical or mechanical issues in cardiac pacemakers/defibrillators. Still others may not be associated with any symptoms at all, but may predispose the patient to potentially life threatening stroke or embolism.

Some arrhythmias are very minor and can be regarded as normal variants. In fact, most people will on occasion feel their heart skip a beat, or give an occasional extra strong beat; neither of these is usually a cause for alarm.

Proarrhythmia is a new or more frequent occurrence of pre-existing arrhythmias, paradoxically precipitated by antiarrhythmic therapy, which means it is a side effect associated with the administration of some existing antiarrhythmic drugs, as well as drugs for other indications. In other words, it is a tendency of antiarrhythmic drugs to facilitate emergence of new arrhythmias.

The term sinus arrhythmia refers to a normal phenomenon of mild acceleration and slowing of the heart rate that occurs with breathing in and out. It is usually quite pronounced in children, and steadily decreases with age. This can also be present during meditation breathing exercises that involve deep inhaling and breath holding patterns.

Classification

Arrhythmia may be classified by rate (normal, tachycardia, bradycardia), or mechanism (automaticity, reentry, fibrillation).

It is also appropriate to classify by site of origin:

Atrial

- Premature Atrial Contractions (PACs)
- Wandering Atrial Pacemaker
- Multifocal atrial tachycardia
- Atrial flutter
- Atrial fibrillation (Afib)

Junctional arrhythmias

- Supraventricular tachycardia (SVT)
- AV nodal reentrant tachycardia is the most common cause of Paroxysmal Supra-ventricular Tachycardia (PSVT)
- Junctional rhythm
- Junctional tachycardia
- Premature junctional complex

Atrio-ventricular

- AV reentrant tachycardia occurs when a re-entry circuit crosses between the atria and ventricles somewhere other than the AV node:
    - Wolff-Parkinson-White syndrome
    - Lown-Ganong-Levine syndrome

Ventricular

- Premature Ventricular Contractions (PVC) sometimes called Ventricular Extra Beats (VEBs)
    - Premature Ventricular beats occurring after every normal beat are termed ventricular bigeminy
    - PVCs that occur at intervals of 2 normal beats to 1 PVC are termed **PVCs in trigeminy**

    - Three premature ventricular grouped together is termed "A Run of PVCs", runs lasting longer than 3 beats are generally referred to as ventricular tachycardia
- Accelerated idioventricular rhythm
- Monomorphic Ventricular tachycardia
- Polymorphic ventricular tachycardia
- Ventricular fibrillation

Heart blocks

These are also known as AV blocks, because the vast majority of them arise from pathology at the atrioventricular node. They are the most common causes of bradycardia:

- First degree heart block, which manifests as PR prolongation
- Second degree heart block
    - Type 1 Second degree heart block, also known as Mobitz I or Wenckebach
    - Type 2 Second degree heart block, also known as Mobitz II
- Third degree heart block, also known as complete heart block.

SADS

SADS, or **sudden arrhythmic death syndrome**, is a term used to describe sudden death due to cardiac arrest brought on by an arrhythmia in the absence of any structural heart disease on autopsy. The most common cause of sudden death in the US is coronary artery disease. Approximately 300,000 people die suddenly of this cause every year in the US. SADS occurs from other causes. There are many inherited conditions and heart diseases that can affect young people and subsequently cause sudden death. Many of these victims have no symptoms before dying suddenly.

Causes of SADS in young people include viral myocarditis, long QT syndrome, Brugada syndrome, Catecholaminergic polymorphic ventricular tachycardia, hypertrophic cardiomyopathy and arrhythmogenic right ventricular dysplasia.

Signs and symptoms

The term cardiac arrhythmia covers a very large number of very different conditions.

The most common symptom of arrhythmia is an abnormal awareness of heartbeat, called palpitations. These may be infrequent, frequent, or continuous. Some of these arrhythmias are harmless (though distracting for patients) but many of them predispose to adverse outcomes.

Some arrhythmias do not cause symptoms, and are not associated with increased mortality. However, some asymptomatic arrhythmias *are* associated with adverse events. Examples include a higher risk of blood clotting within the heart and a higher risk of

insufficient blood being transported to the heart because of weak heartbeat. Other increased risks are of embolisation and stroke, heart failure and sudden cardiac death.

If an arrhythmia results in a heartbeat that is too fast, too slow or too weak to supply the body's needs, this manifests as a lower blood pressure and may cause lightheadedness or dizziness, or fainting.

Some types of arrhythmia result in cardiac arrest, or sudden death.

Medical assessment of the abnormality using an electrocardiogram is one way to diagnose and assess the risk of any given arrhythmia.

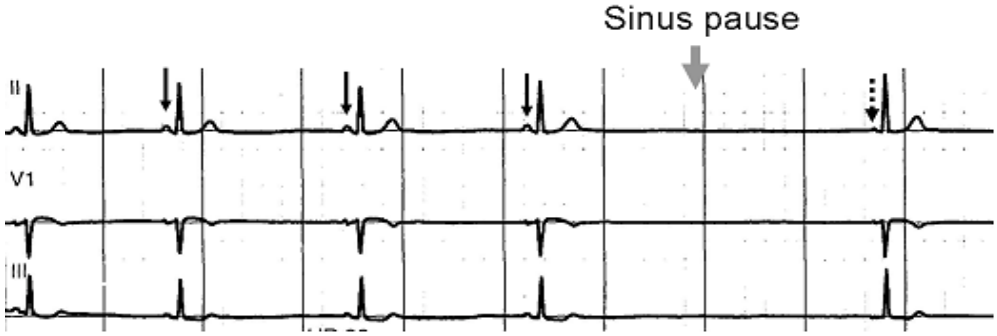
Differential diagnosis

Normal electrical activity

Each heart beat originates as an electrical impulse from a small area of tissue in the right atrium of the heart called the sinus node or Sino-atrial node or SA node. The impulse initially causes both of the atria to contract, then activates the atrioventricular (or AV) node which is normally the only electrical connection between the atria and the ventricles , which can be called as main pumping chambers. The impulse then spreads through both ventricles via the Bundle of His and the Purkinje fibres causing a synchronised contraction of the heart muscle, and thus, the pulse.

In adults the normal resting heart rate ranges from 60 to 80 beats per minute. The resting heart rate in children is much faster.

Bradycardias



Normal sinus rhythm, with solid black arrows pointing to normal P waves representative of normal sinus node function, followed by a pause in sinus node activity (resulting in a transient loss of heart beats). Note that the P wave that disrupts the pause (indicated by the dashed arrow) does not look like the previous (normal) P waves- this last P wave is arising from a different part of the atrium, representing an escape rhythm.

A slow rhythm, (less than 60 beats/min), is labelled bradycardia. This may be caused by a slowed signal from the sinus node (termed sinus bradycardia), a pause in the normal activity of the sinus node (termed sinus arrest), or by blocking of the electrical impulse on its way from the atria to the ventricles (termed AV block or heart block). Heart block comes in varying degrees and severity. It may be caused by reversible poisoning of the AV node (with drugs that impair conduction) or by irreversible damage to the node. Bradycardias may also be present in the normally functioning heart of endurance athletes or other well conditioned persons.

Tachycardias

In adults and children over 15, resting heart rate faster than 100 beats/minute is labelled tachycardia. Tachycardia may result in palpitation, however, tachycardia is not *necessarily* an arrhythmia. Increased heart rate is a normal response to physical exercise or emotional stress. This is mediated by the sympathetic nervous system on the sinus node, and is called sinus tachycardia. Other things that increase sympathetic nervous system activity in the heart include ingested or injected substances such as caffeine or amphetamines, and an overactive thyroid gland (hyperthyroidism).

Tachycardia that is not sinus tachycardia usually results from the addition of abnormal impulses to the normal cardiac cycle. Abnormal impulses can begin by one of three mechanisms: automaticity, reentry or triggered activity. A specialised form of re-entry problem is termed fibrillation.

Automaticity

Automaticity refers to a cardiac muscle cell firing off an impulse on its own. All of the cells in the heart have the ability to initiate an action potential, however, only some of these cells are designed to routinely trigger heart beats. These cells are found in the 'conduction system' of the heart and include the SA node, AV node, Bundle of His and Purkinje fibers. The sinoatrial node is a single specialized location in the atrium which has a higher automaticity (a faster pacemaker) than the rest of the heart, and therefore is usually responsible for setting the heart rate, and initiating each heart beat.

Any part of the heart that initiates an impulse without waiting for the sinoatrial node is called an *ectopic focus*, and is by definition a pathological phenomenon. This may cause a single premature beat now and then, or, if the ectopic focus fires more often than the sinoatrial node, it can produce a sustained abnormal rhythm. Rhythms produced by an ectopic focus in the atria, or by the atrioventricular node, are the least dangerous dysrhythmias; but they can still produce a decrease in the heart's pumping efficiency, because the signal reaches the various parts of the heart muscle with different timing to usual and can be responsible for poorly coordinated contraction.

Conditions that increase automaticity include sympathetic nervous system stimulation and hypoxia. The resulting heart rhythm depends on where the first signal begins: if it is

the sinoatrial node, the rhythm remains normal but rapid; if it is an ectopic focus, many types of dysrhythmia may ensue.

Re-entry

Re-entry arrhythmias occur when an electrical impulse recurrently travels in a tight circle within the heart, rather than moving from one end of the heart to the other and then stopping. Every cardiac cell is able to transmit impulses in every direction, but will only do so once within a short period of time. Normally, the action potential impulse will spread through the heart quickly enough that each cell will only respond once. However, if conduction is abnormally slow in some areas, for example in heart damage, so the myocardial cells are unable to activate the fast sodium channel, part of the impulse will arrive late, and potentially be treated as a new impulse. Depending on the timing, this can produce a sustained abnormal circuit rhythm. Re-entry circuits are responsible for atrial flutter, most paroxysmal supraventricular tachycardia, and dangerous ventricular tachycardia. These types of re-entry circuits are different from WPW syndromes in which the real pathways existed.

Fibrillation

When an entire chamber of the heart is involved in a multiple micro-reentry circuits, and therefore quivering with chaotic electrical impulses, it is said to be in fibrillation.

Fibrillation can affect the atrium (atrial fibrillation) or the ventricle (ventricular fibrillation); ventricular fibrillation is imminently life-threatening.

Atrial fibrillation affects the upper chambers of the heart, known as the atria. Atrial fibrillation may be due to serious underlying medical conditions, and should be evaluated by a physician. It is not typically a medical emergency.

Ventricular fibrillation occurs in the ventricles (lower chambers) of the heart; it is always a medical emergency. If left untreated, ventricular fibrillation (VF, or V-fib) can lead to death within minutes. When a heart goes into V-fib, effective pumping of the blood stops. V-fib is considered a form of cardiac arrest, and an individual suffering from it will not survive unless cardiopulmonary resuscitation (CPR) and defibrillation are provided immediately.

CPR can prolong the survival of the brain in the lack of a normal pulse, but defibrillation is the only intervention which can restore a healthy heart rhythm. Defibrillation is performed by applying an electric shock to the heart, which resets the cells, permitting a normal beat to re-establish itself.

Triggered beats

Triggered beats occur when problems at the level of the ion channels in individual heart cells result in abnormal propagation of electrical activity and can lead to sustained

abnormal rhythm. They are relatively rare, but can result from the action of anti-arrhythmic drugs.

Diagnostic approach

Cardiac dysrhythmias are often first detected by simple but nonspecific means: auscultation of the heartbeat with a stethoscope, or feeling for peripheral pulses. These cannot usually diagnose specific dysrhythmias, but can give a general indication of the heart rate and whether it is regular or irregular. Not all the electrical impulses of the heart produce audible or palpable beats; in many cardiac arrhythmias, the premature or abnormal beats do not produce an effective pumping action and are experienced as "skipped" beats.

The simplest *specific* diagnostic test for assessment of heart rhythm is the electrocardiogram (abbreviated **ECG** or **EKG**). A Holter monitor is an EKG recorded over a 24-hour period, to detect dysrhythmias that may happen briefly and unpredictably throughout the day.

A more advanced study of the heart's electrical activity can be performed to assess the source of the aberrant heart beats. This can be accomplished in an Electrophysiology study. A minimally invasive procedure that uses a catheter to "listen" to the electrical activity from within the heart, additionally if the source of the arrhythmias is found, often the abnormal cells can be ablated and the arrhythmia can be permanently corrected.

Management

The method of cardiac rhythm management depends firstly on whether or not the affected person is stable or unstable. Treatments may include physical maneuvers, medications, electricity conversion, or electro or cryo cautery.

Physical maneuvers

A number of physical acts can increase parasympathetic nervous supply to the heart, resulting in blocking of electrical conduction through the AV node. This can slow down or stop a number of arrhythmias that originate above or at the AV node. Parasympathetic nervous supply to the heart is via the vagus nerve, and these maneuvers are collectively known as vagal maneuvers.

Antiarrhythmic drugs

There are many classes of antiarrhythmic medications, with different mechanisms of action and many different individual drugs within these classes. Although the goal of drug therapy is to prevent arrhythmia, nearly every antiarrhythmic drug has the potential to act as a pro-arrhythmic, and so must be carefully selected and used under medical supervision.

Other drugs

A number of other drugs can be useful in cardiac arrhythmias.

Several groups of drugs slow conduction through the heart, without actually preventing an arrhythmia. These drugs can be used to "rate control" a fast rhythm and make it physically tolerable for the patient.

Some arrhythmias promote blood clotting within the heart, and increase risk of embolus and stroke. Anticoagulant medications such as warfarin and heparins, and anti-platelet drugs such as aspirin can reduce the risk of clotting.

Electricity

Dysrhythmias may also be treated electrically, by applying a shock across the heart — either externally to the chest wall, or internally to the heart via implanted electrodes.

Cardioversion is either achieved pharmacologically or via the application of a shock *synchronised* to the underlying heartbeat. It is used for treatment of supraventricular tachycardias. In elective cardioversion, the recipient is usually sedated or lightly anesthetized for the procedure.

Defibrillation differs in that the shock is not synchronised. It is needed for the chaotic rhythm of ventricular fibrillation and is also used for pulseless ventricular tachycardia. Often, more electricity is required for defibrillation than for cardioversion. In most defibrillation, the recipient has lost consciousness so there is no need for sedation.

Defibrillation or cardioversion may be accomplished by an implantable cardioverter-defibrillator (ICD).

Electrical treatment of dysrhythmia also includes cardiac pacing. Temporary pacing may be necessary for reversible causes of very slow heartbeats, or bradycardia, (for example, from drug overdose or myocardial infarction). A permanent pacemaker may be placed in situations where the bradycardia is not expected to recover.

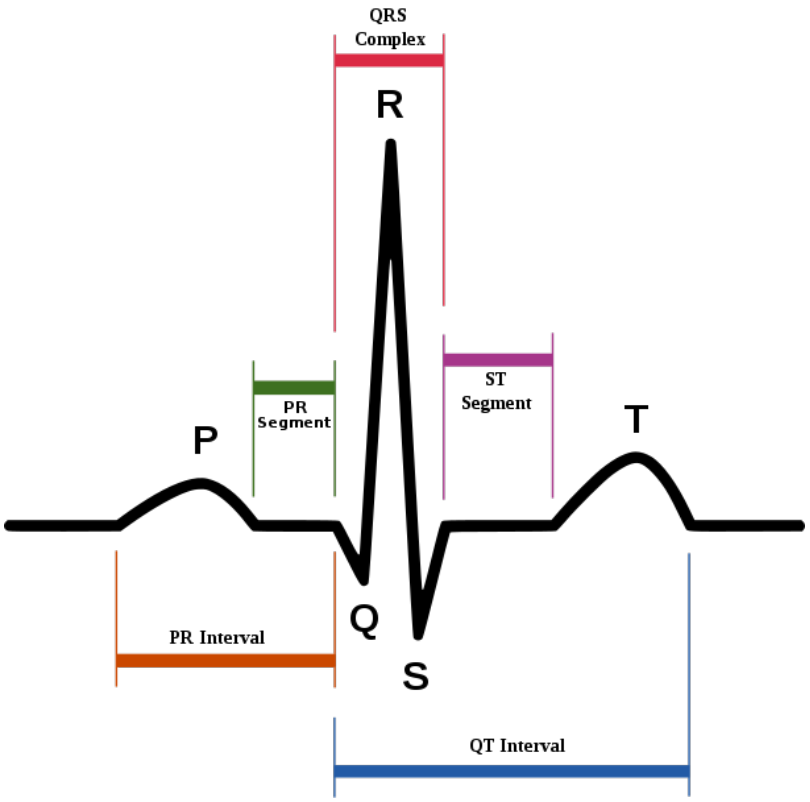
Electrical cautery

Some cardiologists further sub-specialise into electrophysiology. In specialised catheter laboratories, they use fine probes inserted through the blood vessels to map electrical activity from within the heart. This allows abnormal areas of conduction to be located very accurately, and subsequently destroyed with heat, cold, electrical or laser probes.

This may be completely curative for some forms of arrhythmia, but for others, the success rate remains disappointing. AV nodal reentrant tachycardia is often curable. Atrial fibrillation can also be treated with this technique (e.g. pulmonary vein isolation), but the results are less reliable.

Chapter 20

QRS Complex



Schematic representation of normal ECG

	Normal Axis 0 to 90	Left Axis Physiological 0 to -30	Left Axis Pathological -30 to -90	Right Axis 90 to 180	Extreme Axis -90 to -180	Indeterminate Axis ?
Lead I						
Lead II						
Lead III						

Diagram showing how the polarity of the QRS complex in leads I, II, and III can be used to estimate the heart's electrical axis in the frontal plane.

The **QRS complex** is the name for some of the deflections seen on a typical electrocardiogram (ECG). It is usually the central and most visually obvious part of the tracing. It corresponds to the depolarization of the right and left ventricles. Classically the ECG tracing has 5 deflections, arbitrarily named P to T waves (in some conditions there is a U wave as well). The Q, R and S wave occur in rapid succession, do not all appear in all leads and reflect a single event so are thus normally considered as a whole complex. A Q wave is any downward deflection after the P-wave. An R-wave is an upward deflection and the S wave is any downward deflection after the R-wave.

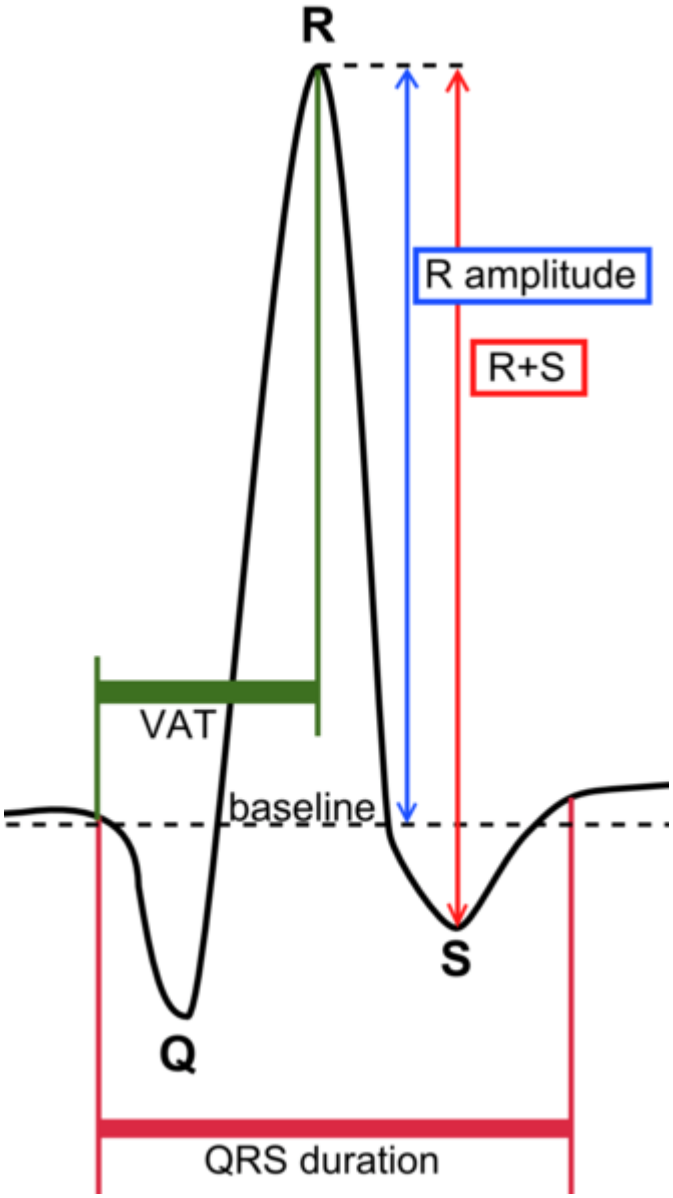
The His/Purkinje specialized muscle cells coordinate the depolarization of both ventricles and if they are working efficiently the QRS complex is 80 to 120 ms in duration (represented by three small squares or less at the standard paper speed of 25mm/s). Any abnormality of conduction takes longer and causes "widened" QRS complexes. In bundle branch block there can be an abnormal second upward deflection within the QRS complex and in this case the second upward deflection is referred to as R' (vocalised as R-prime). This would be described as an RSR' pattern.

Ventricles contain more muscle mass than the atria, therefore the QRS complex is considerably larger than the P wave. The QRS complex is often used to determine the axis of the electrocardiogram (although it is also possible to determine a separate P-wave axis).

The atrial repolarization wave, which resembles an inverse P wave, is buried inside the QRS wave. The atrial repolarization wave is obscured by the QRS because it is far smaller in magnitude.

The duration, amplitude, and morphology of the QRS complex is useful in diagnosing cardiac arrhythmias, conduction abnormalities, ventricular hypertrophy, myocardial infarction, electrolyte derangements, and other disease states.

Parameters



Schematic representation of the QRS complex

Parameter	Normal value	Value comments	Clinical significance
QRS duration	0.06 - 0.10 sec	Shorter in children and in tachycardia	Prolonged duration indicates e.g. hyperkalemia. or bundle branch block
QRS amplitude	• S amplitude in V1 + R amplitude in V5 < 3.5 millivolt (mV)		Increased amplitude indicated cardiac hypertrophy

	• R+S in a precordial lead < 4.5 mV • R in V5 or V6 < 2.6 mV	
Ventricular activation time (VAT)	• < 0.05sec in V5 or V6 • < 0.03sec in V1	Measured in increased QRS amplitude
Q wave	• Duration less than 0.04 secs in leads other than III and AVR • Amplitude less than 1/3 QRS amplitude (R+S) • Amplitude less than 1/4th of R wave	Abnormality indicates presence of infarction

The QRS complex is also included in estimating the QT interval.

Q wave

Normal Q waves, when present, represent depolarization of the interventricular septum. For this reason, they are referred to as septal Q waves, and can be appreciated in the lateral leads I, aVL, V5 and V6.

R wave progression

Looking at the precordial leads, the r wave usually progresses from showing a rS-type complex in V_1, with an increasing R and a decreasing S wave when moving towards the left side. There is usually an qR-type of complex in V_5 and V_6, with the R-wave amplitude usually being taller in V_5 than in V_6. It is normal to have a narrow QS and rSr' patterns in V_1, and so is also the case for qRs and R patterns in V_5 and V_6. The *transition zone* is where the QRS complex changes from predominately negative to predominately positive (R/S ratio becoming >1), and this usually occurs at V_3 or V_4. It is normal to have the transition zone at V_2 (called "early transition"), and at V_5 (called "delayed transition").

The definition of *poor R wave progression* (PRWP) varies in the literature, but a common one is when the R wave is less than 2–4 mm in leads V_3 or V_4 and/or there is presence of a reversed R wave progression, which is defined as R in V_4 < R in V_3 or R in V_3 < R in V_2 or R in V_2 < R in V_1, or any combination of these. *Poor R wave progression* is commonly attributed to anterior myocardial infarction, but it may also be caused by left bundle branch block, Wolff–Parkinson–White syndrome, right and left ventricular hypertrophy as well as by faulty ECG recording technique.

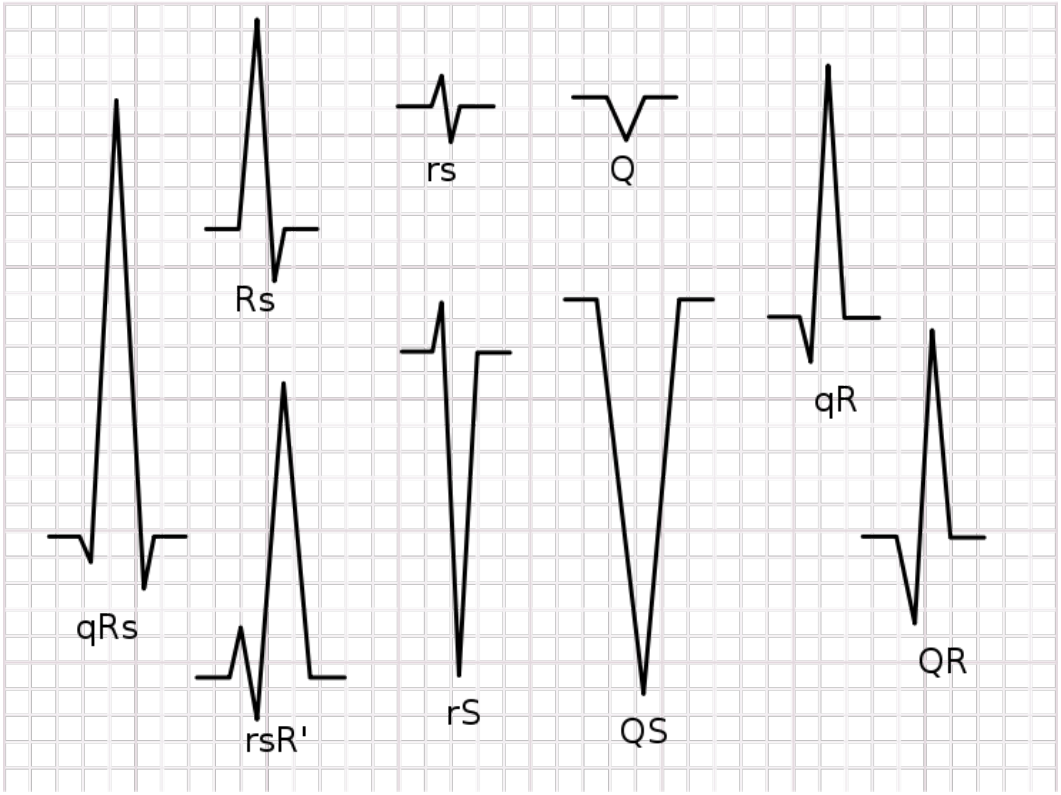
J-point

The point at which the QRS complex meets the ST segment is known as the J-point. Where the ST segment is horizontal it is fairly straightforward to identify where the S-wave finishes and the ST segment begins. A sloping ST segment can cause more difficulty but the J-point can usually be identified by the change in gradient.

Monomorphic or polymorphic

Monomorphic refers to all QRS waves in a single lead being similar in shape. Polymorphic means that the QRS change from complex to complex. These terms are used in the description of ventricular tachycardia.

Terminology

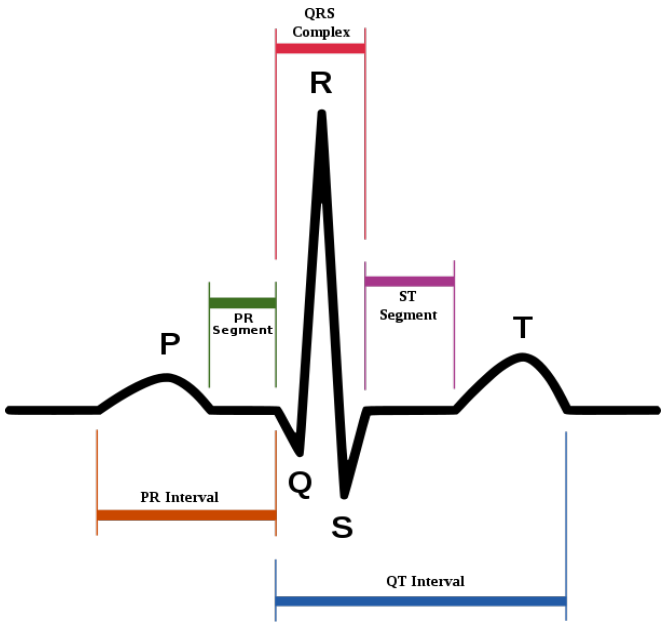


Various QRS complexes with nomenclature

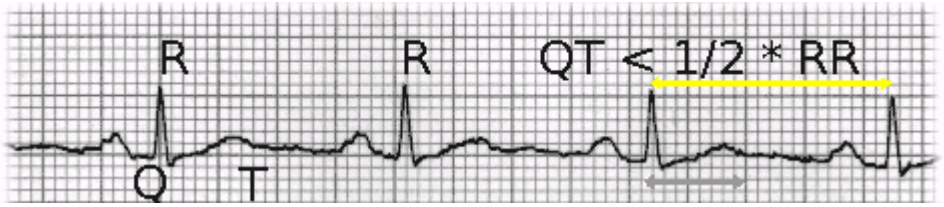
Not every QRS complex contains a Q wave, an R wave, and an S wave. By convention, any combination of these waves can be referred to as a QRS complex. However, correct interpretation of difficult ECGs requires exact labeling of the various waves. Some authors use lowercase and capital letters, depending on the relative size of each wave. For example, an Rs complex would be positively deflected, while an rS complex would be negatively deflected. If both complexes were labeled RS, it would be impossible to appreciate this distinction without viewing the actual ECG.

Chapter 21

QT Interval



Schematic representation of normal ECG trace *(sinus rhythm),* with waves, segments, and intervals labeled.



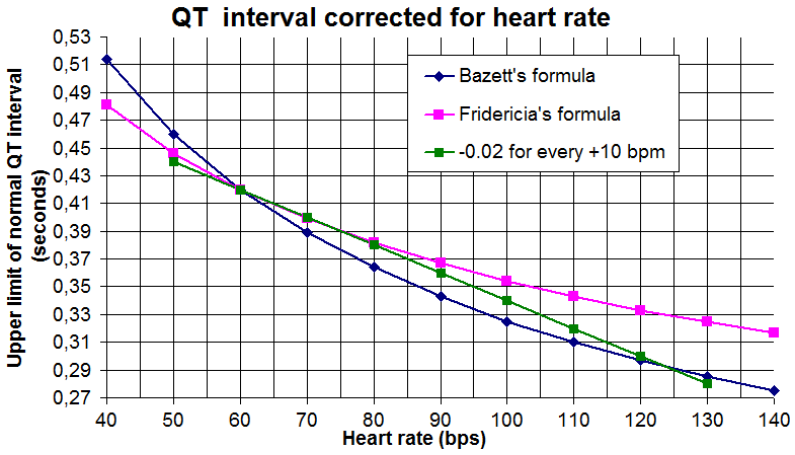
The qt-time is normal, when it is less than half the rr-time.

In medicine, to be specific, cardiology, the **QT interval** is a measure of the time between the start of the **Q wave** and the end of the **T wave** in the heart's electrical cycle. In general, the QT interval represents electrical depolarization and repolarization of the left and right ventricles. A prolonged QT interval is a biomarker for ventricular tachyarrhythmias like torsades de pointes and a risk factor for sudden death.

Measurement

The QT interval is an important ECG parameter and the identification of ECGs with long QT syndrome is of clinical importance. Considering the required standards for precision, the measurement of QT interval is subjective. This is because the end of the T wave is not always clearly defined and usually merges gradually with the baseline. QT interval can be measured manually by different methods such as the threshold method, in which the end of the T wave is determined by the point at which the component of the T wave merges with the isoelectric baseline or the tangent method, in which the end of the T wave is determined by the intersection of a line extrapolated from the isoelectric baseline and the tangent line, which touches the terminal part of the T wave at the point of maximum downslope.

Correction for heart rate



Upper limit of normal QT interval, corrected for heart rate according to *Bazett's formula*, Fridericia's formula and subtracting 0.02s from QT for every 10bpm increase in heart rate. Up to 0.42s (≤420ms) is chosen as normal QTc of QTf in this diagram.

The QT interval is dependent on the heart rate in an obvious way (the faster the heart rate the shorter the QT interval) and may be adjusted to improve the detection of patients at increased risk of ventricular arrhythmia. Modern computer-based ECG machines can easily calculate a corrected QT, but this correction may not aid in the detection of patients at increased risk of arrhythmia.

The standard clinical correction is to use *Bazett's formula*, named after physiologist Henry Cuthbert Bazett, calculating the heartrate-corrected QT interval *QTc*.

Bazett's formula is as follows:

$$QTc = \frac{QT}{\sqrt{RR}},$$

where **QTc** is the QT interval corrected for heart rate, and RR is the interval from the onset of one QRS complex to the onset of the next QRS complex, *measured in seconds*, often derived from the heart rate (HR) as 60/HR (here QT is measured in milliseconds). However, this nonlinear formula, obtained from data in only 39 young men, is not accurate, and over-corrects at high heart rates and under-corrects at low heart rates.

Definitions of normal QTc varies around being equal to or less than 0.40 s (≤400ms), 0.41s (≤410ms), 0.42s (≤420ms) or 0.44s (≤440ms). For risk of sudden cardiac death "Borderline QTc" in males is 431-450 ms, and in females 451-470 ms. An "abnormal" QTc in males is a QTc above 450 ms, and in females, above 470 ms.

If there is not a very high or low heart rate, the upper limits of QT can roughly be estimated by taking QT=QTc at a heart rate of 60 beats per minute (bpm), and subtracting 0.02s from QT for every 10bpm increase in heart rate. For example, taking normal QTc ≤ 0.42s, QT would be expected to be 0.42s or less at a heart rate of 60bpm. For a heart rate of 70 bpm, QT would roughly be expected to be equal to or below 0.40s. Likewise, for 80 bpm, QT would roughly be expected to be equal to or below 0.38s.

Fridericia has published an alternative adjustment:

$$QT_F = \frac{QT}{RR^{1/3}}.$$

There are several other methods as well. For example a regression-based approach that had been developed by Sagie et al., as follows:

$QT_{LC} = QT + 0.154(1 - RR)$.

Abnormal intervals

If abnormally prolonged or shortened, there is a risk of developing ventricular arrhythmias. It is preferred that 3 consecutive measurements of the QT interval be recorded, mainly in lead II or a long lead. Then, the mean is calculated. If lead 2 is not suitable, then leads in the sequence of V5 V4 V3 V2 are selected.

Genetic causes

An abnormal prolonged QT interval could be due to Long QT syndrome, whereas an abnormal shortened QT interval could be due to Short QT syndrome.

The length of the interval was found to associate with variations in NOS1AP gene.

Due to adverse drug reactions

Prolongation of the QT interval may be due to an adverse drug reaction. Many drugs such as haloperidol and methadone can prolong the QT interval. Some antiarrhythmic drugs,

like amiodarone or sotalol work by getting a pharmacological QT prolongation. Additionally, some second generation of antihistamines, such as astemizole, have this effect. Additionally, alcohol in high blood concentrations prolong the QT interval.

Due to pathological conditions

Hypothyroidism, a condition of low function of the thyroid gland, can give QTc prolongation at the electrocardiogram. Acute hypocalcemia causes prolongation of the QT interval, which may lead to ventricular dysrhythmias.

A shortened QT can be associated with hypercalcemia.

Use in drug studies for FDA approval

Since 2005, the FDA has required that new molecular entities are evaluated in a Thorough QT (TQT) study to determine a drug's effect on the QT interval. The TQT study serves to assess the potential arrhythmia liability of a drug. As the pharmaceutical industry has gained experience in performing TQT studies, it has become evident that traditional QT correction formulas such as QTcF, QTcB, and QTcI may not always be suitable for evaluation of drugs impacting autonomic tone. Current efforts are underway by industry and regulators to consider alternative methods to help evaluate QT liability in drugs affecting autonomic tone.

Chapter 22

Electrophysiology Study & Clinical Cardiac Electrophysiology

Electrophysiology Study

An electrophysiology study (**EP test** or **EP study**) is a minimally invasive procedure which tests the electrical conduction system of the heart to assess the electrical activity and conduction pathways of the heart. The study is indicated to investigate the cause, location of origin, and best treatment for various abnormal heart rhythms. This type of study is performed by a specialist (an electrophysiologist) and is performed using a single or multiple catheters situated within the heart through a vein or artery.

Preparation

It is important for patients not to eat or drink for up to 12 hours before the procedure. This is to prevent vomiting, which can result in aspiration, and even cause severe bleed from the insertion site of the catheter. Failure to follow this simple preparation may result in dangerous consequences. Generally small amounts of water can be consumed up to 2 hours before the exam. Patients should try to schedule the exam at a time when they will be having symptoms and will not need to drive for 2 to 3 days.

Procedure

This procedure is performed in a cath lab which is a specially equipped operating room. More modern cath labs contain a video X-ray machine and large magnets (2-3 tesla, 2 ft. diameter) for manipulating the electrodes, in addition to other necessary equipment.

An IV tube is generally inserted to keep the patient hydrated and to allow for the administration of sedatives, anesthesia, or drugs.

In order to reach the heart with a catheter, a site will be prepared that will allow access to the heart via an artery or vein, usually in the wrist or groin. This site is then described as the **insertion point**.

A metal plate is placed underneath the patient between the shoulder blades, directly under the heart. An automated blood pressure cuff is placed on the arm which periodically measures the patient's blood pressure. A pulse oximeter is placed on one of the patient's fingers which steadily monitors the patient's pulse and oxygen saturation of the blood.

The insertion point is cleanly shaved and sterilized. A local anesthetic is injected into the skin to numb the insertion point. A small puncture is then made with a needle in either the femoral vein in the groin or the radial vein in the wrist, before a guide wire is inserted into the venous puncture. A plastic sheath (with a stiffer plastic introducer inside) is then threaded over the wire and pushed into the vein (the Seldinger technique). The wire is then removed and the side-port of the sheath is aspirated to ensure venous blood flows back. It is then flushed with saline. Catheters are inserted using a long guide wire and moved towards the heart. Once in position the guide wire is then removed.

- NOTE It is standard procedure to use the venous system, and place the catheter's tip in the right atrium at the beginning of the procedure. The advantage of this that the SA node is in the right atrium, which is the place where the procedure will start testing the pacing system of the heart.

EP Study

Once the catheter is in and all preparations are complete elsewhere in the lab, the EP study begins. The two large magnets are brought in on either side of the patient. They are large and looming and will sandwich the patient, but are able to precisely control the position of the electrodes that are on the end of the catheters. The X-ray machine will give the doctor a view of the heart and the position of the electrodes, and the magnets will allow the doctor to guide the electrodes through the heart. The magnets are controlled with either a joystick or game controller. The electrophysiologist begins by moving the electrodes along the conduction pathways and along the inner walls of the heart, measuring the electrical activity along the way.

The next step is pacing the heart, this means he/she will speed up or slow down the heart by placing the electrode at certain points along the conductive pathways of the heart and literally controlling the depolarization rate of the heart. The doctor will pace each chamber of the heart one by one, looking for any abnormalities. Then the electrophysiologist tries to provoke arrhythmias and reproduce any conditions that have resulted in the patient's placement in the study. This is done by injecting electric current into the conductive pathways and into the endocardium at various places. Lastly, the electrophysioligst may administer various drugs (proarrhythmic agents) to induce arrhythmia. If the arrhythmia is reproduced by the drugs, the electrophysiologist will search out the source of the abnormal electrical activity. The entire procedure can take several hours.

Ablation

If at any step during the EP study the electrophysiologist finds the source of the abnormal electrical activity, he/she may try to ablate the cells that are misfiring. This is done using high energy radio frequencies (similar to microwaves) to effectively "cook" the abnormal cells.

Recovery

When the necessary procedures are complete, the catheter is removed. Firm pressure is applied to the site to prevent bleeding. This may be done by hand or with a mechanical device. Other closure techniques include an internal suture and plug. If the femoral artery was used, the patient will probably be asked to lie flat for several hours (3 to 6) to prevent bleeding or the development of a hematoma. Trying to sit up or even lift the head is strongly discouraged until an adequate clot has formed. The patient will be moved to a recovery area where he/she will be monitored.

For patients who had a catheterization at the femoral artery or vein (and even some of those with a radial insertion site), generally recovery is fairly quick as the only damage is at the insertion site. The patient will probably feel fine within 8 to 12 hours after the procedure, but may feel a small pinch at the insertion site. After a short period of general rest, the patient may resume some minor activity such as gentle, short, slow walks after the first 24 hours. If stairs must be climbed, they should be taken one step at a time and very slowly. All vigorous activity must be postponed until approved by an physician.

It is also important to note that unless directed by a doctor, some patients should avoid taking blood thinners and foods that contain salicylates, such as cranberry containing products until the clot has healed. (1–2 weeks)

Complications

As with any surgical procedure, cardiac catheterizations come with a generic list of possible complications. One of the complications that is sometimes reported involves some temporary nerve involvement. Some times a small amount of swelling occurs that can put pressure on nerves in the area of the incision. There have been reports of patients feeling like they have hot fluid like blood or urine running down their leg for up to a month or two after the incision has healed. This usually passes with time, but patients should tell their doctor if they have these symptoms and if they last.

More severe but relatively rare complications include: damage or trauma to a blood vessel, which could require repair; infection from the skin puncture or from the catheter itself; cardiac perforation, causing blood to leak into the sac around the heart and compromising the heart's pumping action, requiring removal using a needle under the breast bone (pericardiocentesis); hematoma at the site(s) of the puncture(s); induction of a dangerous cardiac rhythm requiring an external shock(s); a clot may be dislodged, which may travel to a distant organ and impede blood flow or cause a stroke; myocardial

infarction; unanticipated reactions to the medications used during the procedure; damage to the conduction system, requiring a permanent pacemaker; death.

Clinical Cardiac Electrophysiology

Cardiac Electrophysiology (also referred to as **clinical cardiac electrophysiology** , **Arrhythmia Services** , or **electrophysiology**), is a branch of the medical specialty of clinical cardiology and is concerned with the study and treatment of rhythm disorders of the heart. Cardiologists with expertise in this area are usually referred to as electrophysiologists. Electrophysiologists are trained in the mechanism, function, and performance of the electrical activities of the heart. Electrophysiologists work closely with other cardiologists and cardiac surgeons to assist or guide therapy for heart rhythm disturbances (arrhythmias).They are trained to perform interventional and surgical procedures to treat cardiac arrhythmia.

The training required to became an electrophysiologist is long and requires 7 to 8 years after medical school (in the U.S.). Three years of Internal Medicine residency, three years of Clinical Cardiology fellowship, and one to two (in most instances) years of Clinical Cardiac Electrophysiology.

An **electrophysiology study** is a term used to describe a number of invasive (intracardiac) and non-invasive recording of spontaneous electrical activity as well as of cardiac responses to programmed electrical stimulation. These studies are performed to assess arrhythmias, elucidate symptoms, evaluate abnormal electrocardiograms, assess risk of developing arrhythmias in the future, and design treatment.

In addition to diagnostic testing of the electrical properties of the heart, electrophysiologists are trained in therapeutic and surgical methods to treat many of the rhythm disturbances of the heart. Therapeutic modalities employed in this field include antiarrhythmic drug therapy and surgical implantation of pacemakers and implantable cardioverter-defibrillators.

Scope of practice, tests and procedures

Diagnostic testing

- Ambulatory electrocardiographic monitoring - Holter recording and interpretation, loop recording and interpretation;
- Tilt table testing;
- T-wave alternans testing;
- Signal-averaged electrocardiogram (SAECG) interpretation, also referred to as "late potentials" reading;

- Electrophysiology study (EPS) consists in the insertion of pacing and recording electrodes either in the oesophagus (intra-oesophageal EPS) or, through blood vessels, directly into the heart chambers (intra-cardiac EPS) in order to measure electrical properties of the heart and, in the case of intra-cardiac EPS, to electrically stimulate it in the attempt to induce arrhythmias for diagnostic purposes ("programmed electrical stimulation").

Medical treatment

- Initital administration and monitoring of the effect of drugs for treatment of heart rhythm disorders. Electrophysiologists are often involved when severe or life threatening arrhythmias are being treated, or when multiple drugs must be used to treat an arrhythmia.

Catheter ablation

- Ablation therapy - Catheter based creation of lesions in the heart (with radiofrequency energy, cryotherapy (destructive freezing), or ultrasound energy) to cure or control arrhythmias. Ablation is usually performed during the same procedure as the electrophysiology study which induces and confirms the diagnosis of the arrhythmia for which ablation therapy is sought.

- "Non-complex" ablations include ablation for arrhythmias such as: AV nodal reentrant tachycardia, Accessory pathway mediated tachycardia, atrial flutter. These procedures are usually performed using intracardiac catheters (as are used during an electrophysiology study), fluoroscopy (a real-time X-ray camera), and electrical recordings from the inside of the heart.

- "Complex" ablations include ablation for arrhythmias such as multifocal atrial tachycardia, atrial fibrillation, and ventricular tachycardia. In addition to the apparatus used for a "non-complex" ablation, these procedures often make use of sophisticated computer mapping systems to localize the source of the abnormal rhythm and to direct delivery of ablation lesions.

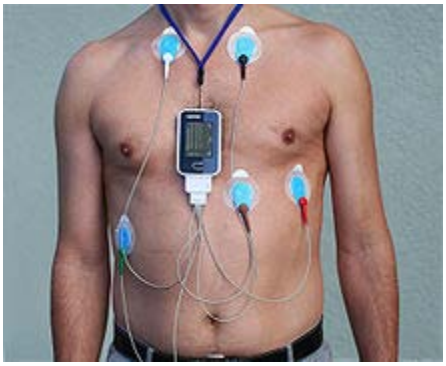
Surgical Procedures: Pacemaker and Defibrillator implantation and follow up

- Implantation of single and dual chamber pacemakers and defibrillators
- Implantation of "biventricular" pacemakers and defibrillators for patients with congestive heart failure
- Implantation of loop recorders (implanted ECG recorders for long term monitoring of ECG to allow for diagnosis of an arrhythmia)
- Clinical follow up and reprogramming of implanted devices

Chapter 23

Holter Monitor

Holter monitor



Holter monitor

Inventor Norman Holter

In medicine, a **Holter monitor** (often simply "Holter" or occasionally **ambulatory electrocardiography device**) is a portable device for continuously monitoring various electrical activity of the central nervous system for at least 24 hours (often for two weeks at a time). The Holter's most common use is for monitoring heart activity (electrocardiography or ECG), but it can also be used for monitoring brain activity (electroencephalography or EEG). Its extended recording period is sometimes useful for observing occasional cardiac arrhythmias or epileptic events which would be difficult to identify in a shorter period of time. For patients having more transient symptoms, a cardiac event monitor which can be worn for a month or more can be used.

The Holter monitor is named for physicist Norman J. Holter who invented telemetric cardiac monitoring in 1949. Clinical use started in the early 1960s.

When used for the heart, much like standard electrocardiography the Holter monitor records electrical signals from the heart via a series of electrodes attached to the chest. Electrodes are placed over bones to minimize artifacts from muscular activity. The number and position of electrodes varies by model, but most Holter monitors employ between three and eight. These electrodes are connected to a small piece of equipment that is attached to the patient's belt or hung around the neck, and is responsible for keeping a log of the heart's electrical activity throughout the recording period.

Older devices used reel to reel tapes or a standard C90 or C120 audio cassette and ran at a 1.7mm or 2mm/second speed to record the data. Once a recording was made, it could be played back and analysed at 60x speed so 24 hours of recording could be analysed in 24 minutes. More modern units record onto digital flash memory devices. The data are uploaded into a computer which then automatically analyzes the input, counting ECG complexes, calculating summary statistics such as average heart rate, minimum and maximum heart rate, and finding candidate areas in the recording worthy of further study by the technician.

Recorder

Each Holter system consists of two basic parts – the hardware (called monitor or recorder) for recording the signal and software for review and analysis of the record. Advanced Holter recorders are able to display the signal, which is very useful for checking the signal quality. Very often there is also a "patient button" located on the front site allowing the patient to press it in specific cases such as sickness, going to bed, taking pills…. A special mark will be then placed into the record so that the doctors or technicians can quickly pinpoint these areas when analyzing the signal. More modern devices also have the ability to record a vocal patient diary entry.

Size of recorder differs depending on manufacturer of the device. The average dimensions of today's Holter monitors are about 110x70x30 mm. Most of the devices operate with two AA batteries. In case the batteries die, some Holters allow their replacement even during monitoring.

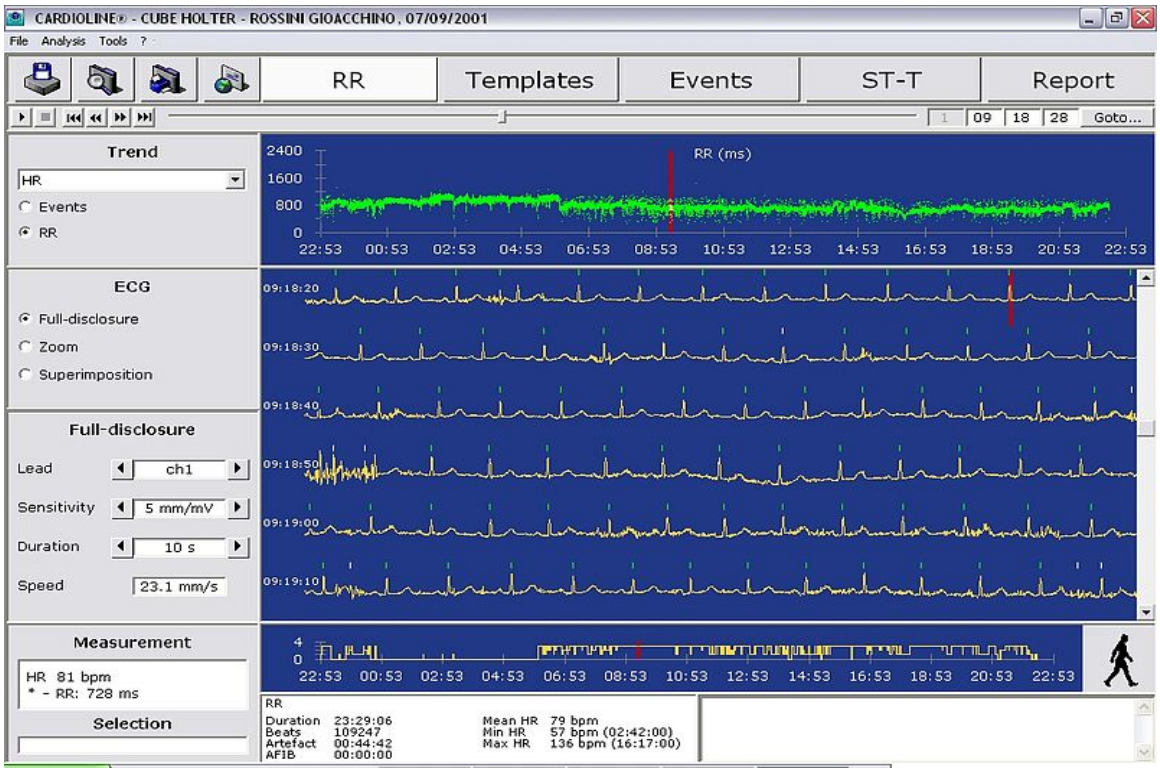
Most of the Holters monitor the ECG just in 2 or 3 channels. Depending on the model (manufacturer), different count of leads and lead systems are used. Today's trend is to minimize such number to insure the patient's comfort during recording. Although 2/3 channel recording has been used for a long time in the Holter monitoring history, recently 12 channel Holters have appeared. These systems use the classic Mason-Likar lead system, thus producing the signal in the same representation as during the common rest ECG and/or stress test measurement. These Holters then allow to substitute stress test examination in cases the stress test is not possible for the current patient. They are also suitable when analyzing patients after myocardial infarction. Recordings from these 12 lead monitors are of a significantly lower resolution than those from a standard 12 lead ECG and in some cases have been shown to provide misleading ST segment representation, even though some device allow to set the sampling frequency up to 1000 Hz for special purposes exams like the late potential.

Another interesting innovation is the presence of a 3 axis movement sensor, which record the patient physical activity, and later show in the software three different status: sleep, stand-up, walking. This helps the cardiologist to better analyze the recorded events belong to the patient activity and diary.

Analysing software

When the recording of ECG signal is finished (usually after 24 or 48 hours), it is up to the physician to perform the signal analysis. Since it would be extremely time demanding to browse through such a long signal, there is an integrated automatic analysis process in each Holter software which automatically determines different sorts of heart beats, rhythms, etc. However the success of the automatic analysis is very closely associated with the signal quality. The quality itself mainly depends on the attachment of the electrodes to the patient body. If these are not properly attached, the electromagnetic disturbance surrounding us will influence the ECG signal resulting thus in a very noisy record. If the patient moves rapidly, the distortion will be even bigger. Such record is then very difficult to process. Besides the attachment and quality of electrodes, there are other factors affecting the signal quality, such as muscle tremors, sampling rate and resolution of the digitized signal (high quality devices offer 2000Hz and 16 bits or higher).

The automatic analysis commonly provides the physician with information about heart beat morphology, beat interval measurement, heart rate variability, rhythm overview and patient diary (moments when the patient pressed the patient button). Advanced systems also perform spectral analysis, ischemic burden evaluation, graph of patient's activity or PQ segment analysis. Another requirement is the ability of pacemaker detection and analysis. Such ability is useful when one wants to check the correct pacemaker function.



Screenshot of an holter ecg software.

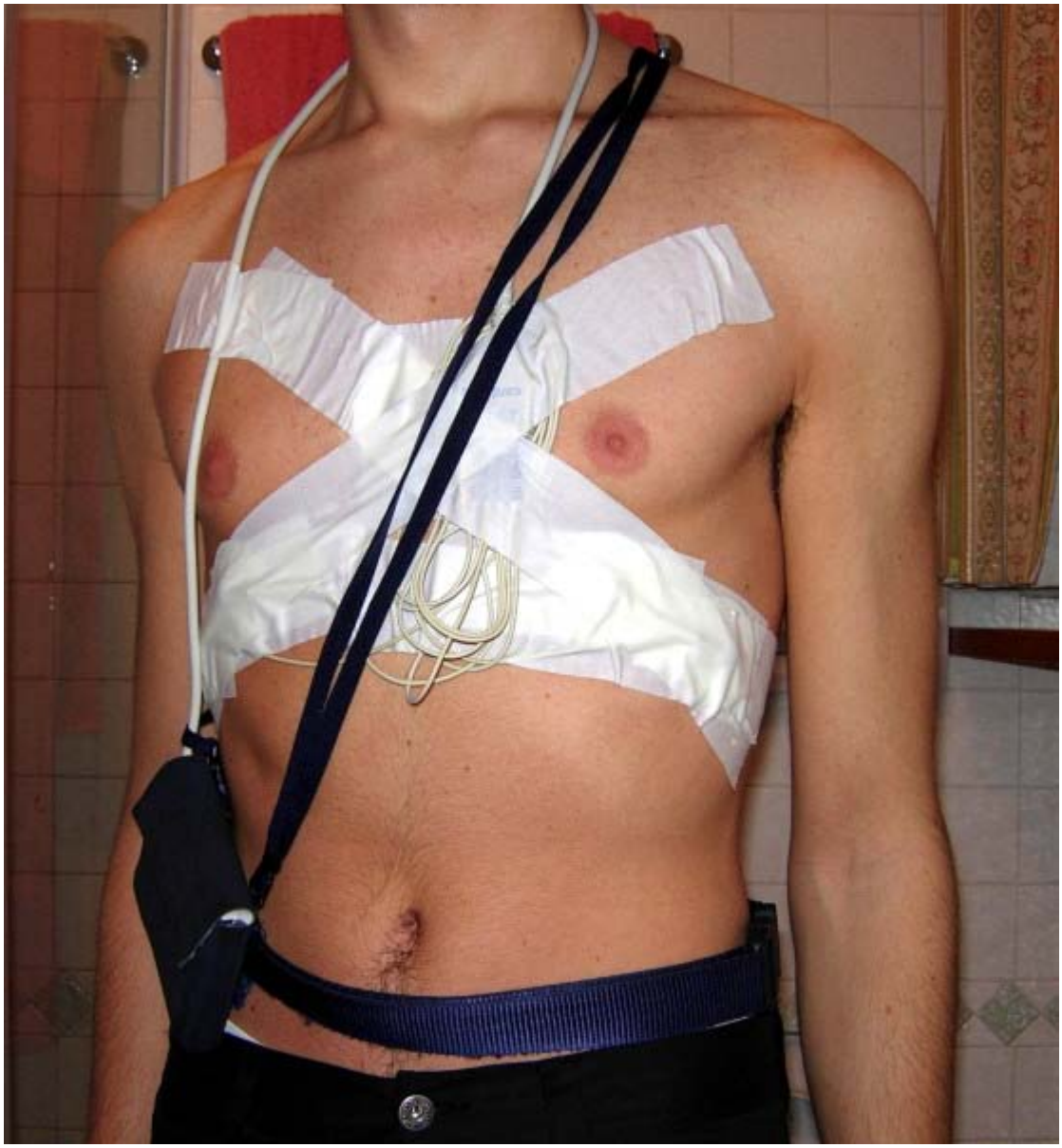
Wearing the monitor

Although some patients may feel uncomfortable about a Holter examination, there is nothing to worry about. No hazards are involved, and it should have little effect on one's normal daily life.

The recording device can be worn in a case on a belt or on a strap across the chest. The device may be visible under light clothing, and those wearing a Holter monitor may wish to avoid shirts with a low neckline.

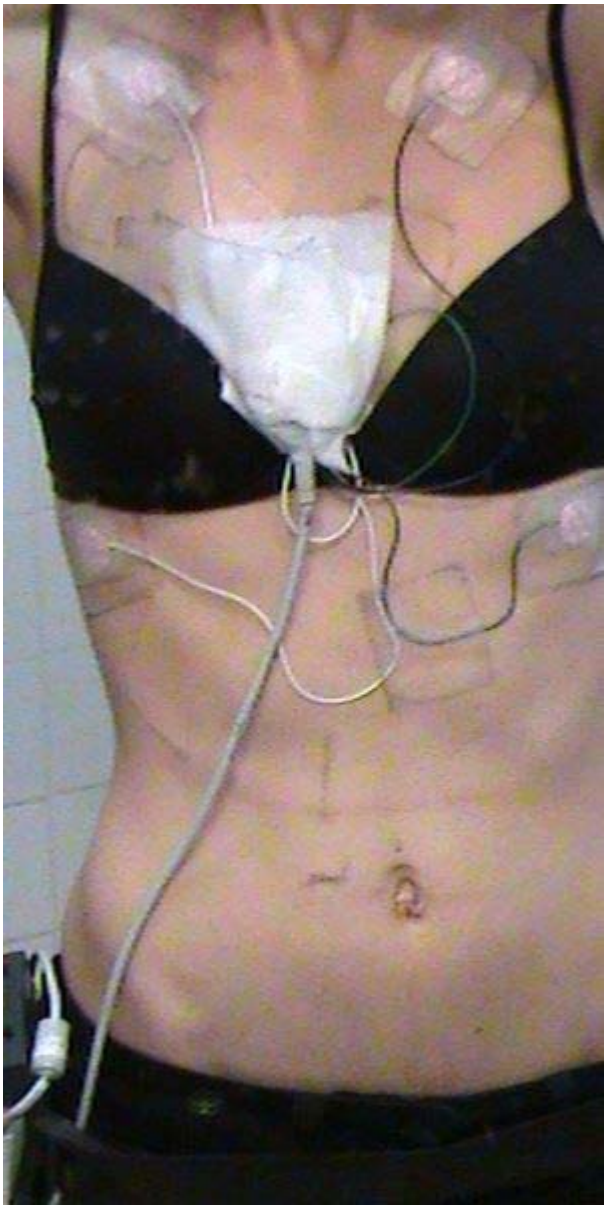
Persons being monitored should not limit normal daily activities, since its purpose is to record how a heart works under various actual conditions over an extended period. It is an electrical device, however, and should be kept dry; showering or swimming should probably be avoided. Monitors can be removed for a few minutes without invalidating collected data, but proper reattachment is critical to avoid degradation of its signals. Beyond changing batteries, one should leave its handling to trained personnel.

Canine Holter Monitor with DogLeggs Vest



A Holter monitor can be worn for many days without causing significant discomfort

A Holter monitor with a US quarter dollar coin to show scale



Holter monitor can be worn with bra on woman, with no discomfort

Chapter 24

Palpitation

Palpitation	
ICD-10	R00.2
ICD-9	785.1
DiseasesDB	29231
MedlinePlus	003081
eMedicine	aaem/337

A **palpitation** is an abnormality of heartbeat that causes a conscious awareness of its beating, whether it is too slow, too fast, irregular, or at its normal frequency. The word may also refer to this sensation itself. It can be caused by (but should not be confused with) ectopic beat, which is a more specific diagnosis.

The difference between an abnormal awareness and a normal awareness is that the former interrupts other thoughts, whereas the latter is almost always caused by a concentration on the beating of one's heart. Palpitations may be brought on by overexertion, adrenaline, alcohol, nicotine, caffeine, cocaine, amphetamines, and other drugs, disease (such as hyperthyroidism and pheochromocytoma) or as a symptom of panic disorder. More colloquially, it can also refer to a shaking motion. It can also happen in mitral stenosis.

Nearly everyone experiences an occasional awareness of their heart beating, but when it occurs frequently, it can indicate a problem. Palpitations may be associated with heart problems, but also with anemias and thyroid malfunction.

Attacks can last for a few seconds or hours, and may occur very infrequently, or more than daily. Palpitations alongside other symptoms, including sweating, faintness, chest pain or dizziness, indicate irregular or poor heart function and should be investigated.

Palpitations may also be associated with anxiety and panic attacks, in which case psychological assessment is recommended. This is a common disorder associated with many common medications such as anti-depressants.

Palpitations can also occur from blood loss, excessive pain, or lack of oxygen.

Causes

Palpitations can be attributed to one of three main causes:

1. **Hyperdynamic circulation** (valvular incompetence, thyrotoxicosis, hypercapnia, pyrexia, anemia, pregnancy).
2. **Sympathetic overdrive** (panic disorders, hypoglycemia, hypoxia, levocetirizine antihistamines, anemia, heart failure, mitral valve prolapse).
3. **Cardiac dysrhythmias** (premature atrial contraction, junctional escape beat, premature ventricular contraction, atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, ventricular fibrillation, heart block).

Anxiety can also cause palpitations in that the heart muscles are affected by the state of one's mind. Psychological problems can thus induce one to palpitate. Clinicians should therefore consider the psycho-social aspect before diagnosis.

Symptoms

Many times, the person experiencing palpitations may not be aware of anything apart from the abnormal heart rhythm itself. But palpitations can be associated with other things such as tightness in the chest, shortness of breath, dizziness or light-headedness. Depending on the type of rhythm problem, these symptoms may be just momentary or more prolonged. Actual blackouts or near blackouts, associated with palpitations, should be taken seriously because they often indicate the presence of important underlying heart disease. Another symptom is pain in arms or legs sometimes lasting through the night before the palpitation.

Diagnosis

The most important initial clue to the diagnosis is one's description of the palpitations. The approximate age of the person when first noticed and the circumstances under which they occur are important, as is information about caffeine intake (tea or coffee drinking). It is also very helpful to know how they start and stop (abruptly or not), whether or not they are regular, and approximately how fast the pulse rate is during an attack. If the person has discovered a way of stopping the palpitations, that is also helpful information.

The diagnosis is usually not made by a routine medical examination and electrical tracing of the heart's activity (ECG), because most people cannot arrange to have their symptoms while visiting the doctor. Nevertheless, findings such as a heart murmur or an abnormality of the ECG, which could point to the probable diagnosis, may be discovered. In particular, ECG changes that can be associated with specific disturbances of the heart rhythm may be picked up; so routine physical examination and ECG remain important in the assessment of palpitations.

Blood tests, particularly tests of thyroid gland function are also important baseline investigations (an overactive thyroid gland is a potential cause for palpitations; the treatment in that case is to treat the thyroid gland over-activity).

The next level of diagnostic testing is usually 24 hour (or longer) ECG monitoring, using a form of tape recorder (a bit like a Walkman) called a Holter monitor, which can record the ECG continuously during a 24-hour period. If symptoms occur during monitoring it is a simple matter to examine the ECG recording and see what the cardiac rhythm was at the time. For this type of monitoring to be helpful, the symptoms must be occurring at least once a day. If they are less frequent, the chances of detecting anything with continuous 24, or even 48-hour monitoring, are substantially lowered.

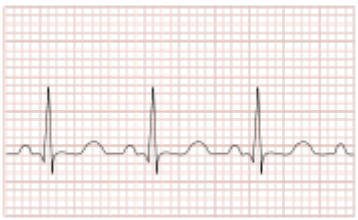
Other forms of monitoring are available, and these can be useful when symptoms are infrequent. A continuous-loop event recorder monitors the ECG continuously, but only saves the data when the wearer activates it. Once activated, it will save the ECG data for a period of time before the activation and for a period of time afterwards - the cardiologist who is investigating the palpitations can program the length of these periods. A new type of continuous-loop recorder has been developed recently that may be helpful in people with very infrequent, but disabling symptoms. This recorder is implanted under the skin on the front of the chest, like a pacemaker. It can be programmed and the data examined using an external device that communicates with it by means of a radio signal.

Investigation of heart structure can also be important. The heart in most people with palpitations is completely normal in its physical structure, but occasionally abnormalities such as valve problems may be present. Usually, but not always, the cardiologist will be able to detect a murmur in such cases, and an ultrasound scan of the heart (echocardiogram) will often be performed to document the heart's structure. This is a painless test performed using sound waves and is virtually identical to the scanning done in pregnancy to look at the fetus.

Chapter 25

Tachycardia

Tachycardia



ECG showing sinus tachycardia with a rate of about 100 beats per minute.

ICD-10 I47.-I49., R00.0

ICD-9 427, 785.0

MeSH D013610

Tachycardia comes from the Greek words *tachys* (*rapid* or *accelerated*) and *kardia* (*of the heart*). Tachycardia typically refers to a heart rate that exceeds the normal range for a resting heartrate (heartrate in an inactive or sleeping individual). It can be dangerous depending on the speed and type of rhythm.

Definition

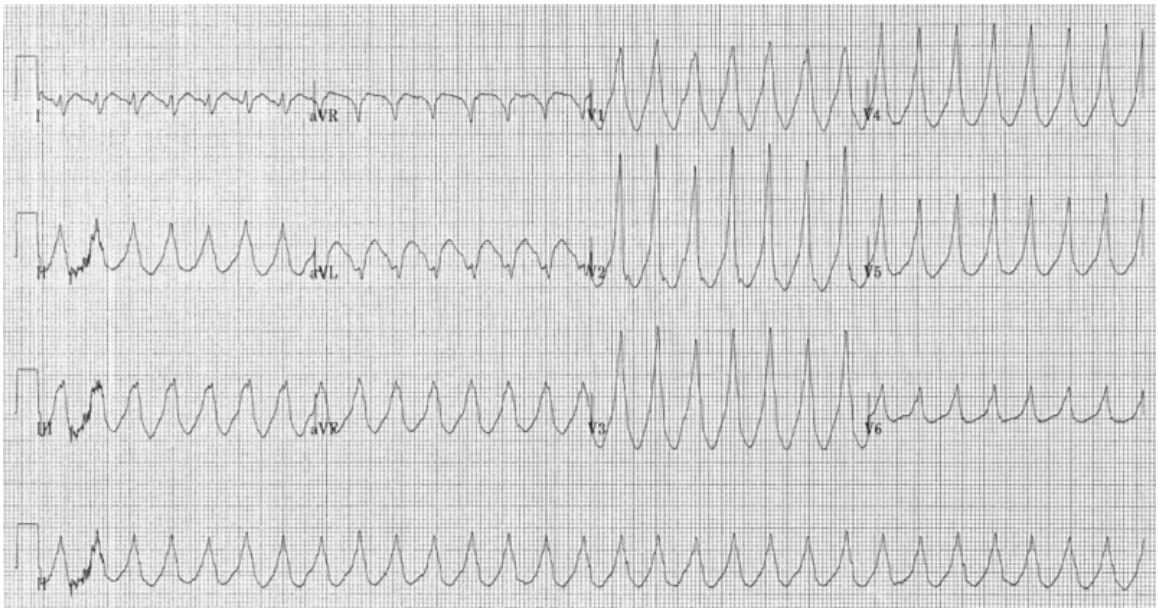
The upper threshold of a normal human heart rate is based upon age. Tachycardia for different age groups is as listed below:

- 1–2 days: >159 beats per minute (bpm)
- 3–6 days: >166 bpm
- 1–3 weeks: >182 bpm
- 1–2 months: >179 bpm
- 3–5 months: >186 bpm
- 6–11 months: >169 bpm
- 1–2 years: >151 bpm
- 3–4 years: >137 bpm
- 5–7 years: >133 bpm

- 8–11 years: >130 bpm
- 12–15 years: >119 bpm
- >15 years – adult: >100 bpm

When the heart beats excessively rapidly, the heart pumps less efficiently and provides less blood flow to the rest of the body, including the heart itself. The increased heart rate also leads to increased work and oxygen demand by the heart, which can lead to rate related ischemia.

Classification



12 lead electrocardiogram showing a run of ventricular tachycardia (VT)

An electrocardiogram (ECG) is used to classify the type of tachycardia. They may be classified into narrow and wide complex based on the QRS complex. Presented in the order of most to least common they are:

Narrow complex

- Sinus tachycardia, which originates from the sino-atrial (SA) node, near the base of the superior vena cava.
- Atrial fibrillation
- Atrial flutter
- AV nodal reentrant tachycardia
- Accessory pathway mediated tachycardia
- Atrial tachycardia
- Multifocal atrial tachycardia
- Junctional tachycardia

Wide complex

- Ventricular tachycardia, any tachycardia which originates in the ventricles.

Tachycardias may be classified as either **narrow complex tachycardias** (supraventricular tachycardias) or **wide complex tachycardias**. "Narrow" and "wide" refer to the width of the QRS complex on the ECG. Narrow complex tachycardias tend to originate in the atria, while wide complex tachycardias tend to originate in the ventricles. Tachycardias can be further classified as either regular or irregular.

Sinus

The body has several feedback mechanisms to maintain adequate blood flow and blood pressure. If blood pressure decreases, the heart beats faster in an attempt to raise it. This is called reflex tachycardia. This can happen in response to a decrease in blood volume (through dehydration or bleeding), or an unexpected change in blood flow. The most common cause of the latter is orthostatic hypotension (also called postural hypotension). Fever, hyperventilation and severe infections can also cause tachycardia, primarily due to increase in metabolic demands.

An increase in sympathetic nervous system stimulation causes the heart rate to increase, both by the direct action of sympathetic nerve fibers on the heart and by causing the endocrine system to release hormones such as epinephrine (adrenaline), which have a similar effect. Increased sympathetic stimulation is usually due to physical or psychological stress. This is the basis for the so-called "Fight or Flight" response, but such stimulation can also be induced by stimulants such as ephedrine, amphetamines or cocaine. Certain endocrine disorders such as pheochromocytoma can also cause epinephrine release and can result in tachycardia independent nervous system stimulation. Hyperthyroidism can also cause tachycardia.

Ventricular

Ventricular tachycardia (VT or V-tach) is a potentially life-threatening cardiac arrhythmia that originates in the ventricles. It is usually a regular, wide complex tachycardia with a rate between 120 and 250 beats per minute. Ventricular tachycardia has the potential of degrading to the more serious ventricular fibrillation. Ventricular tachycardia is a common, and often lethal, complication of a myocardial infarction (heart attack).

Exercise-induced ventricular tachycardia is a phenomenon related to sudden deaths, especially in patients with severe heart disease (ischemia, acquired valvular heart and congenital heart disease) accompanied with left ventricular dysfunction.

Both of these rhythms normally last for only a few seconds to minutes *(paroxysmal tachycardia)*, but if VT persists it is extremely dangerous, often leading to ventricular fibrillation.

Supraventricular

This is a type tachycardia that originates from above the ventricles, such as the atria. It is sometimes known as paroxysmal atrial tachycardia (PAT). Several types of supraventricular tachycardia are known to exist.

Atrial fibrillation

Atrial fibrillation is one of the most common cardiac arrhythmias. It is generally an irregular, narrow complex rhythm. However, it may show wide QRS complexes on the ECG if a bundle branch block is present. At high rates, the QRS complex may also become wide due to the Ashman phenomenon. It may be difficult to determine the rhythm's regularity when the rate exceeds 150 beats per minute. Depending on the patient's health and other variables such as medications taken for rate control, atrial fibrillation may cause heart rates that span from 50 to 250 beats per minute (or even higher if an accessory pathway is present). However, new onset atrial fibrillation tends to present with rates between 100 and 150 beats per minute.

AV nodal reentrant tachycardia (AVNRT)

AV nodal reentrant tachycardia is the most common reentrant tachycardia. It is a regular narrow complex tachycardia that usually responds well to the Valsalva maneuver or the drug adenosine. However, unstable patients sometimes require synchronized cardioversion. Definitive care may include catheter ablation.

AV reentrant tachycardia

AV reentrant tachycardia (AVRT) requires an accessory pathway for its maintenance. AVRT may involve orthodromic conduction (where the impulse travels down the AV node to the ventricles and back up to the atria through the accessory pathway) or antidromic conduction (which the impulse travels down the accessory pathway and back up to the atria through the AV node). Orthodromic conduction usually results in a narrow complex tachycardia, and antidromic conduction usually results in a wide complex tachycardia that often mimics ventricular tachycardia. Most antiarrhythmics are contraindicated in the emergency treatment of AVRT, because they may paradoxically increase conduction across the accessory pathway.

Junctional tachycardia

Junctional tachycardia is an automatic tachycardia originating in the AV junction. It tends to be a regular, narrow complex tachycardia and may be a sign of digitalis toxicity.

Management

The management of tachycardia depends its type (wide complex verses narrow complex), whether or not the person is stable or unstable, and if the instability is due to the

tachycardia. Unstable means that either important organ functions are affected or cardiac arrest is about to occur.

Stable

In those who are stable treatment is determined by the exact ECG findings: wide verses narrow complex, regular verses irregular heart rate, and whether the QRS is monomorphic or polymorphic.

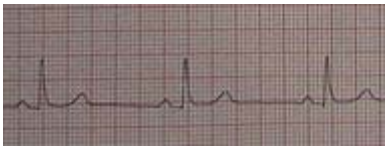
Unstable

In those who are unstable with a narrow complex tachycardia intravenous adenosine may be attempted. In all others immediate cardioversion is recommended.

Chapter 26

Bradycardia

Bradycardia



Sinus bradycardia seen in lead II with a heart rate of about 50.

ICD-10 R00.1

ICD-9 427.81, 659.7, 785.9, 779.81

MeSH D001919

Bradycardia (Greek βραδυκαρδία, *bradykardía*, "heart slowness"), in the context of adult medicine, is the resting heart rate of under 60 beats per minute, though it is seldom symptomatic until the rate drops below 50 beat/min. It may cause cardiac arrest in some patients, because those with bradycardia may not be pumping enough oxygen to their heart. It sometimes results in fainting, shortness of breath, and if severe enough, death.

Trained athletes or young healthy individuals may also have a slow resting heart rate (e.g. professional cyclist Miguel Indurain had a resting heart rate of 28 beats per minute). Resting bradycardia is often considered normal if the individual has no other symptoms such as fatigue, weakness, dizziness, lightheadedness, fainting, chest discomfort, palpitations or shortness of breath associated with it.

The term *relative bradycardia* is used in explaining a heart rate which although not actually below 60 beats per minute still is considered too slow for the individual's current medical condition.

Definition

Bradycardia in an adult is any heart rate less than 60 beats per minute, although symptoms usually manifest only for heart rates less than 50.

Classification

Atrial

Atrial bradycardias come in three different types. The first is sinus bradycardia. This is usually found in young and healthy adults. The symptoms represent with the individual's respirations. Each inhalation corresponds with the heart rate decreasing. Expiration causes an increase in the heart's rate of contraction. This is thought to be caused by changes in the vagal tone during respiration.

Sinus bradycardia is a sinus rhythm of less than 60 bpm. It is a common condition found in both healthy individuals and those who are considered well conditioned athletes. Studies have found that 50 - 85 percent of conditioned athletes have benign sinus bradycardia, as compared to 23 percent of the general population studied. The reason for this is that their heart muscle has become conditioned to have a higher stroke volume and therefore requires fewer contractions to circulate the same volume of blood.

Sick sinus syndrome covers conditions that include severe sinus bradycardia, sinoatrial block, sinus arrest, and bradycardi-tachycardia syndrome (atrial fibillation, flutter, and paroxysmal supraventricular tachycardia).

Atrioventricular nodal

An atrioventricular nodal bradycardia or AV junction rhythm is usually caused by the absence of the electrical impulse from the sinus node. This usually appears on an EKG with a normal QRS complex accompanied with an inverted P wave either before, during, or after the QRS complex.

An AV junctional escape is a delayed heartbeat originating from an ectopic focus somewhere in the AV junction. It occurs when the rate of depolarization of the SA node falls below the rate of the AV node. This dysrhythmia also may occur when the electrical impulses from the SA node fail to reach the AV node because of SA or AV block. This is a protective mechanism for the heart, to compensate for a SA node that is no longer handling the pacemaking activity, and is one of a series of backup sites that can take over pacemaker function when the SA node fails to do so. This would present with a longer PR interval. A junctional escape complex is a normal response that may result from excessive vagal tone on the SA node. Pathological causes include sinus bradycardia, sinus arrest, sinus exit block, or AV block.

Ventricular

A ventricular bradycardia, also known as ventricular escape rhythm or idioventricular rhythm, is a heart rate of less than 50 beats a minute. This is a safety mechanism that arises when there is lack of electrical impulse or stimuli from the atrium. Impulses originating from or below the His bundle, also known as ventricular, will produce a wide QRS complex with heart rates between 20 and 40 beats a minute. Those above the His

bundle, also known as junctional, will typically range between 40 and 60 bpm with a narrow QRS complex. In a third degree heart block, approximately 61% take place at the bundle branch-Purkinje system, 21% at the AV node, and 15% at the His bundle. AV block maybe ruled out with an EKG indicating "a 1:1 relationship between P waves and QRS complexes." Ventricular bradycardias occurs with sinus bradycardia, sinus arrest, and AV block. Treatment often consist of the administration of atropine and cardiac pacing.

Infantile

For infants, bradycardia is defined as a heart rate of less than 100 beats per minute. (Normal is around 120-160 beats per minute.) Premature babies are more likely than full-term babies to have apnea and bradycardia spells; their cause is not clearly understood. Some researchers think the spells are related to centers inside the brain that regulate breathing and that may not be fully developed. Touching the baby gently or rocking the incubator slightly will almost always get the baby to start breathing again, which increases the heart rate. Medications (theophylline or caffeine) can be used to treat these spells in babies if necessary. NICU standard practice is to electronically monitor the heart and lungs for this reason.

Causes

This cardiac arrhythmia can be underlain by several causes, which are best divided into cardiac and non-cardiac causes. Non-cardiac causes are usually secondary, and can involve drug use or abuse; metabolic or endocrine issues, especially in the thyroid; an electrolyte imbalance; neurologic factors; autonomic reflexes; situational factors such as prolonged bed rest; and autoimmunity. Cardiac causes include acute or chronic ischemic heart disease, vascular heart disease, valvular heart disease, or degenerative primary electrical disease. Ultimately, the causes act by three mechanisms: depressed automaticity of the heart, conduction block, or escape pacemakers and rhythms.

There are generally two types of problems that result in bradycardias: disorders of the sinoatrial node (SA node), and disorders of the atrioventricular node (AV node).

With sinus node dysfunction (sometimes called sick sinus syndrome), there may be disordered automaticity or impaired conduction of the impulse from the sinus node into the surrounding atrial tissue (an "exit block"). Only second degree sinostrial blocks can be detected by use of a 12-lead EKG. It is difficult and sometimes impossible to assign a mechanism to any particular bradycardia, but the underlying mechanism is not clinically relevant to treatment, which is the same in both cases of sick sinus syndrome: a permanent pacemaker.

Atrioventricular conduction disturbances (aka: AV block; 1^{o} AV block, 2^{o} type I AV block, 2^{o} type II AV block, 3^{o} AV block) may result from impaired conduction in the AV node, or anywhere below it, such as in the Bundle of His. The clinical relevance pertaining to AV blocks is greater than that of sinoatrial blocks.

Patients with bradycardia have likely acquired it, as opposed to having it congenitally. Bradycardia is more common in older patients.

Diagnosis

A diagnosis of bradycardia in adults is based on a heart rate less than 60. This is determined usually either via palpation or an ECG.

If symptoms occur, a determination of electrolytes may be helpful in determining the underlying cause.

Management

The treatment of bradycardia is dependent on whether or not the person is stable or unstable. If oxygen saturations are low supplemental oxygen should be provided.

Stable

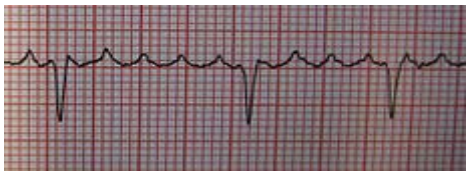
Emergent treatment is not needed if the person is asymptomatic or minimally symptomatic.

Unstable

If a person is unstable the initial recommended treatment is intravenous atropine. Doses less than 0.5 mg should not be used as this may further decrease the rate. If this is not effective intravenous inotrope infusion (dopamine, epinephrine) or transcutaneous pacing should be used. Transvenous pacing may be required if the cause of the bradycardia is not rapidly reversible.

Chapter 27

Atrial Flutter

Atrial flutter	
	
Atrial flutter with variable block (between 3 and 4 to 1)	
ICD-10	I48.
ICD-9	427.32
DiseasesDB	1072
MedlinePlus	000184
eMedicine	med/185
MeSH	D001282

Atrial flutter (AFL) is an abnormal heart rhythm that occurs in the atria of the heart. When it first occurs, it is usually associated with a fast heart rate or tachycardia (beats over 100 per minute), and falls into the category of supra-ventricular tachycardias. While this rhythm occurs most often in individuals with cardiovascular disease (e.g. hypertension, coronary artery disease, and cardiomyopathy), it may occur spontaneously in people with otherwise normal hearts. It is typically not a stable rhythm, and frequently degenerates into atrial fibrillation (AF). However, it does rarely persist for months to years.

Atrial flutter was first identified as an independent medical condition in 1920 by the British physician Sir Thomas Lewis (1881–1945) and colleagues.

Signs and symptoms

While atrial flutter can sometimes go unnoticed, its onset is often marked by characteristic sensations of regular palpitations. Such sensations usually last until the episode resolves, or until the heart rate is controlled.

Atrial flutter is usually well tolerated initially (a high heart rate is for most people just a normal response to exercise), however, people with other underlying heart disease or poor exercise tolerance may rapidly develop symptoms, which can include shortness of breath, chest pains, lightheadedness or dizziness, nausea and, in some patients, nervousness and feelings of impending doom.

Prolonged fast flutter may lead to decompensation with loss of normal heart function (heart failure). This may manifest as effort intolerance (exertional breathlessness), nocturnal breathlessness, or swelling of the legs or abdomen.

Pathophysiology

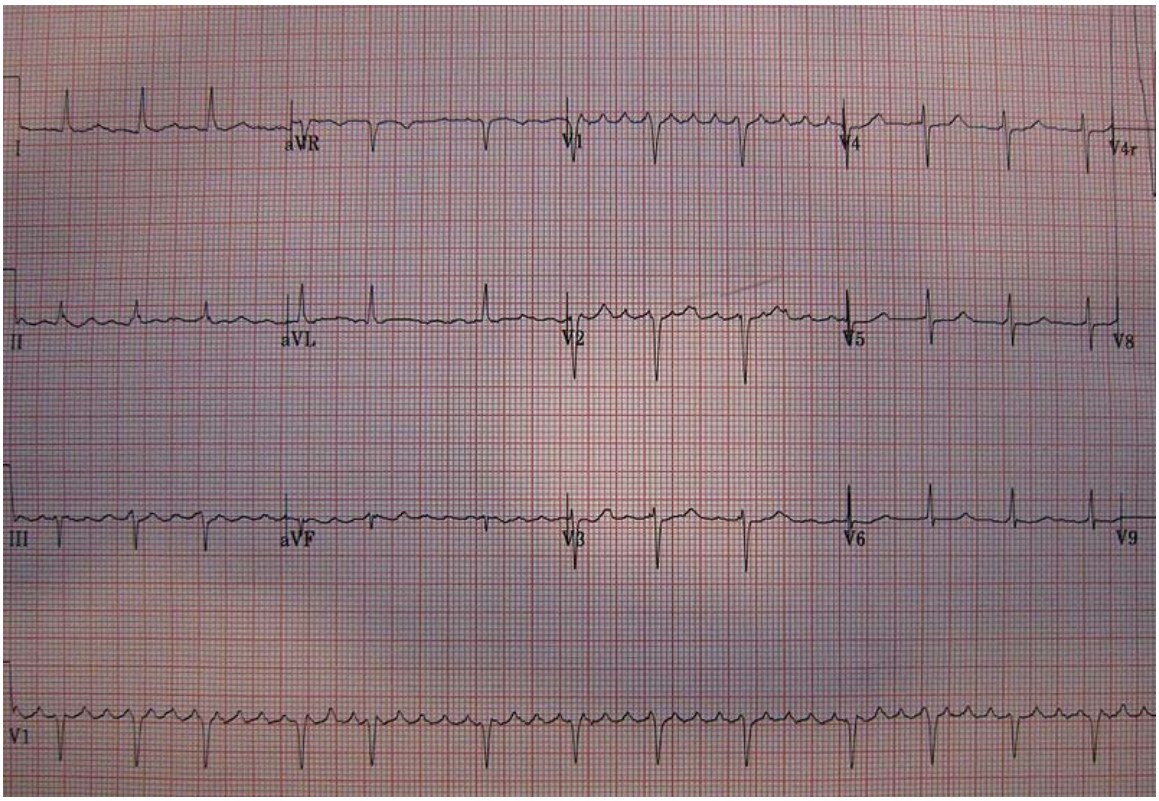
Atrial flutter is caused by a reentrant rhythm in either the right or left atrium. Typically initiated by a premature electrical impulse arising in the atria, atrial flutter is propagated due to differences in refractory periods of atrial tissue. This creates electrical activity that moves in a localized self-perpetuating loop. For each cycle around the loop, there results an electric impulse that propagates through the atria.

The impact and symptoms of atrial flutter depend on the heart rate of the patient. Heart rate is a measure of the ventricular rather than atrial activity. Impulses from the atria are conducted to the ventricles through the atrio-ventricular node. Due primarily to its longer refractory period, the AV node exerts a protective effect on heart rate by blocking atrial impulses in excess of about 180 beats/minute, for the example of a resting heart rate. (This block is dependent on the age of the patient, and can be calculated roughly by subtracting patient age from 220). If the flutter rate is 300/minute only half of these impulses will be conducted, giving a ventricular rate of 150/minute, or a 2:1 heart block. The addition of rate-controlling drugs or conduction system disease can increase this block substantially.

Classification

There are two types of atrial flutter, the common *type I* and rarer *type II*. Most individuals with atrial flutter will manifest only one of these. Rarely someone may manifest both types; however, they can only manifest one type at a time.

Type I



Type I atrial flutter, counterclockwise rotation with 3:1 and 4:1 AV nodal block.

Type I atrial flutter, also known as **common atrial flutter** or **typical atrial flutter**, has an atrial rate of 240 to 350 beats/minute. However, this rate may be slowed by antiarrhythmic agents.

The reentrant loop circles the right atrium, passing through the cavo-tricuspid isthmus - a body of fibrous tissue in the lower atrium between the inferior vena cava, and the tricuspid valve. Type I flutter is further divided into two subtypes, known as **counterclockwise atrial flutter** and **clockwise atrial flutter** depending on the direction of current passing through the loop.

- Counterclockwise atrial flutter (known as cephalad-directed atrial flutter) is more commonly seen. The flutter waves in this rhythm are inverted in ecg leads II, III, and aVF.
- The re-entry loop cycles in the opposite direction in clockwise atrial flutter, thus the flutter waves are upright in II, III, and aVF.

Catheter ablation of the isthmus is a procedure usually available in the electrophysiology laboratory. Eliminating conduction through the isthmus prevents reentry, and if successful, prevents the recurrence of the atrial flutter.

Type II

Type II flutter follows a significantly different re-entry pathway to type I flutter, and is typically faster, usually 340-350 beats/minute. Left atrial flutter is common after incomplete left atrial ablation procedures.

Complications

Although often regarded as a relatively benign rhythm problem, atrial flutter shares the same complications as the related condition atrial fibrillation. There is paucity of published data directly comparing the two, but overall mortality in these conditions appears to be very similar.

Rate Related

Rapid heart rates may produce significant symptoms in patients with pre-existing heart disease. Even in patients whose hearts are normal to start with, prolonged tachycardia tends to produce ventricular decompensation and heart failure.

Clot formation

Because there is little if any effective contraction of the atria there is stasis (pooling) of blood in the atria. Stasis of blood in susceptible individuals can lead to formation of thrombus (blood clots) within the heart. Thrombus is most likely to form in the **atrial appendages**. Clot in the **left atrial appendage** is particularly important since the left side of the heart supplies blood to the entire body. Thus, any thrombus material that dislodges from this side of the heart can embolize to the brain, with the potentially devastating consequence of a stroke. Thrombus material can of course embolize to any other portion of the body, though usually with a less severe outcome.

Sudden cardiac death

Sudden death is not directly associated with atrial flutter. However, in individuals with a pre-existing accessory conduction pathway, such as the bundle of Kent in Wolff-Parkinson-White syndrome, the accessory pathway *may* conduct activity from the atria to the ventricles at a rate that the AV node would usually block. Bypassing the AV node, the atrial rate of 300 beats/minute leads to a ventricular rate of 300 beats/minute (1:1 conduction). Even if the ventricles are able to sustain a cardiac output at such a high rates, 1:1 flutter with time may degenerate into ventricular fibrillation, causing hemodynamic collapse and death.

Treatment

In general, atrial flutter should be treated the same as atrial fibrillation. Because both rhythms can lead to the formation of thrombus in the atria, individuals with atrial flutter usually require some form of anticoagulation or anti-platelet agent. Both rhythms can be

associated with dangerously fast heart rate and thus require medication for rate and or rhythm control. Additionally, there are some specific considerations particular to treatment of atrial flutter.

Cardioversion

Atrial flutter is considerably more sensitive to electrical direct-current cardioversion than atrial fibrillation, and usually requires a lower energy shock. 20-50J is commonly enough to revert to sinus rhythm. Conversely, it is relatively resistant to chemical cardioversion, and often deteriorates into atrial fibrillation prior to spontaneous return to sinus rhythm.

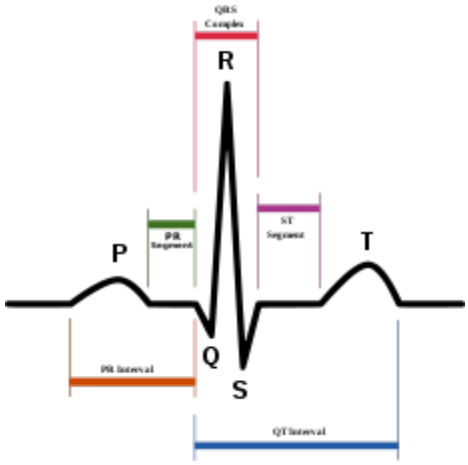
Ablation

Because of the reentrant nature of atrial flutter, it is often possible to ablate the circuit that causes atrial flutter. This is done in the electrophysiology lab by causing a ridge of scar tissue that crosses the path of the circuit that causes atrial flutter. Ablation of the isthmus, as discussed above, is a common treatment for typical atrial flutter.

Chapter 28

Atrial Fibrillation

Atrial fibrillation



The P waves, which represent depolarization of the atria, are absent during atrial fibrillation.

ICD-10	I48.
ICD-9	427.31
DiseasesDB	1065
MedlinePlus	000184
eMedicine	med/184 emerg/46
MeSH	D001281

Atrial fibrillation (**AF** or **A-fib**) is the most common cardiac arrhythmia (abnormal heart rhythm), and involves the two upper chambers (atria) of the heart. Its name comes from the fibrillating (i.e., quivering) of the heart muscles of the atria, instead of a coordinated contraction. It can often be identified by taking a pulse and observing that the heartbeats do not occur at regular intervals. However, a stronger indicator of AF is the absence of P waves on an electrocardiogram (ECG or EKG), which are normally present when there is a coordinated atrial contraction at the beginning of each heart beat. Risk increases with age, with 8% of people over 80 having AF.

In AF, the normal electrical impulses that are generated by the sinoatrial node are overwhelmed by disorganized electrical impulses that originate in the atria and pulmonary veins, leading to conduction of irregular impulses to the ventricles that generate the heartbeat. The result is an irregular heartbeat, which may occur in episodes lasting from minutes to weeks, or it could occur all the time for years. The natural tendency of AF is to become a chronic condition. Chronic AF leads to a small increase in the risk of death.

Atrial fibrillation is often asymptomatic and is not in itself generally life-threatening, but it may result in palpitations, fainting, chest pain, or congestive heart failure. People with AF usually have a significantly increased risk of stroke (up to 7 times that of the general population). Stroke risk increases during AF because blood may pool and form clots in the poorly contracting atria and especially in the left atrial appendage (LAA). The level of increased risk of stroke depends on the number of additional risk factors. If a person with AF has none, the risk of stroke is similar to that of the general population. However, many people with AF do have additional risk factors and AF is a leading cause of stroke.

Atrial fibrillation may be treated with medications which either slow the heart rate or revert the heart rhythm back to normal. Synchronized electrical cardioversion may also be used to convert AF to a normal heart rhythm. Surgical and catheter-based therapies may also be used to prevent recurrence of AF in certain individuals. People with AF are often given anticoagulants such as warfarin to protect them from stroke.

Classification

Classification system

AF Category	**Defining Characteristics**
First detected	only one diagnosed episode
Paroxysmal	recurrent episodes that self-terminate in less than 7 days.
Persistent	recurrent episodes that last more than 7 days
Permanent	an ongoing long-term episode

The American College of Cardiology (ACC), American Heart Association (AHA), and the European Society of Cardiology (ESC) recommend in their guidelines the following classification system based on simplicity and clinical relevance.

All atrial fibrillation patients are initially in the category called *first detected AF*. These patients may or may not have had previous undetected episodes. If a first detected episode self-terminates in less than 7 days and then another episode begins later on, the case has moved into the category of *paroxysmal AF*. Although patients in this category have episodes lasting up to 7 days, in most cases of paroxysmal AF the episodes will self-terminate in less than 24 hours. If instead the episode lasts for more than 7 days, it is unlikely to self-terminate, and it is called *persistent AF*. In this case, the episode may be still terminated by cardioversion. If cardioversion is unsuccessful or it is not attempted, and the episode is ongoing for a long time (e.g. a year or more), the patient's AF is called *permanent*.

Episodes that last less than 30 seconds are not considered in this classification system. Also, this system does not apply to cases where the AF is a secondary condition that occurs in the setting of a primary condition that may be the cause of the AF.

Using this classification system, it's not always clear what an AF case should be called. For example, a case may fit into the paroxysmal AF category some of the time, while other times it may have the characteristics of persistent AF. One may be able to decide which category is more appropriate by determining which one occurs most often in the case under consideration.

In addition to the above four AF categories, which are mainly defined by episode timing and termination, the ACC/AHA/ESC guidelines describe additional AF categories in terms of other characteristics of the patient.

- *Lone atrial fibrillation* (LAF) - absence of clinical or echocardiographic findings of other cardiovascular disease (including hypertension), related pulmonary disease, or cardiac abnormalities such as enlargement of the left atrium, and age under 60 years
- *Nonvalvular AF* - absence of rheumatic mitral valve disease, a prosthetic heart valve, or mitral valve repair
- *Secondary AF* - occurs in the setting of a primary condition which may be the cause of the AF, such as acute myocardial infarction, cardiac surgery, pericarditis, myocarditis, hyperthyroidism, pulmonary embolism, pneumonia, or other acute pulmonary disease

Signs and symptoms

Atrial fibrillation is usually accompanied by symptoms related to a rapid heart rate. Rapid and irregular heart rates may be perceived as palpitations, exercise intolerance, and occasionally produce angina (if the rate is faster and puts the heart under strain) and congestive symptoms of shortness of breath or edema. Sometimes the arrhythmia will be identified only with the onset of a stroke or a transient ischemic attack (TIA). It is not uncommon for a patient to first become aware of AF from a routine physical examination or ECG, as it may be asymptomatic in many cases.

As most cases of atrial fibrillation are secondary to other medical problems, the presence of chest pain or angina, symptoms of hyperthyroidism (an overactive thyroid gland) such as weight loss and diarrhea, and symptoms suggestive of lung disease would indicate an underlying cause. A previous history of stroke or TIA, as well as hypertension (high blood pressure), diabetes, heart failure and rheumatic fever, may indicate whether someone with AF is at a higher risk of complications.

Rapid heart rate

Presentation is similar to other forms of rapid heart rate (tachycardia), and in some cases may actually be asymptomatic. The patient may complain of palpitations or chest

discomfort. The rapid heart rate may result in the heart being unable to provide adequate blood flow and oxygen delivery to the rest of the body. Therefore, common symptoms may include shortness of breath which often worsens with exertion (dyspnea on exertion), shortness of breath when lying flat (orthopnea), and sudden onset of shortness of breath during the night (paroxysmal nocturnal dyspnea), and may progress to swelling of the lower extremities (peripheral edema).Due to inadequate blood flow, patients may also complain of light-headedness, may feel like they are about to faint (presyncope), or may actually lose consciousness (syncope).

The patient may be in significant respiratory distress. Due to inadequate oxygen delivery, the patient may appear blue (cyanosis). By definition, the heart rate will be greater than 100 beats per minute. Blood pressure will be variable, and often difficult to measure as the beat-by-beat variability causes problems for most digital (oscillometric) non-invasive blood pressure monitors. It is most concerning if consistently lower than usual (hypotension). Respiratory rate will be increased in the presence of respiratory distress. Pulse oximetry may confirm the presence of hypoxia related to any precipitating factors such as pneumonia. Examination of the jugular veins may reveal elevated pressure (jugular venous distention). Lung exam may reveal rales or crackles, which are suggestive of pulmonary edema. Heart exam will reveal an irregular but rapid rhythm.

Association with other conditions

- Central sleep apnea (CSA) – A study found that the prevalence of atrial fibrillation among patients with idiopathic central sleep apnea was significantly higher than the prevalence among patients with obstructive sleep apnea or no sleep apnea (27%, 1.7%, and 3.3%, respectively). There was a total of 180 subjects with 60 people in each of the 3 groups. Possible explanations for the association between CSA and AF are a causal relationship between the two conditions, or an abnormality of central cardiorespiratory regulation.
- Left atrial enlargement
- Mitral stenosis

Diagnosis

The evaluation of atrial fibrillation involves diagnosis, determination of the etiology of the arrhythmia, and classification of the arrhythmia. A minimal evaluation should be performed in all individuals with AF. This includes a history and physical examination, ECG, transthoracic echocardiogram, and routine bloodwork. Depending upon given resources, afflicted individuals may benefit from an in-depth evaluation which may include correlation of the heart rate response to exercise, exercise stress testing, chest X-ray, trans-esophageal echocardiography, and other studies.

If a patient presents with a sudden onset of severe symptoms other forms of tachyarrhythmia must be ruled-out, as some may be immediately life threatening, such as ventricular tachycardia. While most patients will be placed on continuous cardiorespiratory monitoring, an electrocardiogram is essential for diagnosis.

Provoking causes should be sought out. A common cause of any tachycardia is dehydration, as well as other forms of hypovolemia. Acute coronary syndrome should be ruled out. Intercurrent illness such as pneumonia may be present.

Screening

Screening for atrial fibrillation is not generally performed, although a study of routine pulse checks or ECGs during routine office visits found that the annual rate of detection of AF in elderly patients improved from 1.04% to 1.63%; selection of patients for prophylactic anticoagulation would improve stroke risk in that age category.

This estimated sensitivity of the routine primary care visit is 64%. This low result probably reflects the pulse not being checked routinely or carefully.

When ECGs are used for screening, the SAFE trial found that electronic software, primary care physicians and the combination of the two had the following sensitivities and specificities:

- Interpreted by software: sensitivity = 83%, specificity = 99%
- Interpreted by a primary care physician: sensitivity = 80%, specificity = 92%
- Interpreted by a primary care physician with software: sensitivity = 92%, specificity = 91%

Minimal evaluation

The minimal evaluation of atrial fibrillation should generally be performed in all individuals with AF. The goal of this evaluation is to determine the general treatment regimen for the individual. If results of the general evaluation warrant it, further studies may then be performed.

History and physical examination

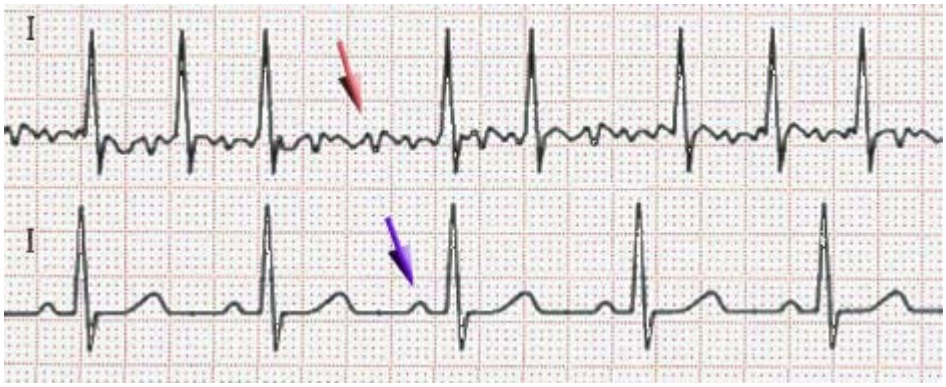
The history of the individual's atrial fibrillation episodes is probably the most important part of the evaluation. Distinctions should be made between those who are entirely asymptomatic when they are in AF (in which case the AF is found as an incidental finding on an ECG or physical examination) and those who have gross and obvious symptoms due to AF and can pinpoint whenever they go into AF or revert to sinus rhythm.

Routine bloodwork

While many cases of AF have no definite cause, it may be the result of various other problems. Hence, renal function and electrolytes are routinely determined, as well as thyroid-stimulating hormone (commonly suppressed in hyperthyroidism and of relevance if amiodarone is administered for treatment) and a blood count.

In acute-onset AF associated with chest pain, cardiac troponins or other markers of damage to the heart muscle may be ordered. Coagulation studies (INR/aPTT) are usually performed, as anticoagulant medication may be commenced.

Electrocardiogram



ECG of atrial fibrillation (top) and normal sinus rhythm (bottom). The purple arrow indicates a P wave, which is lost in atrial fibrillation.

Atrial fibrillation is diagnosed on an electrocardiogram (ECG), an investigation performed routinely whenever an irregular heart beat is suspected. Characteristic findings are the absence of P waves, with unorganized electrical activity in their place, and irregular R-R intervals due to irregular conduction of impulses to the ventricles. However, irregular R-R intervals may be difficult to determine if the rate is extremely rapid.

QRS complexes should be narrow, signifying that they are initiated by normal conduction of atrial electrical activity through the intraventricular conduction system. Wide QRS complexes are worrisome for ventricular tachycardia, although in cases where there is disease of the conduction system, wide complexes may be present in A-Fib with rapid ventricular response.

If paroxysmal AF is suspected but an ECG during an office visit only shows a regular rhythm, AF episodes may be detected and documented with the use of ambulatory Holter monitoring (e.g. for a day). If the episodes are too infrequent to be detected by Holter monitoring with reasonable probability, then the patient can be monitored for longer periods (e.g. a month) with an ambulatory event monitor.

Echocardiography

A non-invasive transthoracic echocardiogram (TTE) is generally performed in newly diagnosed AF, as well as if there is a major change in the patient's clinical state. This ultrasound-based scan of the heart may help identify valvular heart disease (which may greatly increase the risk of stroke), left and right atrial size (which indicates likelihood that AF may become permanent), left ventricular size and function, peak right ventricular

pressure (pulmonary hypertension), presence of left atrial thrombus (low sensivity), presence of left ventricular hypertrophy and pericardial disease.

Significant enlargement of both the left and right atria is associated with long-standing atrial fibrillation and, if noted at the initial presentation of atrial fibrillation, suggests that the atrial fibrillation is likely to be of a longer duration than the individual's symptoms.

Extended evaluation

An extended evaluation is generally not necessary in most individuals with atrial fibrillation, and is only performed if abnormalities are noted in the limited evaluation, if a reversible cause of the atrial fibrillation is suggested, or if further evaluation may change the treatment course.

Chest X-ray

A chest X-ray is generally only performed if a pulmonary cause of atrial fibrillation is suggested, or if other cardiac conditions are suspected (particularly congestive heart failure.) This may reveal an underlying problem in the lungs or the blood vessels in the chest. In particular, if an underlying pneumonia is suggested, then treatment of the pneumonia may cause the atrial fibrillation to terminate on its own.

Transesophageal echocardiogram

A normal echocardiography (transthoracic or TTE) has a low sensitivity for identifying thrombi (blood clots) in the heart. If this is suspected - e.g. when planning urgent electrical cardioversion - a transesophageal echocardiogram (TEE or TOE where British spelling is used) is preferred.

The TEE has much better visualization of the left atrial appendage than transthoracic echocardiography. This structure, located in the left atrium, is the place where thrombus is formed in more than 90% of cases in non-valvular (or non-rheumatic) atrial fibrillation or flutter. TEE has a high sensitivity for locating thrombi in this area and can also detect sluggish bloodflow in this area that is suggestive of thrombus formation.

If no thrombus is seen on TEE, the incidence of stroke, (immediately after cardioversion is performed), is very low.

Ambulatory Holter monitoring

A Holter monitor is a wearable ambulatory heart monitor that continuously monitors the heart rate and heart rhythm for a short duration, typically 24 hours. In individuals with symptoms of significant shortness of breath with exertion or palpitations on a regular basis, a holter monitor may be of benefit to determine if rapid heart rates (or unusually slow heart rates) during atrial fibrillation are the cause of the symptoms.

Exercise stress testing

Some individuals with atrial fibrillation do well with normal activity but develop shortness of breath with exertion. It may be unclear if the shortness of breath is due to a blunted heart rate response to exertion due to excessive AV node blocking agents, a very rapid heart rate during exertion, or due to other underlying conditions such as chronic lung disease or coronary ischemia. An exercise stress test will evaluate the individual's heart rate response to exertion and determine if the AV node blocking agents are contributing to the symptoms.

Cause

AF is linked to several cardiac causes, but may occur in otherwise normal hearts. Known associations include:

- Hypertension (High blood pressure)
- Primary heart diseases including coronary artery disease, mitral stenosis (e.g. due to rheumatic heart disease or mitral valve prolapse), mitral regurgitation, hypertrophic cardiomyopathy (HCM), pericarditis, congenital heart disease, previous heart surgery
- Lung diseases (such as pneumonia, lung cancer, pulmonary embolism, sarcoidosis)
- Excessive alcohol consumption ("binge drinking" or "holiday heart syndrome"). Even otherwise healthy middle-aged women who consumed more than 2 drinks daily were 60% more likely to develop AF.
- Hyperthyroidism
- Carbon monoxide poisoning
- Dual-chamber pacemakers in the presence of normal atrioventricular conduction.
- A family history of AF may increase the risk of AF. A study of more than 2,200 AF patients found that 30 per cent had parents with AF. Various genetic mutations may be responsible.
- Friedreich's ataxia

Pathophysiology

Morphology

The primary pathologic change seen in atrial fibrillation is the progressive fibrosis of the atria. This fibrosis is primarily due to atrial dilation, however genetic causes and inflammation may have a cause in some individuals. One study found that atrial dilation can occur as a consequence of AF, although another study found that AF by itself does not cause it.

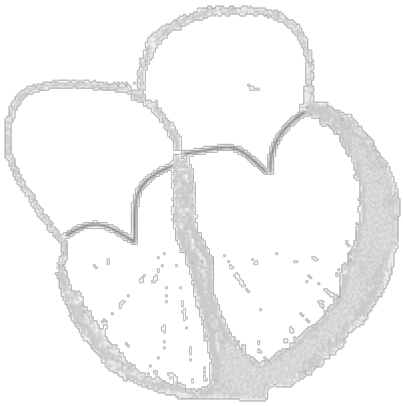
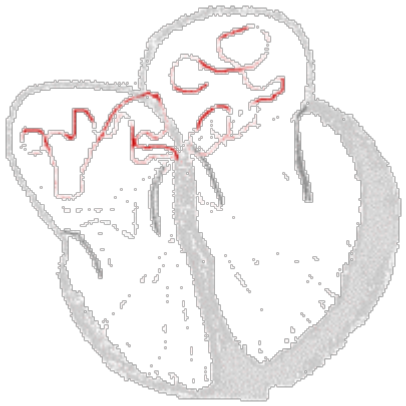
Dilation of the atria can be due to almost any structural abnormality of the heart that can cause a rise in the intra-cardiac pressures. This includes valvular heart disease (such as mitral stenosis, mitral regurgitation, and tricuspid regurgitation), hypertension, and

congestive heart failure. Any inflammatory state that affects the heart can cause fibrosis of the atria. This is typically due to sarcoidosis but may also be due to autoimmune disorders that create autoantibodies against myosin heavy chains. Mutation of the *lamin AC* gene is also associated with fibrosis of the atria that can lead to atrial fibrillation.

Once dilation of the atria has occurred, this begins a chain of events that leads to the activation of the renin aldosterone angiotensin system (RAAS) and subsequent increase in matrix metaloproteinases and disintegrin, which leads to atrial remodeling and fibrosis, with loss of atrial muscle mass. This process is not immediate, and experimental studies have revealed patchy atrial fibrosis may precede the occurrence of atrial fibrillation and may progress with prolonged durations of atrial fibrillation.

Fibrosis is not limited to the muscle mass of the atria, and may occur in the sinus node (SA node) and atrioventricular node (AV node), correlating with sick sinus syndrome. Prolonged episodes of atrial fibrillation have been shown to correlate with prolongation of the sinus node recovery time, suggesting that dysfunction of the SA node is progressive with prolonged episodes of atrial fibrillation.

Electrophysiology

Conduction	
Sinus rhythm	Atrial fibrillation
	

The normal electrical conduction system of the heart allows the impulse that is generated by the sinoatrial node (SA node) of the heart to be propagated to and stimulate the myocardium (muscle of the heart). When the myocardium is stimulated, it contracts. It is the ordered stimulation of the myocardium that allows efficient contraction of the heart, thereby allowing blood to be pumped to the body.

There are multiple theories about the etiology of atrial fibrillation. An important theory is that in atrial fibrillation, the regular impulses produced by the sinus node for a normal heartbeat, are overwhelmed by rapid electrical discharges produced in the atria and adjacent parts of the pulmonary veins. Sources of these disturbances are either automatic foci, often localized at one of the pulmonary veins, or a small number of reentrant sources (rotors) harbored by the posterior wall of the left atrium near the junctions with

the pulmonary veins. The pathology progresses from paroxysmal to persistent AF as the sources multiply and localize anywhere in the atria. Because recovery of the atria from excitation is heterogeneous, the electrical waves generated by the AF sources undergo repetitive, spatially distributed breakup and fragmentation in a process known as "fibrillatory conduction". Another theory is the multiple wavelet theory first formulated by by Moe,, which was experimentally proven by Allessie et al.

AF can be distinguished from atrial flutter (AFL), which appears as an organized electrical circuit usually in the right atrium. AFL produces characteristic saw-toothed F-waves of constant amplitude and frequency on an ECG whereas AF does not. In AFL, the discharges circulate rapidly at a rate of 300 beats per minute (bpm) around the atrium. In AF, there is no regularity of this kind, except at the sources where the local activation rate can exceed 500 bpm.

Although the electrical impulses of AF occur at a high rate, most of them do not result in a heart beat. A heart beat results when an electrical impulse from the atria passes through the atrioventricular (AV) node to the ventricles and causes them to contract. During AF, if all of the impulses from the atria passed through the AV node, there would be severe ventricular tachycardia resulting in severe reduction of cardiac output. This dangerous situation is prevented by the AV node since its limited conduction velocity reduces the rate at which impulses reach the ventricles during AF.

Management

The main goals of treatment are to prevent circulatory instability and stroke. Rate or rhythm control are used to achieve the former, while anticoagulation is used to decrease the risk of the latter. If cardiovascularly unstable due to uncontrolled tachycardia, immediate cardioversion is indicated.

Anticoagulation

Anticoagulation can be achieved through a number of means including the use of aspirin, heparin, warfarin, and dabigatran. Which method is used depends on a number issues including: cost, risk of stroke, risk of falls, compliance, and speed of desired onset of anticoagulation.

Rate control versus rhythm control using drugs

AF can cause disabling and annoying symptoms. Palpitations, angina, lassitude (weariness), and decreased exercise tolerance are related to rapid heart rate and inefficient cardiac output caused by AF. Furthermore, AF with a persistent rapid rate can cause a form of heart failure called tachycardia induced cardiomyopathy. This can significantly increase mortality and morbidity, which can be prevented by early and adequate treatment of the AF.

There are two ways to approach these symptoms using drugs: rate control and rhythm control. *Rate control* seeks to reduce the heart rate to one that is closer to normal, usually 60 to 100 bpm, without trying to convert to a regular rhythm. *Rhythm control* seeks to restore with cardioversion the regular heart rhythm and maintain it with drugs. Studies suggest that rhythm control is mainly a concern in newly diagnosed AF, while rate control is more important in the chronic phase. As far as mortality is concerned, the AFFIRM trial showed that there is no statistical difference with rate control treatment versus rhythm control treatment.

The AFFIRM study also showed no difference in risk of stroke in patients who have converted to a normal rhythm with anti-arrhythmic treatment, compared to those who have only rate control. AF is associated with a reduced quality of life, and while some studies indicate that rhythm control leads to a higher quality of life, the AFFIRM study did not find a difference.

A further study focused on rhythm control in patients with AF and simultaneous heart failure, based on the premise that AF confers a higher mortality risk in heart failure. In this setting, too, rhythm control offered no advantage compared to rate control.

In patients with a fast ventricular response, intravenous magnesium significantly increases the chances of successful rate and rhythm control in the urgent setting without significant side-effects. A patient with hemodynamic instability, mental status changes, preexcitation, or angina will require urgent synchronized DC cardioversion. Otherwise the decision of rate control versus rhythm control using drugs is made. This is based on a number of criteria that includes whether or not symptoms persist with rate control.

Rate control

Rate control is achieved with medications that work by increasing the degree of block at the level of the AV node, effectively decreasing the number of impulses that conduct down into the ventricles. This can be done with:

- Beta blockers (preferably the "cardioselective" beta blockers such as metoprolol, atenolol, bisoprolol, nebivolol)
- Non-dihydropyridine calcium channel blockers (i.e. diltiazem or verapamil)
- Cardiac glycosides (i.e. digoxin) - have limited use, apart from in the sedentary elderly patient

In addition to these agents, amiodarone has some AV node blocking effects (particularly when administered intravenously), and can be used in individuals when other agents are contraindicated or ineffective (particularly due to hypotension).

Diltiazem has been shown to be more effective than either digoxin or amiodarone.

Cardioversion

Cardioversion is a noninvasive conversion of an irregular heartbeat to a normal heartbeat using electrical or chemical means:

- *Electrical cardioversion* involves the restoration of normal heart rhythm through the application of a DC electrical shock.
- *Chemical cardioversion* is performed with drugs, such as amiodarone, dronedarone, procainamide, ibutilide, propafenone or flecainide.

Vernakalant has been found to safely and rapidly covert new onset atrial fibrillation.

Ablation

If rhythm control is desired and cannot be maintained by medication or cardioversion, electrophysiological studies with pathway ablation may be attempted.

Prognosis

Thromboembolism

In atrial fibrillation, the lack of an organized atrial contraction can result in some stagnant blood in the left atrium (LA) or left atrial appendage (LAA). This lack of movement of blood can lead to thrombus formation (blood clotting). If the clot becomes mobile and is carried away by the blood circulation, it is called an embolus. An embolus proceeds through smaller and smaller arteries until it plugs one of them and prevents blood from flowing any farther in that artery. The result can be damage to tissue that depends on that supply of blood. This can occur in various parts of the body, depending on where the embolus ends up. An embolus lodged in an artery of the brain results in a stroke or transient ischemic attack (TIA). The formation of a thrombus, movement of the embolus, and plugging of an artery, is called a thromboembolism.

The LAA is the site of thrombus formation in more than 90% of cases of thrombi associated with non-valvular atrial fibrillation. However, the LAA lies in close relation to the free wall of the left ventricle and thus the LAA's emptying and filling, which determines its degree of blood stagnation, may be helped by the motion of the wall of the left ventricle, if there is good ventricular function.

If the LA is enlarged, there is an increased risk of thrombi that originate in the LA. Moderate to severe, non-rheumatic, mitral regurgitation (MR) reduces this risk of stroke. This risk reduction may be due to a beneficial stirring effect of the MR blood flow into the LA.

Mitral valve

The somewhat circular perimeter of the mitral valve is defined by the mitral annulus. Atrial fibrillation and a corresponding enlargement of the left atrium may cause an increase in the size of the mitral annulus.

With a normal sinus rhythm, the mitral annulus undergoes dynamic changes during the cardiac cycle. For example, at the end of diastole the annular area is smaller than at the end of systole. A possible reason for this dynamic size difference is that the coordinated contraction of the left atrium acts like a sphincter about the mitral annulus and reduces its size. This may be important for mitral valve competence so that it doesn't leak when the left ventricle pumps blood. However, when the left atrium fibrillates, this sphincter action is not possible and may contribute to, or result in, mitral regurgitation in some cases.

Epidemiology

Atrial fibrillation is the most common arrhythmia found in clinical practice. It also accounts for 1/3 of hospital admissions for cardiac rhythm disturbances, and the rate of admissions for AF has risen in recent years. Strokes from AF account for 6-24% of all ischemic strokes. Between 3-11% of those with AF have structurally normal hearts. Approximately 2.2 million individuals in the United States and 4.5 million in the European Union have AF.

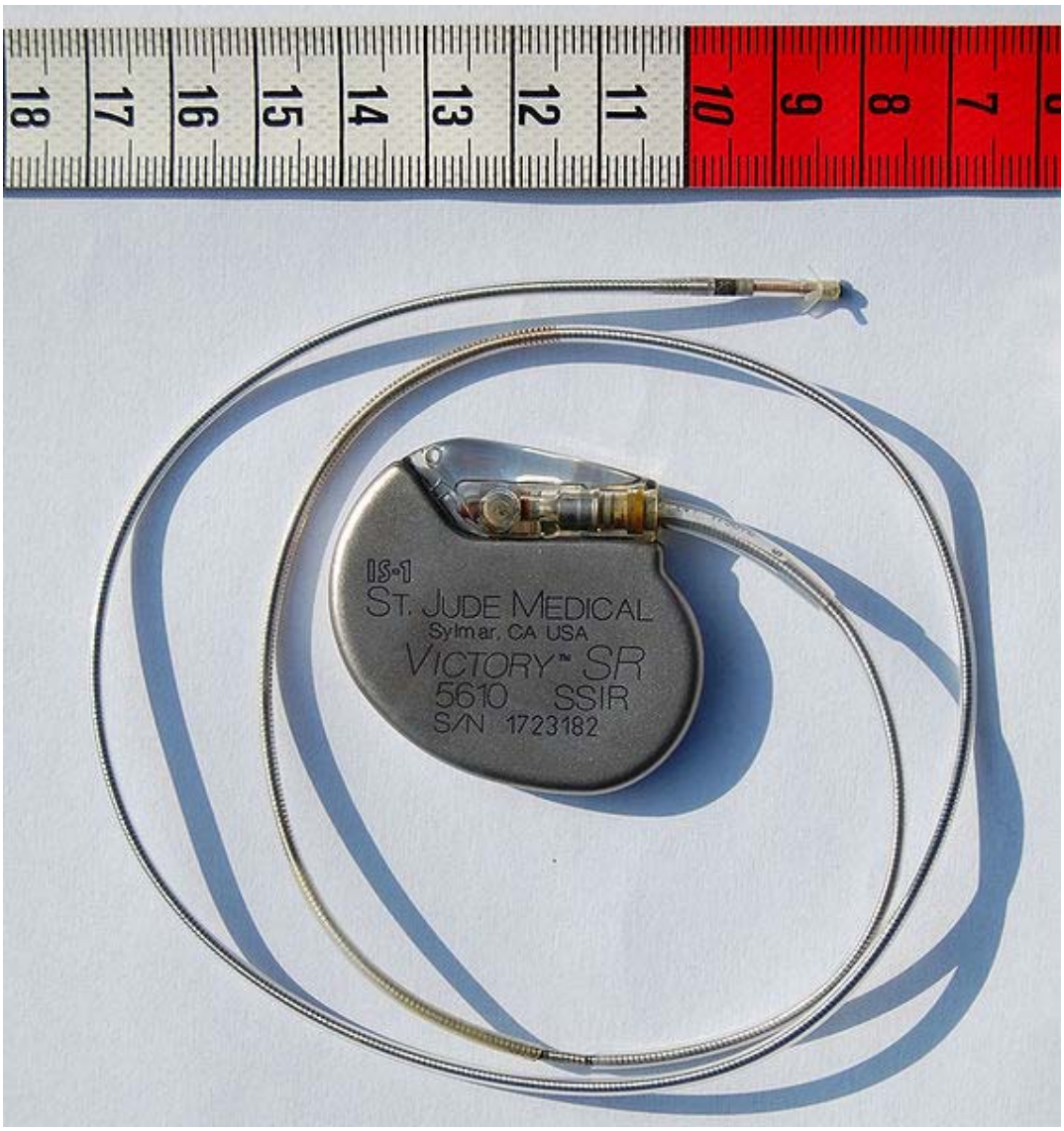
The incidence of atrial fibrillation increases with age. The prevalence in individuals over the age of 80 is about 8%. In developed countries, the number of patients with atrial fibrillation is likely to increase during the next 50 years, due to the growing proportion of elderly individuals.

History

Because the diagnosis of atrial fibrillation requires measurement of the electrical activity of the heart, atrial fibrillation was not truly described until 1874, when Edmé Félix Alfred Vulpian observed the irregular atrial electrical behavior that he termed *"fremissement fibrillaire"* in dog hearts. In the mid-eighteenth century, Jean-Baptiste de Sénac made note of dilated, irritated atria in people with mitral stenosis. The irregular pulse associated with AF was first recorded in 1876 by Carl Wilhelm Hermann Nothnagel and termed *"delirium cordis"*, stating that "[I]n this form of arrhythmia the heartbeats follow each other in complete irregularity. At the same time, the height and tension of the individual pulse waves are continuously changing". Correlation of delirium cordis with the loss of atrial contraction as reflected in the loss of *a waves* in the jugular venous pulse was made by Sir James MacKenzie in 1904. Willem Einthoven published the first ECG showing AF in 1906. The connection between the anatomic and electrical manifestations of AF and the irregular pulse of delirium cordis was made in 1909 by Carl Julius Rothberger, Heinrich Winterberg, and Sir Thomas Lewis.

Chapter 29

Artificial Pacemaker



An artificial pacemaker with electrode for transvenous insertion (from St. Jude Medical). The body of the device is about 4 centimeters long, the electrode measures between 50 and 60 centimeters (20 to 24 inches).

A pacemaker, scale in centimeters

A **pacemaker** (or **artificial pacemaker**, so as not to be confused with the heart's natural pacemaker) is a medical device which uses electrical impulses, delivered by electrodes contacting the heart muscles, to regulate the beating of the heart. The primary purpose of a pacemaker is to maintain an adequate heart rate, either because the heart's native pacemaker is not fast enough, or there is a block in the heart's electrical conduction system. Modern pacemakers are externally programmable and allow the cardiologist to select the optimum pacing modes for individual patients. Some combine a pacemaker and defibrillator in a single implantable device. Others have multiple electrodes stimulating differing positions within the heart to improve synchronisation of the lower chambers of the heart.

History

The first implantable pacemaker

In 1958, Arne Larsson (1915-2001) became the first to receive an implantable pacemaker. He had a total of 26 devices during his life and campaigned for other patients needing pacemakers.

In 1899, J A McWilliam reported in the British Medical Journal of his experiments in which application of an electrical impulse to the human heart in asystole caused a ventricular contraction and that a heart rhythm of 60-70 beats per minute could be evoked by impulses applied at spacings equal to 60-70/minute.

In 1926, Dr Mark C Lidwell of the Royal Prince Alfred Hospital of Sydney, supported by physicist Edgar H Booth of the University of Sydney, devised a portable apparatus which "plugged into a lighting point" and in which "One pole was applied to a skin pad soaked in strong salt solution" while the other pole "consisted of a needle insulated except at its point, and was plunged into the appropriate cardiac chamber". "The pacemaker rate was variable from about 80 to 120 pulses per minute, and likewise the voltage variable from

1.5 to 120 volts" In 1928, the apparatus was used to revive a stillborn infant at Crown Street Women's Hospital, Sydney whose heart continued "to beat on its own accord", "at the end of 10 minutes" of stimulation.

In 1932, American physiologist Albert Hyman, working independently, described an electro-mechanical instrument of his own, powered by a spring-wound hand-cranked motor. Hyman himself referred to his invention as an "artificial pacemaker", the term continuing in use to this day.

An apparent hiatus in publication of research conducted between the early 1930s and World War II may be attributed to the public perception of interfering with nature by 'reviving the dead'. For example, "Hyman did not publish data on the use of his pacemaker in humans because of adverse publicity, both among his fellow physicians, and due to newspaper reporting at the time. Lidwell may have been aware of this and did not proceed with his experiments in humans".

An external pacemaker was designed and built by the Canadian electrical engineer John Hopps in 1950 based upon observations by cardio-thoracic surgeon Wilfred Gordon Bigelow at Toronto General Hospital . A substantial external device using vacuum tube technology to provide transcutaneous pacing, it was somewhat crude and painful to the patient in use and, being powered from an AC wall socket, carried a potential hazard of electrocution of the patient by inducing ventricular fibrillation.

A number of innovators, including Paul Zoll, made smaller but still bulky transcutaneous pacing devices in the following years using a large rechargeable battery as the power supply.

In 1957, Dr. William L. Weirich published the results of research performed at the University of Minnesota. These studies demonstrated the restoration of heart rate, cardiac output and mean aortic pressures in animal subjects with complete heart block through the use of a myocardial electrode. This effective control of postsurgical heart block proved to be a significant contribution to decreasing mortality of open heart surgery in this time period.

The development of the silicon transistor and its first commercial availability in 1956 was the pivotal event which led to rapid development of practical cardiac pacemaking.

In 1958, engineer Earl Bakken of Minneapolis, Minnesota, produced the first wearable external pacemaker for a patient of Dr. C. Walton Lillehei. This transistorised pacemaker, housed in a small plastic box, had controls to permit adjustment of pacing heart rate and output voltage and was connected to electrode leads which passed through the skin of the patient to terminate in electrodes attached to the surface of the myocardium of the heart.

The first clinical implantation into a human of a fully implantable pacemaker was in 1958 at the Karolinska Institute in Solna, Sweden, using a pacemaker designed by Rune Elmqvist and surgeon Åke Senning, connected to electrodes attached to the myocardium

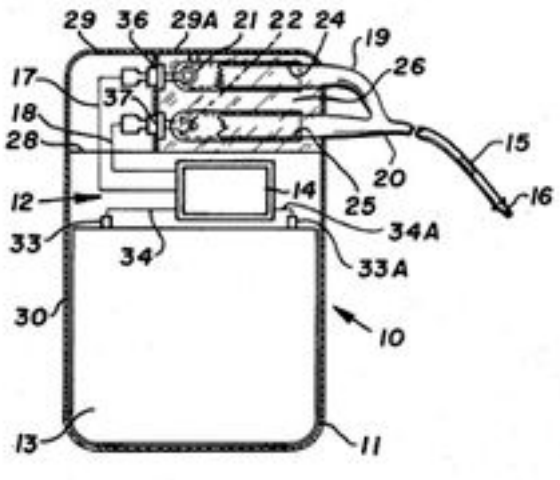
of the heart by thoracotomy. The device failed after three hours. A second device was then implanted which lasted for two days. The world's first implantable pacemaker patient, Arne Larsson, went on to receive 26 different pacemakers during his lifetime. He died in 2001, at the age of 86, outliving the inventor as well as the surgeon.

In 1959, temporary transvenous pacing was first demonstrated by Furman *et al.*. in which the catheter electrode was inserted via the patient's basilic vein.

In February 1960, an improved version of the Swedish Elmqvist design was implanted in Montevideo, Uruguay in the Casmu Hospital by Doctors Fiandra and Rubio. That device lasted until the patient died of other ailments, 9 months later. The early Swedish-designed devices used rechargeable batteries, which were charged by an induction coil from the outside.

Implantable pacemakers constructed by engineer Wilson Greatbatch entered use in humans from April 1960 following extensive animal testing. The Greatbatch innovation varied from the earlier Swedish devices in using primary cells (mercury battery) as the energy source. The first patient lived for a further 18 months.

The first use of transvenous pacing in conjunction with an implanted pacemaker was by Parsonnet in the USA, Lagergren in Sweden and Jean-Jaques Welti in France in 1962-63. The transvenous, or pervenous, procedure involved incision of a vein into which was inserted the catheter electrode lead under fluoroscopic guidance, until it was lodged within the trabeculae of the right ventricle. This method was to become the method of choice by the mid-1960s.



World's first Lithium-iodide cell powered pacemaker. Cardiac Pacemakers Inc. 1972

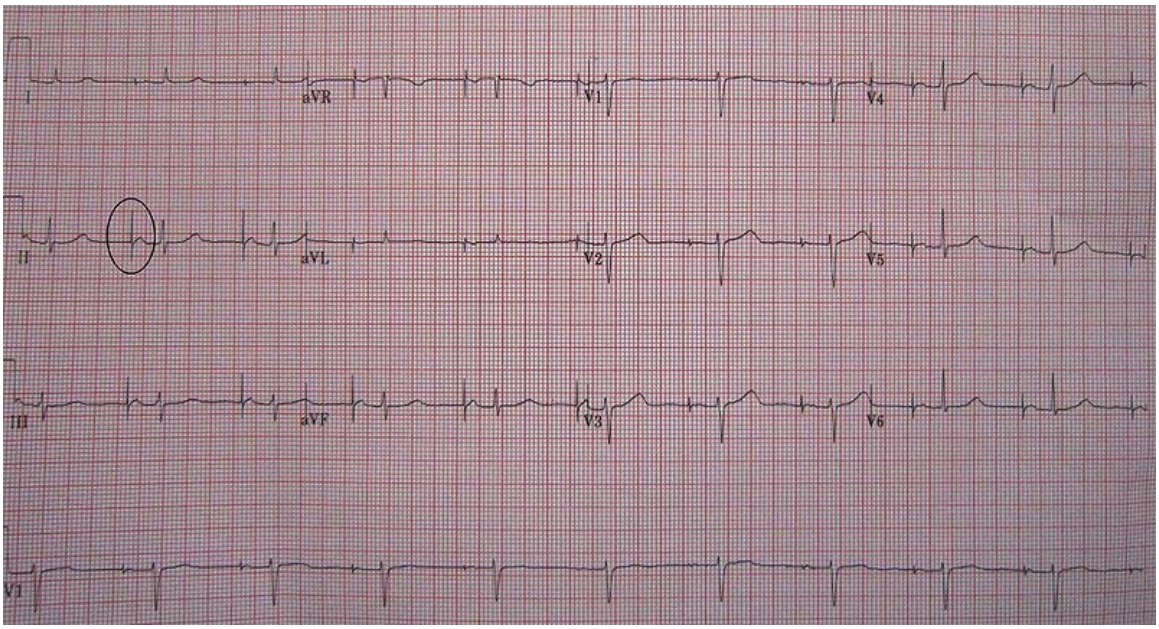
The preceding implantable devices all suffered from the unreliability and short lifetime of the available primary cell technology which was mainly that of the mercury battery.

In the late 1960s, several companies, including ARCO in the USA, developed isotope powered pacemakers, but this development was overtaken by the development in 1971 of the lithium-iodide cell by Wilson Greatbatch. Lithium-iodide or lithium anode cells became the standard for future pacemaker designs.

A further impediment to reliability of the early devices was the diffusion of water vapour from the body fluids through the epoxy resin encapsulation affecting the electronic circuitry. This phenomenon was overcome by encasing the pacemaker generator in an hermetically sealed metal case, initially by Telectronics of Australia in 1969 followed by Cardiac Pacemakers Inc of Minneapolis in 1972. This technology, using titanium as the encasing metal, became the standard by the mid-1970s.

Others who contributed significantly to the technological development of the pacemaker in the pioneering years were Bob Anderson of Medtronic Minneapolis, J.G (Geoffrey) Davies of St George's Hospital London, Barouh Berkovits and Sheldon Thaler of American Optical, Geoffrey Wickham of Telectronics Australia, Walter Keller of Cordis Corp. of Miami, Hans Thornander who joined previously mentioned Rune Elmquist of Elema-Schonander in Sweden, Janwillem van den Berg of Holland and Anthony Adducci of Cardiac Pacemakers Inc.Guidant.

Methods of pacing



An ECG in a person with an atrial pacemaker. Note the circle around one of the sharp electrical spike in the position were one would expect the P wave.

Percussive pacing

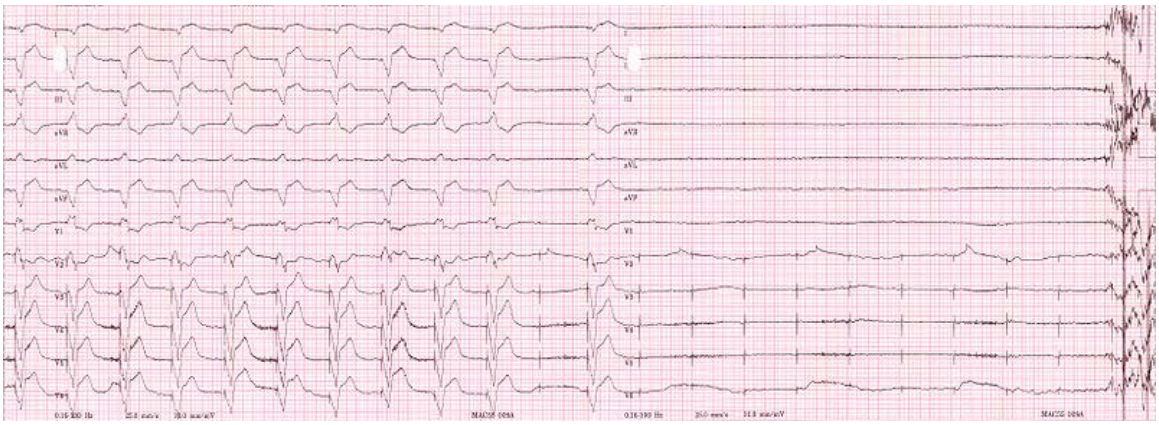
Percussive pacing, also known as transthoracic mechanical pacing, is the use of the closed fist, usually on the left lower edge of the sternum over the right ventricle in the

vena cava, striking from a distance of 20 – 30 cm to induce a ventricular beat (the British Journal of Anesthesia suggests this must be done to raise the ventricular pressure to 10 - 15mmHg to induce electrical activity). This is an old procedure used only as a life saving means until an electrical pacemaker is brought to the patient.

Transcutaneous pacing

Transcutaneous pacing (TCP), also called external pacing, is recommended for the initial stabilization of hemodynamically significant bradycardias of all types. The procedure is performed by placing two pacing pads on the patient's chest, either in the anterior/lateral position or the anterior/posterior position. The rescuer selects the pacing rate, and gradually increases the pacing current (measured in mA) until electrical capture (characterized by a wide QRS complex with a tall, broad T wave on the ECG) is achieved, with a corresponding pulse. Pacing artifact on the ECG and severe muscle twitching may make this determination difficult. External pacing should not be relied upon for an extended period of time. It is an emergency procedure that acts as a bridge until transvenous pacing or other therapies can be applied.

Epicardial pacing (temporary)



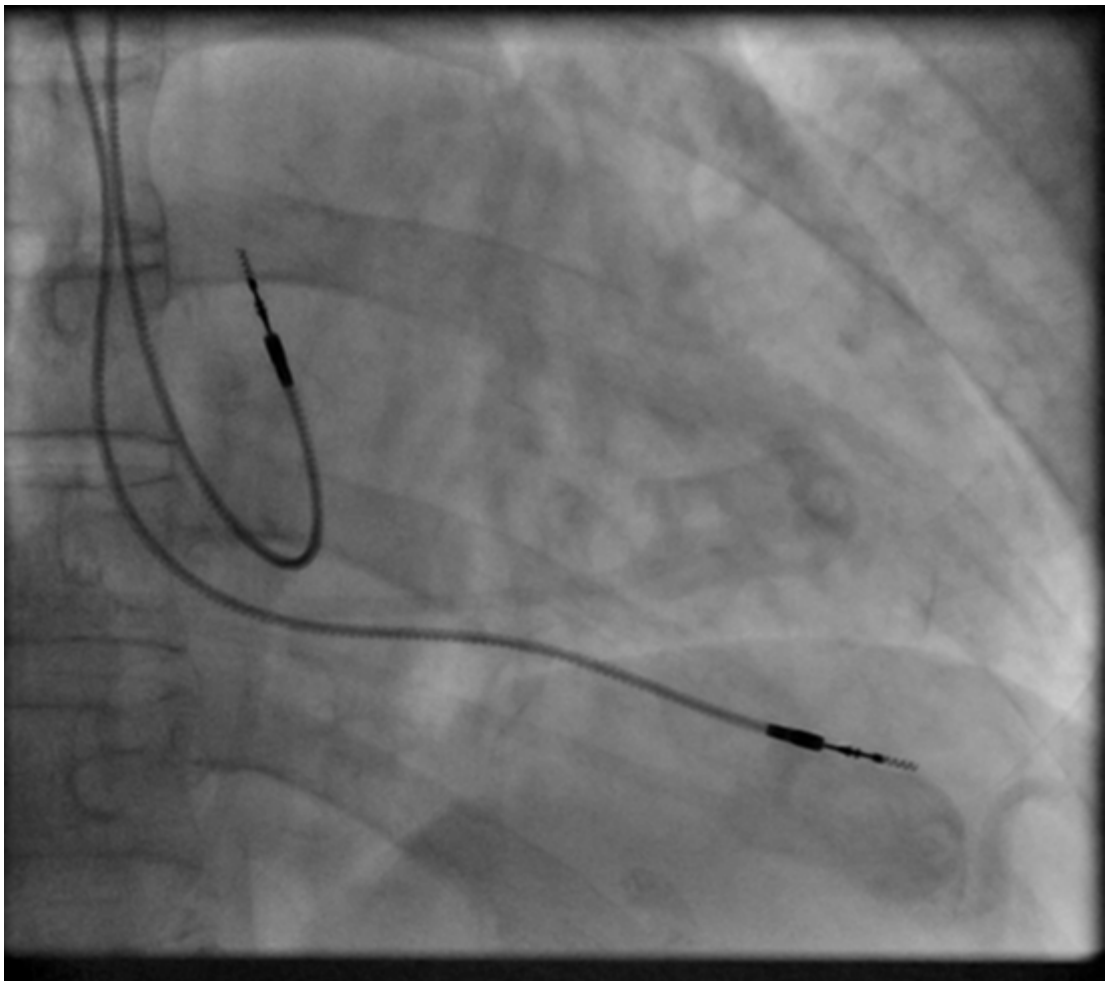
ECG rhythm strip of a threshold determination in a patient with a temporary (epicardial) ventricular pacemaker. The epicardial pacemaker leads were placed after the patient collapsed during aortic valve surgery. In the first half of the tracing, pacemaker stimuli at 60 beats per minute result in a wide QRS complex with a right bundle branch block pattern. Progressively weaker pacing stimuli are administered, which results in asystole in the second half of the tracing. At the end of the tracing, distortion results from muscle contractions due to a (short) hypoxic seizure. Because decreased pacemaker stimuli do not result in a ventricular escape rhythm, the patient can be said to be pacemaker-dependent and needs a definitive pacemaker.

Temporary epicardial pacing is used during open heart surgery should the surgical procedure create atrio ventricular block. The electrodes are placed in contact with the outer wall of the ventricle (epicardium) to maintain satisfactory cardiac output until a temporary transvenous electrode has been inserted.

Transvenous pacing (temporary)

Transvenous pacing, when used for temporary pacing, is an alternative to transcutaneous pacing. A pacemaker wire is placed into a vein, under sterile conditions, and then passed into either the right atrium or right ventricle. The pacing wire is then connected to an external pacemaker outside the body. Transvenous pacing is often used as a bridge to permanent pacemaker placement. It can be kept in place until a permanent pacemaker is implanted or until there is no longer a need for a pacemaker and then it is removed.

Permanent pacing



Right atrial and right ventricular leads as visualized under x-ray during a pacemaker implant procedure. The atrial lead is the curved one making a U shape in the upper left part of the figure.

Permanent pacing with an implantable pacemaker involves transvenous placement of one or more pacing electrodes within a chamber, or chambers, of the heart. The procedure is performed by incision of a suitable vein into which the electrode lead is inserted and passed along the vein, through the valve of the heart, until positioned in the chamber. The procedure is facilitated by fluoroscopy which enables the physician or cardiologist to

view the passage of the electrode lead. After satisfactory lodgement of the electrode is confirmed the opposite end of the electrode lead is connected to the pacemaker generator.

There are three basic types of permanent pacemakers, classified according to the number of chambers involved and their basic operating mechanism:

- *Single-chamber pacemaker*. In this type, only one pacing lead is placed into a chamber of the heart, either the atrium or the ventricle.
- *Dual-chamber pacemaker*. Here, wires are placed in two chambers of the heart. One lead paces the atrium and one paces the ventricle. This type more closely resembles the natural pacing of the heart by assisting the heart in coordinating the function between the atria and ventricles.
- *Rate-responsive pacemaker*. This pacemaker has sensors that detect changes in the patient's physical activity and automatically adjust the pacing rate to fulfill the body's metabolic needs.

The pacemaker generator is a hermetically sealed device containing a power source, usually a lithium battery, a sensing amplifier which processes the electrical manifestation of naturally occurring heart beats as sensed by the heart electrodes, the computer logic for the pacemaker and the output circuitry which delivers the pacing impulse to the electrodes.

Most commonly, the generator is placed below the subcutaneous fat of the chest wall, above the muscles and bones of the chest. However, the placement may vary on a case by case basis.

The outer casing of pacemakers is so designed that it will rarely be rejected by the body's immune system. It is usually made of titanium, which is inert in the body. The whole thing will not be rejected, and will be encapsulated by scar tissue, in the same way a piercing is.

Basic function

Modern pacemakers usually have multiple functions. The most basic form monitors the heart's native electrical rhythm. When the pacemaker fails to sense a heartbeat within a normal beat-to-beat time period, it will stimulate the ventricle of the heart with a short low voltage pulse. This sensing and stimulating activity continues on a beat by beat basis.

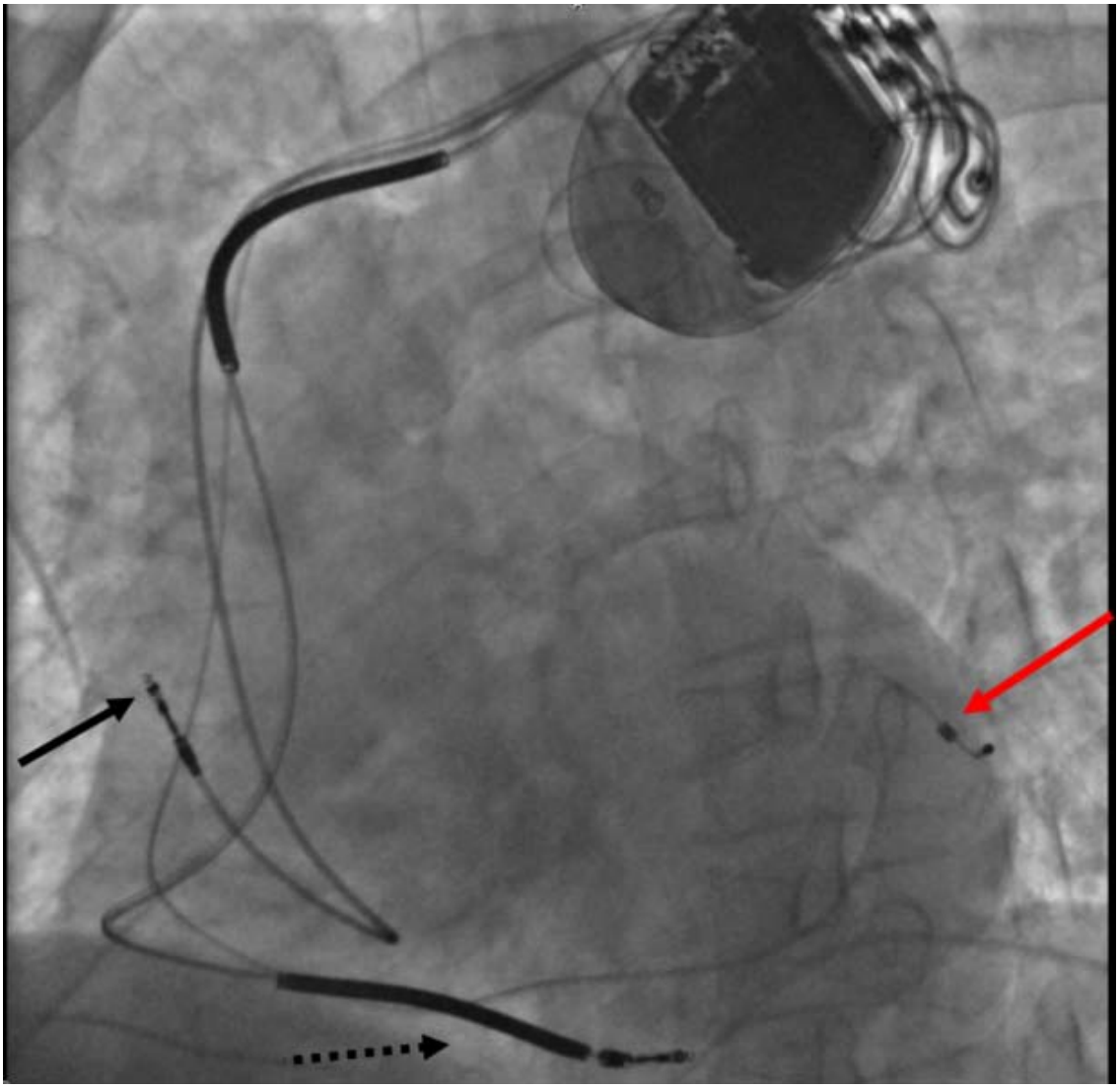
The more complex forms include the ability to sense and/or stimulate both the atrial and ventricular chambers.

The revised NASPE/BPEG generic code for antibradycardia pacing

I	II	III	IV	V
Chamber(s) paced	Chamber(s) sensed	Response to sensing	Rate modulation	Multisite pacing
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	R = Rate modulation	A = Atrium
V = Ventricle	V = Ventricle	I = Inhibited		V = Ventricle
D = Dual (A+V)	D = Dual (A+V)	D = Dual (T+I)		D = Dual (A+V)

From this the basic ventricular "on demand" pacing mode is VVI or with automatic rate adjustment for exercise VVIR - this mode is suitable when no synchronization with the atrial beat is required, as in atrial fibrillation. The equivalent atrial pacing mode is AAI or AAIR which is the mode of choice when atrioventricular conduction is intact but the natural pacemaker the sinoatrial node is unreliable - sinus node disease (SND) or sick sinus syndrome. Where the problem is atrioventricular block (AVB) the pacemaker is required to detect (sense) the atrial beat and after a normal delay (0.1-0.2 seconds) trigger a ventricular beat, unless it has already happened - this is VDD mode and can be achieved with a single pacing lead with electrodes in the right atrium (to sense) and ventricle (to sense and pace). These modes AAIR and VDD are unusual in the US but widely used in Latin America and Europe. The DDDR mode is most commonly used as it covers all the options though the pacemakers require separate atrial and ventricular leads and are more complex, requiring careful programming of their functions for optimal results.

Biventricular pacing (BVP)

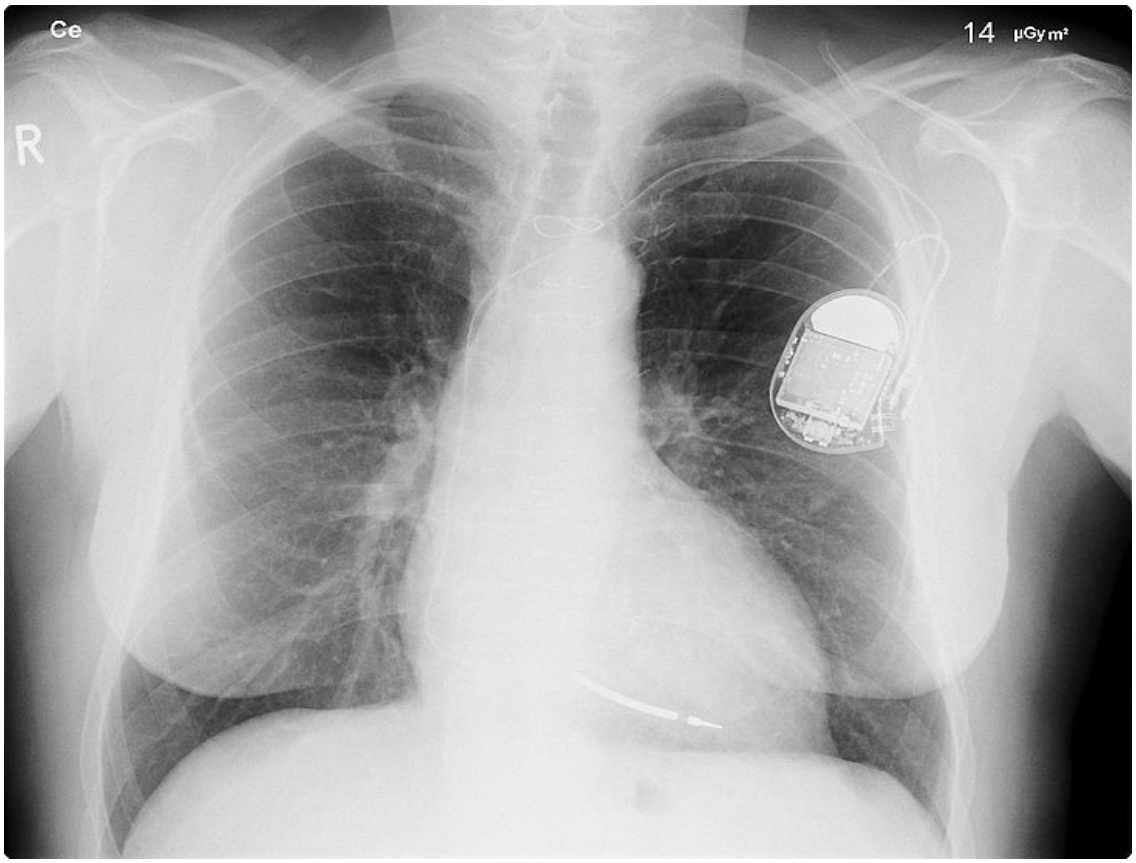


Three leads can be seen in this example of a cardiac resynchronization device: a right atrial lead (solid black arrow), a right ventricular lead (dashed black arrow), and a coronary sinus lead (red arrow). The coronary sinus lead wraps around the outside of the left ventricle, enabling pacing of the left ventricle. Note that the right ventricular lead in this case has 2 thickened aspects that represent conduction coils and that the generator is larger than typical pacemaker generators, demonstrating that this device is both a pacemaker and a cardioverter-defibrillator, capable of delivering electrical shocks for dangerously fast abnormal ventricular rhythms.

A biventricular pacemaker, also known as CRT (cardiac resynchronization therapy) is a type of pacemaker that can pace both the septal and lateral walls of the left ventricle. By pacing both sides of the left ventricle, the pacemaker can resynchronize a heart whose opposing walls do not contract in synchrony, which occurs in approximately 25-50 % of heart failure patients. CRT devices have at least two leads, one in the right ventricle to

stimulate the septum, and another inserted through the coronary sinus to pace the lateral wall of the left ventricle. Often, for patients in normal sinus rhythm, there is also a lead in the right atrium to facilitate synchrony with the atrial contraction. Thus, timing between the atrial and ventricular contractions, as well as between the septal and lateral walls of the left ventricle can be adjusted to achieve optimal cardiac function. CRT devices have been shown to reduce mortality and improve quality of life in patients with heart failure symptoms; a LV ejection fraction less than or equal to 35% and QRS duration on EKG of 120 msec or greater. CRT can be combined with an implantable cardioverter-defibrillator (ICD).

Advancements in function



X-ray image of installed pacemaker showing wire routing

A major step forward in pacemaker function has been to attempt to mimic nature by utilizing various inputs to produce a rate-responsive pacemaker using parameters such as the QT interval, pO_2 - pCO_2 (dissolved oxygen or carbon dioxide levels) in the arterial-venous system, physical activity as determined by an accelerometer, body temperature, ATP levels, adrenaline, etc. Instead of producing a static, predetermined heart rate, or intermittent control, such a pacemaker, a 'Dynamic Pacemaker', could compensate for both actual respiratory loading and potentially anticipated respiratory loading. The first dynamic pacemaker was invented by Dr. Anthony Rickards of the National Health Hospital, London, UK, in 1982.

Dynamic pacemaking technology could also be applied to future artificial hearts. Advances in transitional tissue welding would support this and other artificial organ/joint/tissue replacement efforts. Stem cells may or may not be of interest to transitional tissue welding.

Many advancements have been made to improve the control of the pacemaker once implanted. Many of these have been made possible by the transition to microprocessor controlled pacemakers. Pacemakers that control not only the ventricles but the atria as well have become common. Pacemakers that control both the atria and ventricles are called dual-chamber pacemakers. Although these dual-chamber models are usually more expensive, timing the contractions of the atria to precede that of the ventricles improves the pumping efficiency of the heart and can be useful in congestive heart failure.

Rate responsive pacing allows the device to sense the physical activity of the patient and respond appropriately by increasing or decreasing the base pacing rate via rate response algorithms.

The DAVID trials have shown that unnecessary pacing of the right ventricle can lead to heart failure and an increased incidence of atrial fibrillation. The newer dual chamber devices can keep the amount of right ventricle pacing to a minimum and thus prevent worsening of the heart disease.

Considerations

Insertion

A pacemaker is typically inserted into the patient through a simple surgery using either local anesthetic or a general anesthetic. The patient may be given a drug for relaxation before the surgery as well. An antibiotic is typically administered to prevent infection. In most cases the pacemaker is inserted in the left shoulder area where an incision is made below the collar bone creating a small pocket where the pacemaker is actually housed in the patient's body. The lead or leads (the number of leads varies depending on the type of pacemaker) are fed into the heart through a large vein using a fluoroscope to monitor the progress of lead insertion. The Right Ventricular lead would be positioned away from the apex (tip) of the right ventricle and up on the inter ventricular septum, below the outflow tract, to prevent deterioration of the strength of the heart. The actual surgery may take about 30 to 90 minutes.

Following surgery the patient should exercise reasonable care about the wound as it heals. There is a followup session during which the pacemaker is checked using a "programmer" that can communicate with the device and allows a health care professional to evaluate the system's integrity and determine the settings such as pacing voltage output. The patient should have the strength of their heart analyzed frequently with echocardiography, every 1 or 2 years, to make sure the that placement of the right ventricular lead has not lead to weakening of the left ventricle.

The patient may want to consider some basic preparation before the surgery. The most basic preparation is that people who have body hair on the chest may want to remove the hair by shaving or using a depilatory agent as the surgery will involve bandages and monitoring equipment to be afixed to the body.

Since a pacemaker uses batteries, the device itself will need replacement as the batteries lose power. Device replacement is usually a simpler procedure than the original insertion as it does not normally require leads to be implanted. The typical replacement requires a surgery in which an incision is made to remove the existing device, the leads are removed from the existing device, the leads are attached to the new device, and the new device is inserted into the patient's body replacing the previous device.

Pacemaker patient identification card

International pacemaker patient identification cards carry information such as; patient data (between others, symptom primary, ECG, aetiology), pacemaker center (doctor, hospital), IPG (rate, mode, date of implantation, MFG, type) and lead.

Living with a pacemaker

Periodic pacemaker checkups

Two types of remote monitoring devices used by pacemaker patients

Once the pacemaker is implanted, it is periodically checked to ensure the device is operational and performing appropriately. Depending on the frequency set by the following physician, the device can be checked as often as is necessary. Routine pacemaker checks are typically done in-office every six (6) months, though will vary depending upon patient/device status and remote monitoring availability.

At the time of in-office follow-up, the device will be interrogated to perform diagnostic testing. These tests include:

- Sensing: the ability of the device to "see" intrinsic cardiac activity (Atrial and ventricular depolarization).
- Impedance: A test to measure lead integrity. Large and/or sudden increases in impedance can be indicative of a lead fracture while large and/or sudden decreases in impedance can signify a breach in lead insulation.
- Threshold: this test confirms the minimum amount of energy (Both volts and pulse width) required to reliably depolarize (capture) the chamber being tested. Determining the threshold allows the Allied Professional, Representative, or Physician to program an output that recognizes an appropriate safety margin while optimizing device longevity.

As modern pacemakers are "on-demand", meaning that they only pace when necessary, device longevity is affected by how much it is utilized. Other factors affecting device longevity include programmed output and algorithms (features) causing a higher level of current drain from the battery.

An additional aspect of the in-office check is to examine any events that were stored since the last follow-up. These are typically stored based on specific criteria set by the physician and specific to the patient. Some devices have the availability to display intracardiac electrograms of the onset of the event as well as the event itself. This is especially helpful in diagnosing the cause or origin of the event and making any necessary programming changes.

Lifestyle considerations

A patient's lifestyle is usually not modified to any great degree after insertion of a pacemaker. There are a few activities that are unwise such as full contact sports and activities that involve intense magnetic fields.

The pacemaker patient may find that some types of everyday actions need to be modified. For instance, the shoulder harness of a vehicle seatbelt may be uncomfortable if the harness should fall across the pacemaker insertion site.

Any kind of an activity that involves intense magnetic fields should be avoided. This includes activities such as arc welding possibly, with certain types of equipment, or maintaining heavy equipment that may generate intense magnetic fields (such as an MRI (Magnetic Resonance Imaging Machine)).

However, in February 2011 the FDA approved a new pacemaker device called the Revo MRI SureScan which is the first to be proven safe for MRI use. There are several limitations to its use including certain patients qualifications, body parts, and scan settings.

A 2008 U.S. study has found that the magnets in some portable music players, when placed within an inch of pacemakers, may cause interference.

Some medical procedures may require the use of antibiotics to be administered before the procedure. The patient should inform all medical personnel that they have a pacemaker. Some standard medical procedures such as the use of Magnetic resonance imaging (MRI) may be ruled out by the patient having a pacemaker.

In addition, according to the American Heart Association, some home devices have a remote potential to cause interference by occasionally inhibiting a single beat. Cellphones available in the United States (less than 3 watts) do not seem to damage pulse generators or affect how the pacemaker works.

Turning off the pacemaker

According to a consensus statement by the Heart Rhythm Society, it is legal and ethical to honor requests by patients, or by those with legal authority to make decisions for patients, to deactivate implanted cardiac devices. Lawyers say that the legal situation is similar to removing a feeding tube. A patient has a right to refuse or discontinue treatment, including a pacemaker that keeps him or her alive. Physicians have a right to refuse to turn it off, but they should refer the patient to a physician who will. Some patients believe that hopeless, debilitating conditions like strokes, in combination with dementia, can cause so much suffering to themselves and their families that they would prefer not to prolong their lives with supportive measures, such as cardiac devices.

Privacy and security

Security and privacy concerns have been raised with pacemakers that allow wireless communication. Unauthorized third parties may be able to read patient records contained in the pacemaker, or reprogram the devices, as has been demonstrated by a team of researchers. The demonstration worked at short range; they did not attempt to develop a long range antenna. The proof of concept exploit helps demonstrate the need for better security and patient alerting measures in remotely accessible medical implants.

Complications

A possible complication of dual-chamber artificial pacemakers is *pacemaker-mediated tachycardia* (PMT), a form of reentrant tachycardia. In PMT, the artificial pacemaker forms the anterograde (atrium to ventricle) limb of the circuit and the atrioventricular (AV) node forms the retrograde limb (ventricle to atrium) of the circuit. Treatment of PMT typically involves reprogramming the pacemaker.

Other devices with pacemaker function

Sometimes devices resembling pacemakers, called implantable cardioverter-defibrillators (ICDs) are implanted. These devices are often used in the treatment of patients at risk

from sudden cardiac death. An ICD has the ability to treat many types of heart rhythm disturbances by means of pacing, cardioversion, or defibrillation. Some ICD devices can distinguish between ventricular fibrillation and ventricular tachycardia (VT), and may try to pace the heart faster than its intrinsic rate in the case of VT, to try to break the tachycardia before it progresses to ventricular fibrillation. This is known as *fast-pacing*, *overdrive pacing*, or *anti-tachycardia pacing* (ATP). ATP is only effective if the underlying rhythm is ventricular tachycardia, and is never effective if the rhythm is ventricular fibrillation.

NASPE / BPEG Defibrillator (NBD) code - 1993

I	II	III	IV
Shock chamber	Antitachycardia pacing chamber	Tachycardia detection	Antibradycardia pacing chamber
O = None	O = None	E = Electrogram	O = None
A = Atrium	A = Atrium	H = Hemodynamic	A = Atrium
V = Ventricle	V = Ventricle		V = Ventricle
D = Dual (A+V)	D = Dual (A+V)		D = Dual (A+V)

Short form of the NASPE/BPEG Defibrillator (NBD) code

ICD-S ICD with shock capability only

ICD-B ICD with bradycardia pacing as well as shock

ICD-T ICD with tachycardia (and bradycardia) pacing as well as shock