

**UKRAINIAN MINISTRY OF HEALTH CARE  
UKRAINIAN ACADEMY OF MEDICINE AND DENTISTRY**

**CLINICAL MEDICINE**

**Part 1. CARDIORHEUMATOLOGY**

**EDUCATIONAL MATERIALS FOR INDEPENDENT STUDY WITH  
TESTS AND EXPLANATIONS INCLUDED**

**FOR THIRD YEAR DENTAL FACULTY STUDENTS**

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## Preface

Beginning students of medicine and dentistry must acquire a set of skills that prepare them to become clinicians. This includes establishing rapport and a therapeutic relationship with the patient, basic interviewing, the specific conduct and content of medical data collection (the history and the physical examination), formulation of a problem list and diagnostic hypotheses, documentation and record-keeping, and communication with others involved in the patient's care. An introduction to these skills during the first years of medical school focuses on the basics of data collection and information synthesis rather than the specifics of disease, diagnosis, and treatment—that is, the emphasis is on process rather than specialized content.

There are many fine texts that provide detailed discussions of the medical history and physical examination. This instruction is not intended to replace these comprehensive approaches but rather to summarize methods and outline the basic principles essential to data collection.

The authors of this book have all been involved in teaching the Introduction to Clinical Medicine course at the Ukrainian Academy of Medicine and Dentistry. Their experience has informed the **problem based approach** used in this book. This book is structured to allow students to review a set of skills that will enable them to approach undifferentiated medical problems systematically and with confidence in preparation for clinical clerkships.

**I. Kajdashev, M. Rasin**

## Arterial hypertension

Persistent hypertension is one of the risk factors for strokes, heart attacks, heart failure and arterial aneurysm, and is a leading cause of chronic renal failure.

### Definition

Blood pressure is a continuously distributed variable and the risk of associated cardiovascular disease likewise rises continuously. The point at which blood pressure is defined as hypertension is therefore somewhat arbitrary. Presently finding sustained blood pressure of 140/90 mmHg or above, measured on both arms is generally regarded as diagnostic. Because blood pressure readings in many individuals are highly variable — especially in the office setting — the diagnosis of hypertension should be made only after noting a mean elevation on two or more readings on two or more office visits, unless the elevations are severe or associated with compelling indications such as diabetes mellitus, chronic kidney disease, heart failure, post-myocardial infarction, stroke, and high coronary disease risk.

Recently, the JNC 7 (The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure)<sup>[1]</sup> has defined blood pressure 120/80 mmHg to 139/89 mmHg as "prehypertension." Prehypertension is not a disease category; rather, it is a designation chosen to identify individuals at high risk of developing hypertension.

In patients with diabetes mellitus or kidney disease studies have shown that blood pressure over 130/80 mmHg should be considered a risk factor and may warrant treatment. Even lower numbers are considered diagnostic using home blood pressure monitoring devices.

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## Etiology of Essential Hypertension

### Environment

A number of environmental factors have been implicated in the development of hypertension, including salt intake, obesity, occupation, alcohol intake, family size, excessive noise exposure.<sup>[2]</sup>, and crowding.

### Salt Sensitivity

Sodium is the environmental factor that has received the greatest attention. It is to be noted that approximately 60% of the essential hypertension population is responsive to sodium intake.

### **Role of Renin**

Renin is an enzyme secreted by the juxtaglomerular cells of the kidney and linked with aldosterone in a negative feedback loop. The range of plasma renin activities observed in hypertensive subjects is broader than in normotensive individuals. In consequence, some hypertensive patients have been defined as having low-renin and others as having high-renin essential hypertension.

### **Insulin Resistance**

Insulin is a [hormone] secreted by the pancreas. Its main purpose is to regulate the levels of glucose in the body, it also has some other effects. Insulin resistance and/or hyperinsulinemia have been suggested as being responsible for the increased arterial pressure in some patients with hypertension. This feature is now widely recognized as part of syndrome X, or the metabolic syndrome.

**Genetics** Hypertension is one of the most common complex genetic disorders, with genetic heritability averaging 30%. Data supporting this view emerge from animal studies as well as in population studies in humans. Most of these studies support the concept that the inheritance is probably multifactorial or that a number of different genetic defects each have an elevated blood pressure as one of their phenotypic expressions.

More than 50 genes have been examined in association studies with hypertension, and the number is constantly growing.

### **Other Etiologies**

There are some anecdotal or transient causes of high blood pressure. These are not to be confused with the disease called hypertension in which there is an intrinsic physiopathological mechanism as described above.

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### **Etiology of Secondary Hypertension**

Only in a small minority of patients with elevated arterial pressure can a specific cause be identified. These individuals will probably have an endocrine or renal defect that if corrected would bring blood pressure back to normal values.

### **Renal Hypertension**

Hypertension produced by renal disease. A simple explanation for renal vascular hypertension is that decreased perfusion of renal tissue due to stenosis of a main or branch renal artery activates the renin-angiotensin system.

## **Adrenal Hypertension**

Hypertension is a feature of a variety of adrenal cortical abnormalities. In primary aldosteronism there is a clear relationship between the aldosterone-induced sodium retention and the hypertension.

In patients with pheochromocytoma increased secretion of epinephrine and norepinephrine by a tumor (most often located in the adrenal medulla) causes excessive stimulation of [adrenergic receptors], which results in peripheral vasoconstriction and cardiac stimulation. This diagnosis is confirmed by demonstrating increased urinary excretion of epinephrine and norepinephrine and/or their metabolites (vanillylmandelic acid).

## **Hypercalcemia**

## **Coarctation of the Aorta**

- Age. Over time, the number of collagen fibers in artery and arteriole walls increases, making blood vessels stiffer. With the reduced elasticity comes a smaller cross-sectional area in systole, and so a raised mean arterial blood pressure.

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## **Pathophysiology**

Most of the secondary mechanisms associated with essential hypertension are generally fully understood, and are outlined at secondary hypertension. However, those associated with essential (primary) hypertension are far less understood.

What is known is that cardiac output is raised early in the disease course, with total peripheral resistance (TPR) normal; over time cardiac output drops to normal levels but TPR is increased. Three theories have been proposed to explain this:

- Inability of the kidneys to excrete sodium, resulting in natriuretic factor (note: the existence of this substance is theoretical) being secreted to promote salt excretion with the side-effect of raising total peripheral resistance.
- An overactive renin / angiotension system leads to vasoconstriction and retention of sodium and water. The increase in blood volume leads to hypertension.

- An overactive sympathetic nervous system, leading to increased stress responses.

It is also known that hypertension is highly hereditary and polymorphic (more than one gene) and a few candidate genes have been postulated as participating in the etiology of this condition.<sup>[3] [4] [5]</sup>

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## Signs and symptoms

Hypertension is usually found incidentally - "case finding" - by healthcare professionals. It normally produces no symptoms.

Malignant hypertension (or accelerated hypertension) is distinct as a late phase in the condition, and may present with headaches, blurred vision and end-organ damage.

It is recognised that stressful situations can increase the blood pressure;

Hypertension is often confused with mental tension, stress and anxiety. While chronic anxiety is associated with poor outcomes in people with hypertension, it alone does not cause it.

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## Hypertensive urgencies and emergencies

Hypertension is rarely severe enough to cause symptoms. These typically only surface with a systolic blood pressure over 240 mmHg and/or a diastolic blood pressure over 120 mmHg. These pressures without signs of end-organ damage (such as renal failure) are termed "accelerated" hypertension. When end-organ damage is possible or already ongoing, but in absence of raised intracranial pressure, it is called hypertensive emergency. Hypertension under this circumstance needs to be controlled, but prolonged hospitalization is not necessarily required. When hypertension causes increased intracranial pressure, it is called malignant hypertension. Increased intracranial pressure causes papilledema, which is visible on ophthalmoscopic examination of the retina.

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## Complications

While elevated blood pressure alone is not an illness, it often requires treatment due to its short- and long-term effects on many organs. The risk is increased for:

- Cerebrovascular accident (CVAs or strokes)

- Myocardial infarction (heart attack)
- Hypertensive cardiomyopathy (heart failure due to chronically high blood pressure)
- Hypertensive retinopathy - damage to the retina
- Hypertensive nephropathy - chronic renal failure due to chronically high blood pressure

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## Pregnancy

*Main article: Hypertension of pregnancy*

Although few women of childbearing age have high blood pressure, up to 10% develop hypertension of pregnancy. While generally benign, it may herald three complications of pregnancy: pre-eclampsia, HELLP syndrome and eclampsia. Follow-up and control with medication is therefore often necessary.

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## Diagnosis

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## Measuring blood pressure

Diagnosis of hypertension is generally on the basis of a persistently high blood pressure. Usually this requires three separate measurements at least one week apart. Exceptionally, if the elevation is extreme, or end-organ damage is present then the diagnosis may be applied and treatment commenced immediately.

Obtaining reliable blood pressure measurements relies on following several rules and understanding the many factors that influence blood pressure reading.

For instance, measurements in control of hypertension should be at least 1 hour after caffeine, 30 minutes after smoking and without any stress. Cuff size is also important. The bladder should encircle and cover two-thirds of the length of the arm. The patient should be sitting for a minimum of five minutes. The patient should not be on any adrenergic stimulants, such as those found in many cold medications.

When taking manual measurements, the person taking the measurement should be careful to inflate the cuff suitably above anticipated systolic pressure. A stethoscope should be placed lightly over the brachial artery. The cuff should be at the level of the heart and the cuff should be deflated at a rate of 2 to 3 mmHg/s. Systolic pressure is the pressure reading at the onset of the sounds described by



Korotkoff (Phase one). Diastolic pressure is then recorded as the pressure at which the sounds disappear (K5) or sometimes the K4 point, where the sound is abruptly muffled. Two measurements should be made at least 5 minutes apart, and, if there is a discrepancy of more than 5 mmHg, a third reading should be done. The readings should then be averaged. An initial measurement should include both arms. In elderly patients who particularly when treated may show orthostatic hypotension, measuring lying sitting and standing BP may be useful. The BP should at some time have been measured in each arm, and the higher pressure arm preferred for subsequent measurements.

BP varies with time of day, as may the effectiveness of treatment, and archetypes used to record the data should include the time taken. Analysis of this is rare at present.

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### **Distinguishing primary vs. secondary hypertension**

Once the diagnosis of hypertension has been made it is important to attempt to exclude or identify reversible (secondary) causes.

- Over 90% of adult hypertension has no clear cause and is therefore called **essential/primary hypertension**. Often, it is part of the metabolic "syndrome X" in patients with insulin resistance: it occurs in combination with diabetes mellitus (type 2), combined hyperlipidemia and central obesity.
- In hypertensive children most cases are secondary hypertension, and the cause should be pursued diligently.

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### **Blood tests commonly performed in a newly diagnosed hypertension patient**

- Creatinine (renal function)
- Electrolytes (sodium, potassium)
- Glucose (to identify diabetes mellitus)
- Cholesterol

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### **Epidemiology**

The level of blood pressure regarded as deleterious has been revised down during years of epidemiological studies. A widely-quoted and important series of such studies is the Framingham Heart Study carried out in an American town: Framingham, Massachusetts. The results from Framingham and of similar work in

Busselton, Western Australia have been widely applied. To the extent that people are similar this seems reasonable, but there are known to be genetic variations in the most effective drugs for particular sub-populations. Recently (2004), the Framingham figures have been found to overestimate risks for the UK population considerably. The reasons are unclear. Nevertheless the Framingham work has been an important element of UK health policy.

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## Treatment

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## Lifestyle modification

Doctors recommend weight loss and regular exercise as the first steps in treating mild to moderate hypertension. These steps are highly effective in reducing blood pressure, but easier to suggest than to achieve, and most patients with moderate or severe hypertension end up requiring indefinite drug therapy to bring their blood pressure down to a safe level. Discontinuing smoking does not directly reduce blood pressure, but is very important for people with hypertension because it reduces the risk of many dangerous outcomes of hypertension, such as stroke and heart attack.

Mild hypertension is usually treated by diet, exercise and improved physical fitness. A diet rich in fruits and vegetables and fat-free dairy foods and low in fat and sodium lowers blood pressure in people with hypertension. Dietary sodium (salt) causes hypertension in some people and reducing salt intake decreases blood pressure in a third of people. Regular mild exercise improves blood flow, and helps to lower blood pressure.

Reduction of environmental stressors such as high sound levels and over-illumination can be an additional method of ameliorating hypertension.

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## Medications

*See main article: Antihypertensives*

There are many classes of medications for treating hypertension, together called antihypertensives, which — by varying means — act by lowering blood pressure. Evidence suggests that reduction of the blood pressure by 5-6 mmHg can decrease

the risk of stroke by 40%, of coronary heart disease by 15-20%, and reduces the likelihood of dementia, heart failure, and mortality from vascular disease.

Which type of medication to use initially for hypertension has been the subject of several large studies. The *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (JNC 7) recommends starting with a thiazide diuretic if single therapy is being initiated and another medication is not indicated.<sup>[11]</sup> This is based on a slightly better outcome for chlortalidone in the ALLHAT study versus other anti-hypertensives and because thiazide diuretics are relatively cheap.<sup>[6]</sup> A subsequent smaller study (ANBP2) published after the JNC7 did not show this small difference in outcome and actually showed a slightly better outcome for ACE-inhibitors in older male patients.<sup>[7]</sup>

Despite thiazides being cheap, effective, and recommended as the best first-line drug for hypertension by many experts, they are not prescribed as often as some newer drugs. Arguably, this is because they are off-patent and thus rarely promoted by the drug industry.<sup>[8]</sup>

Physicians may start with non-thiazide antihypertensive medications if there is a compelling reason to do so. An example is the use of ACE-inhibitors in diabetic patients who have evidence of kidney disease, as they have been shown to both reduce blood pressure and slow the progression of diabetic nephropathy.<sup>[9]</sup> In patients with coronary artery disease or a history of a heart attack, beta blockers and ACE-inhibitors both lower blood pressure and protect heart muscle over a lifetime, leading to reduced mortality.

Commonly used drugs include:

- Beta blockers such as metoprolol (Lopressor®), atenolol, labetalol, carvedilol (Coreg®)
- ACE inhibitors such as lisinopril (Zestril®), quinapril, fosinopril (Monopril®), captopril, enalapril, ramipril (Altace®)
- Angiotensin receptor blockers (ARBs): eg, losartan (Cozaar®), valsartan (Diovan®), irbesartan (Avapro®)
- Calcium channel blockers such as amlodipine (Norvasc®), verapamil
- Diuretics: eg, chlortalidone, hydrochlorothiazide (also called HCTZ)
- Combination products (which usually contain HCTZ and one other drug)
- Alpha blockers such as terazosin, prazosin

The aim of treatment should be blood pressure control (<140/90 mmHg for most patients, and lower in certain contexts such as diabetes or kidney disease (some medical professionals recommend keeping levels below 130/80 mmHg)). Each added drug may reduce the systolic blood pressure by 5-10 mmHg, so often multiple drugs are necessary to achieve blood pressure control.

## Atherosclerosis



Changes in endothelial dysfunction in atherosclerosis (note text comments about geometry error)

**Atherosclerosis** is a disease affecting the arterial blood vessel. It is commonly referred to as a "hardening" or "furring" of the arteries. It is caused by the formation of multiple plaques within the arteries.

Pathologically, the **atheromatous plaque** is divided into three distinct components:

1. The atheroma ("lump of porridge", from *Athera*, porridge in Greek,) is the nodular accumulation of a soft, flaky, yellowish material at the center of large plaques, composed of macrophages nearest the lumen of the artery, sometimes with
2. Underlying areas of cholesterol crystals, and possibly also
3. Calcification at the outer base of older/more advanced lesions.

The following terms are similar, yet distinct, in both spelling and meaning, and can be easily confused: arteriosclerosis, arteriolosclerosis and atherosclerosis.

**Arteriosclerosis**, is a general term describing any hardening (and loss of elasticity) of medium or large arteries (in Latin, Arterio meaning artery and sclerosis meaning hardening), **arteriolosclerosis** is arteriosclerosis mainly affecting the arterioles (small arteries), **atherosclerosis** is a hardening of an artery specifically due to an atheromatous plaque (in Latin, "athero" means "porridge"). Therefore, atherosclerosis is a form of arteriosclerosis.

**Arteriosclerosis** ("hardening of the artery") results from a deposition of tough, rigid collagen inside the vessel wall and around the atheroma. This increases the stiffness, decreases the elasticity of the artery wall. **Arteriolosclerosis** (hardening of small arteries, the arterioles) is the result of collagen deposition, but also muscle wall thickening and deposition of protein ("hyaline").

Calcification, sometimes even ossification (formation of complete bone tissue) occurs within the deepest and oldest layers of the sclerosed vessel wall.

Atherosclerosis causes two main problems. First, the atheromatous plaques, though long compensated for by artery enlargement, eventually lead to plaque ruptures and *stenosis* (narrowing) of the artery and, therefore, an insufficient blood supply to the organ it feeds. Alternatively, if the compensating artery enlargement process is excessive, then a net aneurysm results.

These complications are chronic, slowly progressing and cumulative. Most commonly, soft plaque suddenly *ruptures* (see vulnerable plaque), causing the formation of a blood clot (thrombus) that will rapidly slow or stop blood flow, e.g. 5 minutes, leading to death of the tissues fed by the artery. This catastrophic event is called an *infarction*. One of the most common recognized scenarios is called coronary thrombosis of a coronary artery causing myocardial infarction (a heart attack). Another common scenario in very advanced disease is claudication from insufficient blood supply to the legs, typically due to a combination of both stenosis and aneurysmal segments narrowed with clots. Since atherosclerosis is a body wide process, similar events also occur in the arteries to the brain, intestines, kidneys, legs, etc.

## Symptoms

Atherosclerosis typically begins in early adolescence, is usually found in most major arteries, yet is asymptomatic and not detected by most diagnostic methods during life. It most commonly becomes seriously symptomatic when interfering with the coronary circulation supplying the heart or cerebral circulation supplying the brain, and is considered the most important underlying cause of strokes, heart attacks, various heart diseases including congestive heart failure and most cardiovascular diseases in general. Atheroma in arm or more often leg arteries and producing decreased blood flow is called Peripheral artery occlusive disease (PAOD).

According to United States data for the year 2004, for about 65% of men and 47% of women, the first symptom of atherosclerotic cardiovascular disease is heart attack or sudden cardiac death (death within one hour of onset of the symptom).

Most artery flow disrupting events occur at locations with less than 50% lumen narrowing (~20% stenosis is average. [The reader might reflect that the illustration above, like most illustrations of arterial disease, over emphasizes lumen narrowing as opposed to compensatory external diameter enlargement (at least within smaller, e.g. heart arteries) typical of the atherosclerosis process as it progresses, see Reference 1, Glagov S, below and the [ASTEROID] trial, the IVUS photographs on page 8, as examples for a more accurate understanding.] The relative geometry error within the illustration is common to many older illustrations, an error slowly being more commonly recognized within the last decade.

Cardiac stress testing, traditionally the most commonly performed non-invasive testing method for blood flow limitations generally only detects lumen narrowing of ~75% or greater, although some physicians advocate that nuclear stress methods can detect as little as 50%.

## Atherogenesis

*Atherogenesis* is the developmental process of atheromatous plaques. It is characterized by a remodeling of arteries involving the concomitant accumulation fatty substances called plaques. One recent theory suggests that for unknown reasons, leukocytes such as monocytes or basophils begin to attack the endothelium of the artery lumen in cardiac muscle. The ensuing inflammation leads to formation of *atheromatous plaques* in the arterial intima, a region of the vessel wall located between the endothelium and the media and adventitia. The bulk of these lesions is comprised of excess fat, collagen, and elastin. The plaques initially grow without producing any narrowing, stenosis, of the artery opening, called the lumen.

## **Cellular**

The first step of atherogenesis is the development of fatty streaks, small subendothelial deposits of lipid. The exact cause for this process is unknown, and fatty streaks may appear and disappear.

LDL in blood plasma poses a risk for cardiovascular disease when it invades the endothelium and becomes oxidized. A complex set of biochemical reactions regulates the oxidation of LDL, chiefly stimulated by presence of free radicals in the endothelium.

The initial damage to the blood vessel wall results in a "call for help," an inflammation response. Monocytes (a type of white blood cell) enter the artery wall from the bloodstreams, with platelets adhering to the area on insult. The monocytes differentiate into macrophages, which ingest oxidized LDL, slowly turning into large "foam cells" – so-described because of their changed appearance resulting from the numerous internal cytoplasmic vesicles and resulting high lipid content. Under the microscope, the lesion now appears as a fatty streak. Foam cells eventually die, and further propagate the inflammatory process.

## **Calcification and lipids**

Intracellular microcalcifications form within vascular smooth muscle cells of the surrounding muscular layer, specifically in the muscle cells adjacent to the atheromas. In time, as cells die, this leads to extracellular calcium deposits between the muscular wall and outer portion of the atheromatous plaques.

Cholesterol is delivered into the vessel wall by cholesterol-containing low-density lipoprotein (LDL) particles. To attract and stimulate macrophages, the cholesterol must be released from the LDL particles and oxidized, a key step in the ongoing inflammatory process. The process is worsened if there is insufficient high-density lipoprotein (HDL), the lipoprotein particle that removes cholesterol from tissues and carries it back to the liver.



The foam cells and platelets encourage the migration and proliferation of smooth muscle cells, which in turn become replaced by collagen and transform into foam cells themselves. A protective fibrous cap normally forms between the fatty deposits and the artery lining (the intima).

These capped fatty deposits (now called *atheromas*) produce enzymes that cause the artery to enlarge over time. As long as the artery enlarges sufficiently to compensate for the extra thickness of the atheroma, then no narrowing, stenosis, of the opening, lumen, occurs. The artery becomes expanded with an egg-shaped cross-section, still with a circular opening. If the enlargement is beyond proportion to the atheroma thickness, then an aneurysm is created<sup>[1]</sup>.

[edit]

### Visible features



Severe atherosclerosis of the aorta. Autopsy specimen.

Although arteries are not typically studied microscopically, two plaque types can be distinguished<sup>[2]</sup>:

1. *The fibro-lipid (fibro-fatty) plaque* is characterized by an accumulation of lipid-laden cells underneath the intima of the arteries, typically without narrowing the lumen due to compensatory expansion of the bounding muscular layer of the artery wall. Beneath the endothelium there is a "fibrous cap" covering the atheromatous "core" of the plaque. The core consists of lipid-laden cells (macrophages and smooth muscle cells) with elevated tissue cholesterol and cholesterol ester content, fibrin,

proteoglycans, collagen, elastin and cellular debris. In advanced plaques, the central core of the plaque usually contains extracellular cholesterol deposits (released from dead cells), which form areas of cholesterol crystals with empty, needle-like clefts. At the periphery of the plaque are younger "foamy" cells and capillaries. These plaques usually produce the most damage to the individual when they rupture.

2. *The fibrous plaque* is also localized under the intima, within the wall of the artery resulting in thickening and expansion of the wall and, sometimes, spotty localized narrowing of the lumen with some atrophy of the muscular layer. The fibrous plaque contains collagen fibres (eosinophilic), precipitates of calcium (hematoxylinophilic) and, rarely, lipid-laden cells.

In effect, the muscular portion of the artery wall forms small aneurysms just large enough to hold the atheroma that are present. The muscular portion of artery walls usually remain strong, even after they have remodeled to compensate for the atheromatous plaques.

However, atheromas within the vessel wall are soft and fragile with little elasticity. Arteries constantly expand and contract with each heartbeat, i.e., the pulse. In addition, the calcification deposits between the outer portion of the atheroma and the muscular wall, as they progress, lead to a loss of elasticity and stiffening of the artery as a whole.

The calcification deposits, after they have become sufficiently advanced, are partially visible on coronary artery computed tomography or electron beam tomography (EBT) as rings of increased radiographic density, forming halos around the outer edges of the atheromatous plaques, within the artery wall. On CT, >130 units on the Hounsfield scale (some argue for 90 units) has been the radiographic density usually accepted as clearly representing tissue calcification within arteries. These deposits demonstrate unequivocal evidence of the disease, relatively advanced, even though the lumen of the artery is often still normal by angiographic or intravascular ultrasound.

## **Rupture and stenosis**

Although the disease process tends to be slowly progressive over decades, it usually remains asymptomatic until an atheroma obstructs the bloodstream in the artery. This is typically by rupture of an atheroma, clotting and fibrous organization of the clot within the lumen, covering the rupture but also producing stenosis, or over time and after repeated ruptures, resulting in a persistent, usually localized stenosis. Stenoses can be slowly progressive, while plaque rupture is a sudden event that occurs specifically in atheromas with thinner/weaker fibrous caps that have become "unstable".

Repeated plaque ruptures, ones not resulting in total lumen closure, combined with the clot patch over the rupture and healing response to stabilize the clot, is the



process that produces most stenoses over time. The stenotic areas tend to become more stable, despite increased flow velocities at these narrowings. Most major blood-flow-stopping events occur at large plaques, which, prior to their rupture, produced very little if any stenosis.

From clinical trials, 20% is the average stenosis at plaques that subsequently rupture with resulting complete artery closure. Most severe clinical events do not occur at plaques that produce high-grade stenosis. From clinical trials, only 14% of heart attacks occur from artery closure at plaques producing a 75% or greater stenosis prior to the vessel closing.

If the fibrous cap separating a soft atheroma from the bloodstream within the artery ruptures, tissue fragments are exposed and released, and blood enters the atheroma within the wall and sometimes results in a sudden expansion of the atheroma size. Tissue fragments are very clot-promoting, containing collagen and tissue factor; they activate platelets and activate the system of coagulation. The result is the formation of a thrombus (blood clot) overlying the atheroma, which obstructs blood flow acutely. With the obstruction of blood flow, downstream tissues are starved of oxygen and nutrients. If this is the myocardium (heart muscle), angina (cardiac chest pain) or myocardial infarction (heart attack) develops.

### **Diagnosis of plaque-related disease**

Areas of severe narrowing, stenosis, detectable by angiography, and to a lesser extent "stress testing" have long been the focus of human diagnostic techniques for cardiovascular disease, in general. However, these methods focus on detecting only severe narrowing, not the underlying atherosclerosis disease. As demonstrated by human clinical studies, most severe events occur in locations with heavy plaque, yet little or no lumen narrowing present before debilitating events suddenly occur. Plaque rupture can lead to artery lumen occlusion within seconds to minutes, and potential permanent debility and sometimes sudden death.

77% lumen stenosis used to be considered by cardiologists as the hallmark of clinically significant disease because it is only at this severity of narrowing of the larger heart arteries that recurring episodes of angina and detectable abnormalities by stress testing methods are seen. However, clinical trials have shown that only about 14% of clinically-debilitating events occur at locations with this, or greater severity of narrowing. The majority of events occur due to atheroma plaque rupture at areas without narrowing sufficient enough to produce any angina or stress test abnormalities. Thus, since the later-1990s, greater attention is being focused on the "vulnerable plaque."

Though any artery in the body can be involved, usually only severe narrowing or obstruction of some arteries, those that supply more critically-important organs are recognized. Obstruction of arteries supplying the heart muscle result in a heart attack. Obstruction of arteries supplying the brain result in a stroke. These events

are life-changing, and often result in irreversible loss of function because lost heart muscle and brain cells do not grow back to any significant extent, typically less than 2%.

### Physiologic factors that increase risk

Various anatomic, physiological & behavioral risk factors for atherosclerosis are known. These can be divided into various categories: congenital vs acquired, modifiable or not, classical or non-classical. The points labelled '+' in the following list form the core components of "metabolic syndrome":

- Advanced age
- Male sex
- Having Diabetes or Impaired glucose tolerance (IGT) +
- Dyslipidemia (elevated serum cholesterol or triglyceride levels): +
  - High serum concentration of low density lipoprotein (LDL, "bad cholesterol"), lipoprotein little a (a variant of LDL), and / or very low density lipoprotein (VLDL) particles
  - Low serum concentration of functioning high density lipoprotein (HDL, "good cholesterol") particles
- Tobacco smoking
- Having high blood pressure +
- Being obese (in particular central obesity, also referred to as *abdominal* or *male-type* obesity) +
- A sedentary life-style
- Having close relatives who have had some complication of atherosclerosis (eg. coronary heart disease or stroke)
- Elevated serum levels of homocysteine
- Elevated serum levels of uric acid (also responsible for gout)
- Elevated serum fibrinogen concentrations +
- Chronic systemic inflammation as reflected by upper normal WBC concentrations, elevated hs-CRP and many other blood chemistry markers, most only research level at present, not clinically done.<sup>[2]</sup>
- Stress or symptoms of clinical depression
- Hypothyroidism (a slow-acting thyroid)

### Treatment

If atherosclerosis leads to symptoms, the symptoms (such as angina pectoris) can be treated. Non-pharmaceutical means are usually the first method of treatment, such as cessation of smoking and/or regular exercise. If these methods do not work, medicines are usually the next step in treating cardiovascular diseases, and with improvements, have increasingly become the most effective method over the long term. However, medicines are criticized for their expense, patented control and occasional undesired effects.

Lipoprotein imbalances, upper normal and especially elevated blood sugar, i.e. diabetes, high blood pressure, homocysteine, stopping smoking, taking anticoagulants (anti-clotting agents) which target clotting factors, taking Omega 3 oils from salt-water fish meats, exercising and losing weight are the usual focus of treatments which have proved to be helpful in clinical trials. The target serum cholesterol level is ideally equal or less than 4mmol/L (with triglycerides equal or less than 2mmol/L).

In general, the group of medications referred to as statins have been the most successful, with the lowest rates of undesirable side-effects, approach to reducing atherosclerotic disease events. The newest statin, rosuvastatin, has been the first to demonstrate regression of atherosclerotic plaque within the coronary arteries by IVUS evaluation<sup>[31]</sup>, see the *Effect of Very High-Intensity Statin Therapy* reference below. However, for most people, changing their physiologic behaviors, from the usual high risk to greatly reduced risk, requires a combination of several compounds, taken on a daily basis and indefinitely. More and more human treatment trials have been done and are ongoing which demonstrate improved outcome for those people using more complex and effective treatment regimens which change physiologic behaviour patterns to more closely resemble those humans exhibit in childhood at a time before fatty streaks begin forming.

Lowering lipoprotein little a, a genetic variant of LDL, can be achieved with large daily doses of vitamin B3, niacin. Niacin also tends to shift LDL particle distribution to larger particle size and improve HDL functioning. Work on increasing HDL particle concentration and function, beyond the niacin effect, perhaps even more important, is slowly advancing. Combinations of statins, niacin, intestinal cholesterol absorption inhibiting supplements (ezetimibe and others, and to a much lesser extent fibrates have been the most successful in changing dyslipidemia patterns and improving clinical outcomes in secondary prevention. In primary prevention, cholesterol lowering agents have also reduced the mortality rates, (e.g. the AFCAPS/TexCAPS trail), however longer periods are sometimes required to demonstrate the effect because of the usual delay until enough people show the effects of advancing disease without effective treatment. Dietary changes to achieve this have been more controversial, generally far less effective and less widely adhered to with success.

Evidence has increased that people with diabetes, despite not having clinically detectable atherosclerotic disease, have more severe debility from atherosclerotic events over time than even non-diabetics who have already suffered atherosclerotic events. Thus diabetes has been upgraded to be viewed as an advanced atherosclerotic disease equivalent.

Lowering homocysteine levels, including within the normal range and dietary supplements of Omega 3 oils, especially those from the muscle of some deep salt

water living fish species, also have clinical evidence of significant protective effects as confirmed by 6 double blind placebo controlled human clinical trials.

Aerobic exercise, weight loss, and dietary changes can also help, but are generally much less effective and often more problematic for many to achieve and continue long term.

Medical treatments often focus predominantly on the symptoms. However, over time, the treatments which focus on decreasing the underlying atherosclerosis processes, as opposed to simply treating the symptoms resulting from the atherosclerosis, have been shown by clinical trials to be more effective.

Other physical treatments, helpful in the short term, include minimally invasive angioplasty procedures to physically expand narrowed arteries and major invasive surgery, such as bypass surgery, to create additional blood supply connections which go around the more severely narrowed areas.

High dose supplements of vitamin E or C, with the goal of improving antioxidant protection, have failed to produce any beneficial trends in human, double blind, clinical research trials. However, these trials have consistently used lower doses than those claimed to be effective and have ignored the short half life of high intakes of vitamin C in the body.

On the other hand, the statins, and some other medications have been shown to have significant antioxidant effects, perhaps part of their basis for major therapeutic success.

The success of statin drugs in clinical trials is based on large reductions in actual human mortality rates. For example, in 4S, the first large placebo controlled, randomized clinical trial of a statin in people with advanced disease who had already suffered a heart attack, the overall mortality rate reduction for those taking the statin, vs. placebo, was 30%. For the subgroup of people in the trial who had Diabetes Mellitus, the mortality rate reduction between statin and placebo was 54%. 4S was a 5.4 year trial which started in 1989 and was published in 1995 after completion. Many later trials, using more aggressive statin treatments, especially in combination with additional treatment strategies, have shown greater reductions in mortality rates. The [ASTEROID] trial, mentioned above and in reference 3, has been the first to show actual disease volume regression (see page 8 of the paper which shows cross-sectional areas of the total heart artery wall at start and 2 years of rosuvastatin 40 mg/day treatment); however, its design was not large enough or long enough to statistically "prove" the mortality reduction issue. The trials to test this issue with this agent are currently in progress; all current evidence and signs are that the outcomes will be very favorable.

Over the last about 18 years, the treatment data results have become so encouraging that some physician leaders are anticipating the day, probably within

another 10 to 15 years, that clinical disability from atherosclerotic disease will become a disease only of the past, at least for those who enjoy the benefit of using the treatment advances.

In summary, the key to the more effective approaches has been better understanding of the widespread and insidious nature of the disease and to combine multiple different treatment strategies, not rely on just one or a few approaches. Additionally, for those approaches, such as lipoprotein transport behaviors, which have been shown to produce the most success, adopting more aggressive combination treatment strategies has generally produced better results, both before and especially after people are symptomatic. However, treating asymptomatic people remains controversial in the medical community.

Patients at risk for atherosclerosis-related diseases are increasingly being treated prophylactically with low-dose aspirin and a statin. The high incidence of cardiovascular disease led Wald and Law<sup>[4]</sup> to propose a Polypill, a once-daily pill containing these two types of drugs in addition to an ACE inhibitor, diuretic and beta blocker and folic acid. They maintain that high uptake by the general population by such a Polypill would reduce cardiovascular mortality by 80%. It must be emphasized however that this is purely theoretical, as the Polypill has never been tested in a clinical trial.

## **Recent research**

Progress on methods to improve HDLipoprotein particle concentrations and function, which in some animal studies largely reverses and remove atheromas, are being developed and researched. The most dramatic demonstrations of potential HDL efficacy to reverse atherosclerosis has been with the rare Apo-A1 Milano human genetic variant of the HDL protein. Ongoing work starting in the 1990s, leading to human clinical trials probably by about 2008, on using either synthesized Apo-A1 Milano HDL directly or gene-transfer methods to pass the ability to synthesize the Apo-A1 Milano HDL protein is in progress.

The ASTEROID trial, relying on more aggressive treatment of LDLipoproteins, has been the most successful trial, achieving plaque regression, so far using commercially available products, see the *Effect of Very High-Intensity Statin Therapy* reference below.

Since about 2002, progress in understanding and developing techniques for modulating immune system function so as to significantly suppress the action of macrophages to drive atherosclerotic plaque progression are being developed with considerable success in reducing plaque development in both mice and rabbits. Plans for human trials, hoped for by about 2008, are in progress. Generally these techniques are termed immunomodulation of atherosclerosis. Genetic expression and control mechanism research, including (a) the PPAR peroxisome proliferator activated receptors known to be important in blood sugar and variants



of lipoprotein production and function and (b) of the multiple variants with the proteins which form the lipoprotein transport particles, is progressing. Some controversial research has suggested a link between atherosclerosis and the presence of several different nanobacteria in the arteries, e.g. Chlamydophila pneumoniae, though trials of current antibiotic treatments known to usually be effective in suppressing growth or killing these bacteria have not been successful in improving outcomes. The immunomodulation approaches mentioned above, because they deal with innate responses of the host to promote atherosclerosis, have far greater prospects for major success.

## Coronary heart disease

**Coronary heart disease** (CHD), also called **coronary artery disease** (CAD) and atherosclerotic heart disease, is the end result of the accumulation of atheromatous plaques within the walls of the arteries that supply the myocardium (the muscle of the heart). While the symptoms and signs of coronary heart disease are noted in the advanced state of disease, most individuals with coronary heart disease show no evidence of disease for decades as the disease progresses before the first onset of symptoms, often a "sudden" heart attack, finally arise. 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.

[edit]

## Overview

Atherosclerotic heart disease can be thought of as a wide spectrum of disease of the heart. At one end of the spectrum is the asymptomatic individual with atheromatous streaks within the walls of the coronary arteries (the arteries of the heart). These streaks represent the early stage of atherosclerotic heart disease and do not obstruct the flow of blood. A coronary angiogram performed during this stage of disease may not show any evidence of coronary artery disease, because the lumen of the coronary artery has not decreased in caliber.

Over a period of many years, these streaks increase in thickness. While the atheromatous plaques initially expand into the walls of the arteries, eventually they will expand into the lumen of the vessel, affecting the flow of blood through the arteries. While it was originally believed that the growth of atheromatous plaques was a slow, gradual process, some recent evidence suggests that the gradual buildup of plaque may be complemented by small plaque ruptures which cause the sudden increase in the plaque burden due to accumulation of thrombus material.

Atheromatous plaques that cause obstruction of less than 70 percent of the diameter of the vessel rarely cause symptoms of obstructive coronary artery disease. As the plaques grow in thickness and obstruct more than 70 percent of the diameter of the vessel, the individual develops symptoms of obstructive coronary artery disease. At this stage of the disease process, the patient can be said to have ischemic heart disease. The symptoms of ischemic heart disease are often first noted during times of increased workload of the heart. For instance, the first symptoms include exertional angina or decreased exercise tolerance.

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 heart 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 oxygen 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 heart disease. The acute rupture of a plaque may lead to an acute myocardial infarction (heart attack). It is unclear at present which plaques in an individual are more likely to rupture in the future and cause a heart attack.

[edit]

## **Pathophysiology**

Limitation of blood flow to the heart causes ischemia (cell starvation secondary to a lack of oxygen) of the myocardial cells. When myocardial cells die from lack of oxygen, this is called a myocardial infarction (commonly called a heart attack). It leads to heart muscle damage, heart muscle death and later scarring without heart muscle regrowth.

Myocardial infarction usually results from the sudden occlusion of a coronary artery when a plaque ruptures, activating the clotting system and atheroma-clot interaction fills the lumen of the artery to the point of sudden closure. The typical narrowing of the lumen of the heart artery before sudden closure is typically 20%, according to clinical research completed in the late 1990s and using IVUS examinations within 6 months prior to a heart attack. High grade stenoses as such

exceeding 75% blockage, such as detected by stress testing, were found to be responsible for only 14% of acute heart attacks the rest being due to plaque rupture/ spasm. The events leading up to plaque rupture are only partially understood. Myocardial infarction is also caused, far less commonly, by spasm of the artery wall occluding the lumen, a condition also associated with atheromatous plaque and CHD.

CHD is associated with smoking, obesity, hypertension and a chronic sub-clinical lack of vitamin C. A family history of CHD is one of the strongest predictors of CHD. Screening for CHD includes evaluating homocysteine levels, high-density and low-density lipoprotein (cholesterol) levels and triglyceride levels.

[edit]

## Angina

The pain associated with very advanced CHD is known as angina, and usually presents as a sensation of pressure in the chest, arm pain, jaw pain, and other forms of discomfort. The word *discomfort* is preferred over the word *pain* for describing the sensation of angina, because it varies considerably among individuals in character and intensity and most people do not perceive angina as painful, unless it is severe. There is evidence that angina and CHD present differently in women and men.

Angina that occurs regularly with activity, upon awakening, 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 nitrate preparations such as nitroglycerin, which come in short-acting and long-acting forms, and may be administered transdermally, sublingually or orally. 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 is treated with oxygen, intravenous nitroglycerin, and morphine. Interventional procedures such as angioplasty may be done.

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## Risk Factors

**The following are confirmed independent risk factors for the development of CAD, in order of decreasing importance:**

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. Hereditary differences in such diverse aspects as lipoprotein structure and that of their associated receptors, homocysteine processing/metabolism, etc.

### **Significant, but indirect risk factors include:**

- Male sex (by far the most significant of this group)
- Lack of exercise
- Stress
- Diet rich in saturated fats
- Obesity

[edit]

### **Prevention**

Coronary heart 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 uric acid and homocysteine levels may contribute. In diabetes mellitus, there is little evidence that blood sugar control actually improves cardiac risk. Some recommend a diet rich in omega-3 fatty acids and vitamin C.

An increasingly growing number of other physiological markers and homeostatic mechanisms are currently under scientific investigation. Among these markers are low density lipoprotein and asymmetric dimethylarginine. Patients with CHD and those trying to prevent CHD 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 while increasing High density lipoproteins, keeping blood pressure normal, exercise and stop smoking. These measures limit the progression of the disease. Recent studies have shown that dramatic reduction in LDL levels can cause mild regression of coronary heart disease.

Risk factor management 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.

[edit]

### **Preventive diets**

*Main article: Diet and Heart Disease*

- Vegetarian diet: Vegetarians have been shown to have a 24% reduced risk of dying of heart disease (source: Key TJ, Fraser GE, et al. 1999, Sep. Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. Am J Clin Nutr, 70:516S-524S).
- Cretan Mediterranean-style 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 a small amount of animal products. 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.<sup>[*citation needed*]</sup>

[edit]

## Recent research

*Further information: atheroma and atherosclerosis*

A 2006 study found a region on Chromosome 17 was confined to families with multiple cases of myocardial infarction<sup>[1]</sup>.

Controversial research has recently suggested a link between the atherosclerosis-causing CHD and the presence of nanobacteria in the arteries.<sup>[*citation needed*]</sup> However, trials of currently available antibiotics known to inhibit or kill some of these microorganisms have not shown much benefit to patients. If an infectious role were found to be a significant factor, this could have important implications for treatment and prevention of the disease beyond the many current, proven strategies.

Ornish has suggested that coronary heart disease is partially reversible using an intense dietary regime such as the Cretan diet coupled with regular cardio exercise

## Cardiac arrest

A **cardiac arrest**, or **circulatory arrest**, is the abrupt cessation of normal circulation of the blood due to failure of the heart to contract effectively during systole.<sup>[1]</sup>

The resulting lack of blood supply results in cell death from oxygen starvation. Cerebral hypoxia, or lack of oxygen supply to the brain, causes victims to lose consciousness and to stop breathing, which in turn causes the heart to stop. Brain

damage is likely to occur after 3-4 minutes, except in cases of hypothermia. To improve survival and neurological recovery immediate response is paramount.<sup>[2]</sup>

Cardiac arrest is a medical emergency that, in certain groups of patients, is potentially reversible if treated early enough. When cardiac arrest leads to death this is called **sudden cardiac death** (SCD).<sup>[1]</sup> The primary first-aid treatment for cardiac arrest is cardiopulmonary resuscitation (commonly known as **CPR**).

## **Etiology**

Ventricular fibrillation (VF) constitutes the most common electrical mechanism in cardiac arrest, and is responsible for 65 to 80% of occurrences. Another 20-30% is caused by severe bradyarrhythmias, pulseless electrical activity (PEA) and asystole. Other conditions are associated with impaired circulation due to a state of shock.<sup>[1]</sup>

Among adults ischemic heart disease is the predominant cause.<sup>[3]</sup> At autopsy 30% of victims show signs of recent myocardial infarction. Other conditions include structural abnormalities, arrhythmias and cardiomyopathies. Secondary cardiac arrest may be elicited by non-cardiac conditions such as hypoxia from a variety of causes,<sup>[4]</sup> overwhelming infection (sepsis), massive pulmonary embolus, arrhythmias, cardiac tamponade, shock, pneumothorax, ventricular rupture, as well as other conditions such as electrocution and near-drowning. Non-cardiac conditions constitute the principal cause of cardiac arrest in in-hospital patients.<sup>[5]</sup>

Coronary heart disease (CHD) -also known as coronary artery disease, or (CAD)- is the predominant disease process associated with sudden cardiac death in the United States and elsewhere in the developed world. The incidence of CHD in individuals who suffer sudden cardiac death is between 64 and 90%.

In children, cardiac arrest is typically caused by hypoxia from other causes such as near-drowning. With prompt treatment survival rates are high.

## **Treatable causes**

There are 8 reversible causes of cardiac arrest, known as the "4Hs and 4Ts".<sup>[5]</sup> They are looked for and treated by ambulance technicians/paramedics or by medical staff at the hospital while undertaking advanced life support, protocols for which will be used alongside any specific treatments for each of the causes. Lay rescuers performing basic life support can generally neither identify nor treat them (with the exception of hypoxia due to choking), and so can offer only supportive treatment pending the arrival of emergency medical services.

## **4 Hs**

- **Hypoxia** - A lack of oxygen to the heart, brain and other vital organs. This is treated by providing the patient with oxygen, either through a bag-valve-mask device, or through mechanical ventilation by inserting an endotracheal tube (intubation)
- **Hypovolemia** - A lack of circulating body fluids, principally blood. This is usually (though not exclusively) caused by some form of bleeding. Peri-arrest treatment includes giving IV fluids and blood transfusions, and controlling the source of any bleeding - by direct pressure for external bleeding, or emergency surgical techniques such as esophagogastroduodenoscopy (i.e. esophageal varices) and thoracotomy for internal bleeding.
- **Hypo/Hyper-metabolic disorders** - An abnormally high or low level of electrolytes such as potassium and calcium circulating the body. An arterial blood gas and blood electrolyte test are performed to find the problem, then IV crystalloids are given to correct it.
- **Hypothermia** - A low core body temperature, defined clinically as a temperature of less than 35 degrees Celsius. The patient is re-warmed either by using a cardiac bypass or by irrigation of the body cavities (such as thorax, peritoneum, bladder) with warm fluids; or warmed IV fluids. CPR only is given until the core body temperature reached 30 degrees Celsius, as defibrillation is ineffective at lower temperatures. Patients have been known to be successfully resuscitated after periods of hours in hypothermia and cardiac arrest, and this has given rise to the often-quoted medical truism, "You're not dead until you're warm and dead."

#### 4 Ts

- **Tension pneumothorax** - A rush of air into one of the pleural cavities which is not able to escape compresses the lungs and causes the trachea to deviate away from the mid-line, often putting pressure on the heart so it is not able to beat effectively. This is relieved in an emergency by inserting a needle into the 2nd intercostal space at the mid-clavicular line, releasing the air and the pressure on the thoracic organs.
- **Tamponade (Cardiac)** - Blood or other fluids building up in the pericardium can put pressure on the heart so that it is not able to beat. This is treated in an emergency by inserting a needle into the pericardium to drain the fluid (pericardiocentesis), or if the fluid is too thick then an emergency thoracotomy is performed to cut the pericardium and release the fluid.
- **Toxins** - Toxic substances which have been ingested, injected, absorbed or inhaled into the body can lead to cardiac arrest. This may be evidenced by items found on or around the patient, the patient's medical history (i.e. drug

abuse, medication) taken from family and friends, checking the medical records to make sure no interacting drugs were prescribed, or sending blood and urine samples to the toxicology lab for report. Treatment is mainly supportive, unless there is an antidote which can be administered.

- **Thrombosis** - Blood clots in the heart (myocardial infarction) or lungs (pulmonary embolism) are both well known causes of cardiac arrest. Treatment includes thrombolysis, and possibly surgical interventions such as percutaneous transluminal coronary angioplasty (PTCA), coronary bypass or surgical embolectomy.

In addition to the specific treatments for the causes of cardiac arrest, full resuscitation (using advanced life support protocols) is offered to patients as soon as possible, and continues until the patient is either declared dead or regains a pulse and stable heart rhythm.

Cardiac Arrest is an abrupt cessation of pump function (evidenced by absence of a palpable pulse) of the heart that with prompt intervention could be reversed, but without it will lead to death.<sup>[1]</sup> In many cases, lack of carotid pulse is the gold standard for diagnosing cardiac arrest, but pulselessness (particularly in the peripheral pulses) may be a result of other conditions (i.e. shock, or other conditions leading to poor circulation)

In a hospital or ambulance, cardiac arrest is identified by the lack of a pulse (or lack of heartbeat if listened to through a stethoscope), and advanced life support is given.

Out of hospital, lay rescuers are now being taught to identify cardiac arrest in as simple a manner as possible. With the latest standard as set by the ILCOR, lay rescuers are taught that a lack of normal breathing is evidence of cardiac arrest, and they begin CPR without checking a pulse.

An ECG clarifies the exact diagnosis and guides treatment, but basic life support should begin without awaiting an ECG. The ECG may reveal:

- Asystole (known colloquially as a flatline) - a complete stoppage of the heart
- Pulseless electrical activity (formerly called electromechanical dissociation) - where the heart's electrical system is working normally but there is a problem with mechanical function (so the rhythm on the heart monitor appears normal, but there is no pulse)
- ventricular fibrillation - A quivering of the ventricles
- ventricular tachycardia - The ventricles contract so rapidly that they do not refill fully between beats, so they do not pump enough blood to maintain circulation.

## First aid

First aid treatment of cardiac arrest varies from country to country, but the general principles of the guidelines in all locales are to summon help (in the form of an ambulance) and then begin CPR.

## Angina pectoris

**Angina pectoris** is chest pain due to ischemia (a lack of blood and hence oxygen supply) of the heart muscle, generally due to obstruction or spasm of the coronary arteries (the heart's blood vessels). Coronary artery disease, the main cause of angina, is due to atherosclerosis of the cardiac arteries. The term derives from the Greek *ankhon* ("strangling") and the Latin *pectus* ("chest"), and can therefore be translated as "a strangling feeling in the chest". American author and humorist Mark Twain suffered from angina pectoris and died in 1910. Angina is a symptom, not a disease, so it is likely that Twain died of a heart attack, caused by sudden blockage of a coronary artery, which may have been preceded by anginal symptoms.

It is common to equate severity of angina with risk of fatal cardiac events. There is a weak relationship between severity of pain and degree of oxygen deprivation in the heart muscle ie there can be severe pain with little or no risk of a heart attack, and a heart attack can occur without pain)

Worsening ("crescendo") angina attacks, sudden-onset angina at rest, and angina lasting more than 15 minutes are symptoms of *unstable angina* (usually grouped with similar conditions as the acute coronary syndrome). As these may herald myocardial infarction (a heart attack), they require urgent medical attention and are generally treated as a presumed heart attack.

## Symptoms

Most patients with angina complain of chest discomfort rather than actual pain: the discomfort is usually described as a pressure, heaviness, squeezing, burning, or choking sensation. Apart from chest discomfort, anginal pains may also be experienced in the epigastrium (upper central abdomen), back, neck, jaw, or shoulders. Typical locations for radiation of pain are arms, shoulders, and neck. Angina is typically precipitated by exertion or emotional stress. It is exacerbated by having a full stomach and by cold temperatures. Pain may be accompanied by breathlessness, sweating and nausea in some cases. It usually lasts for about 1 to 5 minutes, and is relieved by rest or specific anti-angina medication. Chest pain lasting only a few seconds is normally not angina.

Myocardial ischemia comes about when the myocardium, which is more commonly called as the heart's muscles, fails to take in the much needed blood and



oxygen in order to function correctly. The inability to acquire blood and oxygen, on the other hand, is due to blocked or narrowed blood vessels.

Some experience "autonomic symptoms" (related to increased activity of the autonomic nervous system) such as nausea, vomiting and pallor.

Major risk factors for angina include family history of premature heart disease, cigarette smoking, diabetes, high cholesterol, and high blood pressure.

A variant form of angina (Prinzmetal's angina) occurs in patients with normal coronary arteries or insignificant atherosclerosis. It is thought to be caused by spasms of the artery. It occurs more in younger women.

## **Diagnosis**

In patients with the occasional angina who are not having chest pain, an electrocardiogram (ECG) is typically normal, unless there have been other cardiac problems in the past. During pain, depression or elevation of the ST segment may be observed. To elicit these changes, an exercise ECG test ("treadmill test") may be performed, during which the patient exercises to their maximum ability before fatigue, breathless or, importantly, pain supervenes; if characteristic ECG changes are documented (typically more than 1mm of flat or downsloping ST depression), the test is considered diagnostic for angina. The exercise test is also useful in looking for other markers of myocardial ischaemia: blood pressure response (or lack thereof, particularly a drop in systolic pressure), dysrhythmia and chronotropic response. Other alternatives to a standard exercise test include a thallium scintigram (in patients that cannot exercise enough for the purposes of the treadmill tests, e.g., due to asthma or arthritis or in whom the ECG is too abnormal at rest) or Stress Echocardiography.

In patients in whom such noninvasive testing is diagnostic, a coronary angiogram is typically performed to identify the nature of the coronary lesion, and whether this would be a candidate for angioplasty, coronary artery bypass graft (CABG), treatment only with medication, or other treatments. In patients who are in hospital with unstable angina (or the newer term of "high risk acute coronary syndromes"), those with resting ischaemic ECG changes or those with raised cardiac enzymes such as troponin may undergo coronary angiography directly.

## **Pathophysiology**

Increase in heart rate result in increased oxygen demand by the heart. The heart has a limited ability to increase its oxygen intake during episodes of increased demand. Therefore, an increase in oxygen demand by the heart (eg, during exercise) has to be met by a proportional increase in blood flow to the heart.

Myocardial ischemia can result from:

1. a reduction of blood flow to the heart caused by the stenosis or spasm of the heart's arteries
2. resistance of the blood vessels
3. reduced oxygen-carrying capacity of the blood.

Atherosclerosis is the most common cause of stenosis (narrowing of the blood vessels) of the heart's arteries and, hence, angina pectoris. Some people with chest pain have normal or minimal narrowing of heart arteries; in these patients, vasospasm is a more likely cause for the pain, sometimes in the context of Prinzmetal angina and syndrome X.

Myocardial ischemia also can be the result of factors affecting blood composition, such as reduced oxygen-carrying capacity of blood, as seen with severe anemia (low number of red blood cells), or long-term smoking.

## **Epidemiology**

Roughly 6.3 million Americans are estimated to experience angina. Angina is more often the presenting symptom of coronary artery disease in women than in men. The prevalence of angina rises with an increase in age. Similar figures apply in the remainder of the Western world. All forms of coronary heart disease are much less-common in the Third World, as its risk factors are much more-common in Western and Westernized countries; it could therefore be termed a disease of affluence. The increase of smoking, obesity and other risk factors has already led to an increase in angina and related diseases in countries such as China.

## **Treatment**

The main goals of treatment in angina pectoris are relief of symptoms, slowing progression of the disease, and reduction of future events, especially heart attacks and of course death. An aspirin (75 mg to 100 mg) per day has been shown to be beneficial for all patients with stable angina that have no problems with its use. Beta-blockers have a large body of evidence in morbidity and mortality benefits (fewer symptoms and disability and live longer) and short-acting nitroglycerin medications are used for symptomatic relief of angina. Calcium channel blockers (such as nifedipine and amlodipine), Isosorbide mononitrate and nicorandil are vasodilators commonly used in chronic stable angina. ACE inhibitors are also vasodilators with both symptomatic and prognostic benefit and lastly, statins are the most frequently used lipid/cholesterol modifiers which probably also stabilise existing atheromatous plaque.

Surprising perhaps is that exercise is also a very good long term treatment for angina[1](but only particular regimes - gentle and sustained exercise rather than dangerous intense short bursts), probably working by complex mechanisms such improving blood pressure and promoting coronary artery collateralisation.



Identifying and treating risk factors for further coronary heart disease is a priority in patients with angina. This means testing for elevated cholesterol and other fats in the blood, diabetes and hypertension (high blood pressure), encouraging stopping smoking and weight optimisation.

Even though known victims may wear a necklace or bracelet identifying the medical condition, EMS (ambulance) is still required

## Myocardial infarction

Acute **myocardial infarction** (AMI or MI), commonly known as a **heart attack**, is a disease that occurs when the blood supply to a part of the heart is interrupted, causing death of heart tissue. It is the leading cause of death for both men and women all over the world.<sup>[1]</sup>

The term *myocardial infarction* is derived from *myocardium* (the heart muscle) and *infarction* (tissue death due to oxygen starvation or ischemia). The phrase "heart attack" sometimes refers to heart problems other than MI, such as unstable angina pectoris and sudden cardiac death.

## Symptoms

Acute myocardial infarction is usually characterized by varying degrees of chest pain, discomfort, sweating, weakness, nausea, vomiting, and arrhythmia, sometimes causing loss of consciousness and even sudden death. Chest pain is the most common symptom of acute myocardial infarction (MI) and is often described as a sensation of tightness, pressure, or squeezing. Pain radiates most often to the left arm, but may also radiate to the jaw, neck, right arm, back, and epigastrium. The patient may complain of shortness of breath (dyspnea) especially if the decrease in myocardial contractility due to the infarct is sufficient to cause left ventricular failure with pulmonary congestion or even pulmonary edema. Approximately half of all MI patients have experienced warning symptoms like angina pectoris prior to the infarction.

Women often experience different symptoms than men. The most common symptoms of MI in women include dyspnea, weakness, and fatigue. *Fatigue*, *sleep disturbances*, and dyspnea have been reported as frequently occurring prodromal symptoms which may manifest as long as one month before the actual clinically manifested ischemic event. In women, chest pain may be less predictive of coronary ischemia than in men<sup>[2]</sup>

Approximately one third of all myocardial infarctions are silent, without chest pain or other symptoms.<sup>[3]</sup> This happens more often in elderly patients and patients with diabetes mellitus.<sup>[4]</sup>

## Diagnosis

Myocardial infarctions vary greatly in severity. Many cases of myocardial infarction are identified by ambulance staff, emergency room doctors and cardiac specialist nurse practitioners quickly. Other, often smaller myocardial infarctions sometimes are not recognized by victims, never receive medical attention, and can result in heart weakness and other complications. Adequate diagnosis requires a medical history, an electrocardiogram, and blood tests for heart muscle cell damage. Other information, including results of myocardial perfusion tests (see stress tests) and echocardiograms can also help establish the diagnosis of MI.

## Electrocardiogram

Electrocardiogram (ECG/EKG) findings suggestive of MI are elevations of the *ST segment* and changes in the *T wave*. After a myocardial infarction, changes can often be seen on the ECG called *Q waves*, representing scarred heart tissue. However, a normal ECG/EKG does not rule out a myocardial infarction.

The ST segment elevation distinguishes between:

- STEMI ("ST-Elevation Myocardial Infarction")
- NSTEMI ("Non-ST-Elevation Myocardial Infarction") -- diagnosed when cardiac enzymes are elevated.

The leads with abnormalities on the ECG may help identify the location:<sup>[5]</sup>

Wall affected	Leads	Artery involved	Reciprocal changes
<u>Anterior</u>	V <sub>2</sub> -V <sub>4</sub>	<u>Left coronary artery, Left Anterior descending (LAD)</u>	II, III, aV <sub>F</sub>
<u>Anterolateral</u>	I, aV <sub>L</sub> , V <sub>3</sub> -V <sub>6</sub>	<u>LAD</u> and diagonal branches, <u>circumflex</u> and <u>marginal</u> branches	II, III, aV <sub>F</sub>
<u>Anteroseptal</u>	V <sub>1</sub> -V <sub>4</sub>	<u>LAD</u>	-
<u>Inferior</u>	II, III, aV <sub>F</sub>	<u>right coronary artery (RCA)</u>	I, aV <sub>L</sub>
<u>Lateral</u>	I, aV <sub>L</sub> , V <sub>5</sub> , V <sub>6</sub>	<u>circumflex branch</u> or <u>left coronary artery</u>	II, III, aV <sub>F</sub>
<u>Posterior</u>	V <sub>8</sub> , V <sub>9</sub>	<u>RCA</u> or <u>circumflex artery</u>	V <sub>1</sub> -V <sub>4</sub> (R greater than S in V <sub>1</sub> )

			& V <sub>2</sub> , ST-segment depression, elevated T wave)
<u>Right ventricular</u>	V <sub>4R</sub> -V <sub>6R</sub>	<u>RCA</u>	-

[edit]

## Cardiac markers

Cardiac markers or cardiac enzymes are proteins from cardiac tissue found in the blood. Until the 1980s, the enzymes SGOT and LDH were used to assess cardiac injury. Then it was found that disproportional elevation of the *MB* subtype of the enzyme creatine phosphokinase (CPK) was very specific for myocardial injury. Current guidelines are generally in favor of troponin sub-units I or T, which are very specific for the myocardium and are thought to rise before permanent injury develops. A positive troponin in the setting of chest pain may accurately predict a high likelihood of a myocardial infarction in the near future.

The diagnosis of myocardial infarction requires two out of three components (history, ECG, and enzymes) to be positive for MI. Currently the cardiac markers, namely the troponins have become so reliable that enzyme elevations alone are considered reliable measures of cardiac injury, with ECG serving to determine where in the heart the damage has occurred, and history serving to screen patients for further enzyme and ECG testing.

In difficult cases or in situations where intervention to restore blood flow is appropriate, an angiogram can be done (see below for an image). Using a catheter inserted into an artery (usually the femoral artery), obstructed or narrowed vessels can be identified, and angioplasty applied as a therapeutic measure (see below). Angiography requires extensive skill, especially in emergency settings, and may not always be available out of hours. It is commonly performed by cardiologists. There is a very small risk of plaque and vessel rupture on balloon inflation; should this occur, then emergency open-chest cardiac surgery may be required. Patients commonly experience bruising at the catheter insertion point in the groin and occasionally a hematoma. Dissection (tearing) of the blood vessel is rare but usually managed with a local thrombotic injection.

## Diagnostic criteria

WHO criteria<sup>[6]</sup> have classically been used to diagnose MI; a patient is diagnosed with myocardial infarction if two (probable) or three (definite) of the following criteria are satisfied:

1. Clinical history of ischaemic type chest pain lasting for more than 20 minutes
2. Changes in serial ECG tracings

3. Rise and fall of serum cardiac enzymes (biomarkers) such as creatine kinase, troponin I, and lactate dehydrogenase isozymes specific for the heart.

The WHO criteria were refined in 2000 to give more prominence to cardiac biomarkers.<sup>[7]</sup> According to the new guidelines, a cardiac troponin rise accompanied by either typical symptoms, pathological Q waves, ST elevation or depression or coronary intervention are diagnostic of MI.



 Angiogram

The blood flow problem is nearly always a result of exposure of atheroma tissue within the wall of the artery to the blood flow inside the artery, atheroma being the primary lesion of the atherosclerotic process. The many blood stream column irregularities, visible in the single frame angiogram image to the right, reflects artery lumen changes as a result of decades of advancing atherosclerosis.

Heart attacks rates are higher in association with intense exertion, be it stress or physical exertion, especially if the exertion is unusually more intense than the individual usually performs. Quantitatively, the period of intense exercise and subsequent recovery is associated with about a 6-fold higher myocardial infarction rate (compared with other more relaxed times frames) for people who are physically very fit. For those in poor physical condition, the rate differential is over 35-fold higher. One observed mechanism for this phenomenon is the increased arterial pulse pressure stretching and relaxation of arteries with each heart beat which, as has been observed with IVUS, increases mechanical "shear stress" on atheromas and the likelihood of plaque rupture.

Increased spasm/contraction of coronary arteries and left ventricular hypertrophy in association with cocaine abuse can also precipitate myocardial infarction.

Acute severe infection, such as pneumonia, can trigger myocardial infarction. A more controversial link is that between *Chlamydomphila 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.

## First aid

### Immediate care

As myocardial infarction is a common medical emergency, the signs are often part of first aid courses. General management in the acute setting is:

- Seek emergency medical assistance immediately.
- Help the patient to rest in a position which minimises breathing difficulties. A half-sitting position with knees bent is often recommended.
- Give access to more oxygen, e.g. by opening the window and widening the collar for easier breathing; but keep the patient warm, e.g. by a blanket or a jacket
- Give aspirin, if the patient is not allergic to aspirin. Aspirin has an antiplatelet effect which inhibits formation of further thrombi (blood clots).
  - Non-enteric coated or soluble preparations are preferred. These should be chewed or dissolved, respectively, to facilitate quicker absorption. If the patient cannot swallow, the aspirin can be used sublingually.
  - U.S. guidelines recommend a dose of 160 – 325 mg.<sup>[8]</sup>
  - Australian guidelines recommend a dose of 150 – 300 mg.<sup>[9]</sup>
- Give glyceryl trinitrate (nitroglycerin) sublingually (under the tongue) if it has been prescribed for the patient.
- Monitor pulse, breathing, level of consciousness and, if possible, the blood pressure of the patient continually.
- Administer cardiopulmonary resuscitation (CPR) if cardiac arrest occurs due to ventricular arrhythmia

### Automatic external defibrillation (AED)

Since the publication of data showing that the availability of automated external defibrillators (AEDs) in public places may significantly increase chances of survival, many of these have been installed in public buildings, public transport facilities, and in non-ambulance emergency vehicles (e.g. police cars and fire engines). AEDs are also becoming popular for use in the home, where most attacks occur. AEDs analyze the heart's rhythm and determine whether the rhythm is amenable to defibrillation ("shockable"), as in ventricular tachycardia and ventricular fibrillation.

### Emergency services

Emergency services may recommend the patient to take nitroglycerin tablets or patches, in case these are available, particularly if they had prior heart attacks or angina.

In an ambulance, an intravenous line is established, and the patient is transported immediately if breathing and pulse are present. Oxygen first aid is provided and the patient is calmed. Close cardiac monitoring (with an electrocardiogram) is initiated if available.

Recent attempts to reduce the damage to the heart from an acute myocardial infarction have resulted in studies of prehospital use of thrombolytics or clot busters. In rural areas or congested urban areas trained paramedics are giving thrombolytics to patients who meet specific rigid criteria. Determining the effectiveness of this treatment is done through various studies. Studies, like the TIMI-19, evaluate time of the onset of symptoms and time of administration of thrombolytics and the patients outcome. Studies have also been done comparing prehospital thrombolytics and in-hospital administration of thrombolytics and interventional angioplasty. The specific medication utilized and the criteria the patient must meet are factors for each of several different studies.

If the patient has lost breathing or circulation advanced cardiac life support (including defibrillation) may be necessary and (at the paramedic level) injection of medications may be given per protocol. CPR is performed if there is no satisfactory cardiac output.

About 20% of patients die before they reach the hospital – the cause of death is often ventricular fibrillation.

### **Wilderness first aid**

In wilderness first aid, a possible heart attack justifies evacuation by the fastest available means, including MEDEVAC, even in the earliest or precursor stages. The patient will rapidly be incapable of further exertion and have to be carried out. A sublingual aspirin tablet may help.

### **Air travel**

Doctors traveling by commercial aircraft may be able to assist an MI patient by using the on-board first aid kit, which contains some cardiac drugs used in advanced cardiac life support, and oxygen. Flight attendants are generally aware of the location of these materials. Pilots may divert the flight to land at a nearby airport.

### **Treatment**

A heart attack, especially because of cardiac arrhythmias, is often a life-threatening medical emergency which demands both immediate attention and activation of the emergency medical services. Immediate termination of arrhythmias and transport by ambulance to a hospital where advanced cardiac life support (ACLS) is available can greatly improve both chances for survival and recovery. The more



time that passes, even 1 – 2 minutes, before medical attention is available/sought, the more likely the occurrence of both (a) life threatening arrhythmias/death and (b) more severe and permanent heart damage.

## First line

In the hospital, oxygen, aspirin, glyceryl trinitrate (nitroglycerin) and analgesia (usually morphine, hence the popular mnemonic MONA, *m*orphine, *o*xygen, *n*itro, *a*spirin) are administered as soon as possible. In many areas, first responders can be trained to administer these prior to arrival at the hospital.

## Reperfusion

The ultimate goal of the management in the acute phase of the disease is to salvage as much myocardium as possible and restore contractile function of heart chambers. This is achieved primarily with thrombolytic drugs, such as streptokinase, urokinase, alteplase (recombinant tissue plasminogen activator, rtPA) or reteplase. Heparin alone as an anticoagulant is ineffective. Aspirin is a standard therapy that is part of all reperfusion regimens. Because irreversible ischemic injury occurs within 2-4 hours of the infarction, there is a limited window of time available for reperfusion to work.

Although clinical trials suggest better outcomes, angioplasty via cardiac catheterization as a first-line measure is probably still underused. This is largely dependent on the availability of an experienced interventional cardiologist on-site, or the availability of rapid transport to a referral centre. The goal of primary angioplasty is to open the artery within 90 minutes of the patient presenting to the emergency room. This time is referred to as the door-to-balloon time. If this door-to-balloon time exceeds the time required to administer a thrombolytic agent by > 60 minutes, then the administration of a thrombolytic agents is preferred.

Emergency coronary surgery, in the form of coronary artery bypass surgery is another option, although this option is in decline since the development of primary angioplasty. The same limitations apply here: cardiothoracic surgery services are not available in many hospitals.

NSTEMI (non-ST elevation MI) is initially indistinguishable from unstable angina in most cases, and is therefore managed similarly with aspirin, heparin, and usually with clopidogrel.

## Monitoring and follow-up

Additional objectives are to prevent life-threatening arrhythmias or conduction disturbances. This requires monitoring in a coronary care unit and protocolised administration of antiarrhythmic agents.

Patients are discouraged from working and sexual activity for about two months, while they undergo cardiac rehabilitation training. Local authorities may place limitations on driving motorised vehicles.

During a follow-up outpatient visit, or increasingly before discharge from hospital, further investigations are performed to objectivate coronary artery disease. If rescue angioplasty has not already been performed, a coronary angiogram (or alternatively a thallium scintigram or treadmill test) may be done to identify treatable causes, as this will decrease the risk of future myocardial infarction.

## Secondary prevention

Patients are usually commenced on several long-term medications post-MI, with the aim of preventing secondary cardiovascular events such as further myocardial infarctions or cerebrovascular accident (CVA). Unless contraindicated, such medications may include.<sup>[10][9]</sup>

- Antiplatelet drug therapy such as aspirin and/or clopidogrel should be continued to reduce the risk of thrombus formation. Aspirin is first-line, owing to its low cost and comparable efficacy, with clopidogrel reserved for patients intolerant of aspirin. The combination of clopidogrel and aspirin may further reduce risk of cardiovascular events, however the risk of hemorrhage is increased.
- β-Blocker therapy such as bisoprolol or metoprolol should be commenced.<sup>[11]</sup> These have been particularly beneficial in high-risk patients such as those with left ventricular dysfunction (LVD) and/or continuing cardiac ischaemia. β-Blockers decrease mortality and morbidity. They also improve symptoms of cardiac ischemia in NSTEMI.
- ACE inhibitor therapy should be commenced 24 – 48 hours post-MI in hemodynamically-stable patients, particularly in patients with a history of MI, diabetes mellitus, hypertension, anterior location of infarct (as assessed by ECG), tachycardia, and/or evidence of left ventricular dysfunction. ACE inhibitors reduce mortality, the development of heart failure, and decrease ventricular remodelling post-MI.
- Statin therapy has been shown to reduce mortality and morbidity post-MI, irrespective of the patient's cholesterol level.
- The aldosterone antagonist agent eplerenone has been shown to further reduce risk of cardiovascular death post-MI in patients with heart failure and left ventricular dysfunction, when used in conjunction with standard therapies above.<sup>[12]</sup>

Patients' blood pressure is also treated to target, and lifestyle changes are suggested, chiefly smoking cessation, regular aerobic exercise, a sensible diet, and limitation of alcohol intake.



## Cardiac arrhythmia

**Cardiac arrhythmia** is a group of conditions in which the muscle contraction of the heart is irregular or is faster or slower than normal. **Cardiac dysrhythmia** is technically more correct, as arrhythmia would imply that there is "no rhythm," but this term is not used frequently.

Some arrhythmias are life-threatening medical emergencies that can cause cardiac arrest and sudden death. Others cause aggravating symptoms, such as an awareness of a different heart beat, or palpitation, which can be annoying. Some are quite benign and normal. Sinus arrhythmia is the mild acceleration followed by slowing of the normal rhythm that occurs with breathing. In adults the normal heart rate ranges from 60 beats per minute to 100 beats per minute. The normal heart beat is controlled by a small area in the upper chamber of the heart called the sinoatrial node or sinus node. The sinus node contains specialized cells that have spontaneous electrical activity that starts each normal heart beat.

### Frequency too high or too low

A heart rate faster than 100 beats/minute is considered a tachycardia. This number varies with age, as the heartbeat of a younger person is naturally faster than that of an older person's. With exercise the sinus node increases its rate of electrical activity to accelerate the heart rate. The normal fast rate that develops is called sinus tachycardia. Arrhythmias that are due to fast, abnormal electrical activity can cause tachycardias that are dangerous. If the ventricles of the heart experiences one of these tachycardias for a long period of time, there can be deleterious effects. Individuals may sense a tachycardia as a pounding sensation of the heart, known as palpitations. If a tachycardia lowers blood pressure it may cause lightheadedness or dizziness, or even fainting (syncope). If the tachycardia is too fast, the pump function of the heart is impeded, which may lead to a sudden death.

Most tachycardias are not dangerous. Anything that increases adrenaline or its effects on the heart will increase the heart rate and potentially cause palpitations or tachycardias. Causes include stress, ingested or injected substances (ie: caffeine, alcohol (see Holiday heart syndrome), and an overactive thyroid gland (hyperthyroidism). Individuals who have a tachycardia are often advised to limit or remove exposure to any causative agent.

A slow rhythm, known as bradycardia (less than 60 beats/min), is usually not life threatening, but may cause symptoms. When it causes symptoms implantation of a permanent pacemaker may be needed.

Either dysrhythmia requires medical attention to evaluate the risks associated with the arrhythmia.

## Fibrillation

A serious variety of arrhythmia is known as fibrillation. Fibrillation occurs when the heart muscle begins a quivering motion instead of a normal, healthy pumping rhythm. Fibrillation can affect the atrium (atrial fibrillation) or the ventricle (ventricular fibrillation); ventricular fibrillation is imminently life-threatening.

*Atrial fibrillation* is the quivering, chaotic motion in the upper chambers of the heart, known as the atria. Atrial fibrillation is often 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 intervention which is most likely to restore a more healthy heart rhythm. It does this by applying an electric shock to the heart, after which sometimes the heart will revert to a rhythm that can once again pump blood.

Almost every person goes into ventricular fibrillation in the last few minutes of life as the heart muscle reacts to diminished oxygen or general blood flow, trauma, irritants, or depression of electrical impulses themselves from the brain.

## **Origin of impulse**

When an electrical impulse begins in any part of the heart, it will spread throughout the myocardium and cause a contraction; see Electrical conduction system of the heart. Abnormal impulses can begin by one of two mechanisms: automaticity or reentry.

### **Automaticity**

Automaticity refers to a cardiac muscle cell firing off an impulse on its own. Every cardiac cell has this potential: if it does *not* receive any impulses from elsewhere, its internal "pacemaker" will fire off an impulse after a certain amount of time. A single specialized location in the atria, the sinoatrial node, has a higher automaticity (a faster pacemaker) than the rest of the heart, and therefore is usually the one to start the heartbeat.

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 slightly different timing than usual and causes a 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 can result.

## **Reentry**

Reentrant dysrhythmias occur when an electrical impulse travels in a circle within the heart, rather than moving outward 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 impulse spreads through the heart quickly enough that each cell will only respond once, but if conduction is abnormally slow in some areas, part of the impulse will arrive late and will be treated as a new impulse, which can then spread backward. Depending on the timing, this can produce a sustained abnormal rhythm, such as atrial flutter, a self-limiting burst of supraventricular tachycardia, or the dangerous ventricular tachycardia.

By analogy, imagine a room full of people all given these instructions: "If you see anyone starting to stand up, then stand up for three seconds and sit back down." If the people are quick enough to respond, the first person to stand will trigger a single wave which will then die out; but if there are stragglers on one side of the room, people who have already sat down will see them and start a second wave, and so on.

## **Diagnosis**

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 ECG recorded over a 24-hour period, to detect dysrhythmias that may happen briefly and unpredictably throughout the day.

## **SADS**

**SADS**, or **sudden arrhythmia death syndrome**, is a term used to describe sudden death due to cardiac arrest brought on by an arrhythmia. 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 can also occur from other causes. Tragically there are many inherited conditions and heart diseases that can affect young people that can cause sudden death. Many of these victims have no symptoms before dying suddenly.

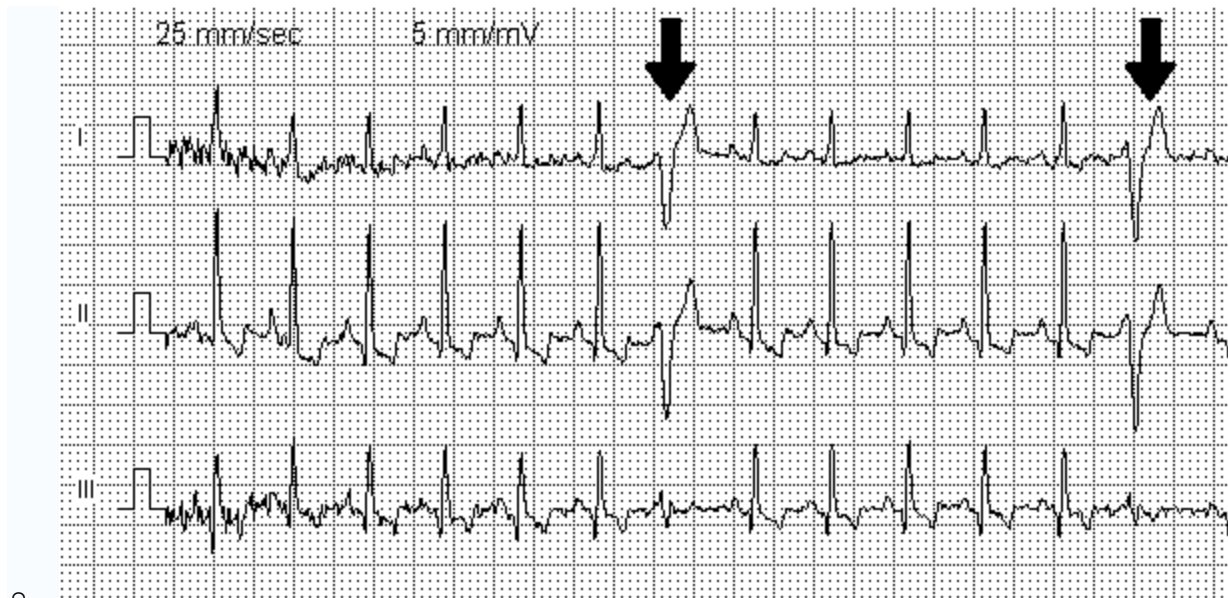
The most common causes of SADS in young people are long QT syndrome, Brugada syndrome, and hypertrophic cardiomyopathy and arrhythmogenic right ventricular dysplasia ("arrhythmia"-causing, "right ventricle"-involving, pre-cancerous malformation(bad-growth)).

[edit]

### List of common cardiac dysrhythmias

- . Atrial Arrhythmias
  - o Atrial fibrillation
- . Ventricular Arrhythmias
  - o Ventricular fibrillation
- . Ventricular Dysrhythmias
  - o Premature ventricular contraction





- 
- Ventricular tachycardia
- Asystole
- Heart Blocks
  - Third degree heart block, also known as complete heart block

### Antiarrhythmic therapies

There are many classes of antiarrhythmic medications and many individual drugs within these classes. See the article on **antiarrhythmic agents**.

Dysrhythmias may also be treated electrically. Cardioversion is the application of electrical current across the chest wall to the heart and it is used for treatment of supraventricular or pulsed ventricular tachycardia. Defibrillation differs in that it is used for ventricular fibrillation and pulseless ventricular tachycardia, and more electricity is delivered with defibrillation than with cardioversion. In cardioversion, the recipient is either sedated or lightly anesthetized for the procedure. In defibrillation, the recipient has lost consciousness so there is no need for sedation.

Electrical treatment of dysrhythmia includes cardiac pacing. Temporary pacing may be done for very slow heartbeats, or bradycardia, from drug overdose or myocardial infarction. A pacemaker may be placed in situations where the bradycardia is not expected to recover.

Atrial fibrillation can also be treated through a procedure, e.g. pulmonary vein isolation. This is performed by a cardiologist who specializes in electrophysiology and is done percutaneously with catheters. Alternatively, a maze procedure can be performed through cardiothoracic surgery.

### Congestive heart failure

**Congestive heart failure (CHF)**, also called **congestive cardiac failure (CCF)** or just **heart failure**, 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. It is not to be confused with "*cessation of heartbeat*", which is known as asystole, or with cardiac arrest, which is the cessation of normal cardiac function in the face of heart disease. Because not all patients have volume overload at the time of initial or subsequent evaluation, the term "heart failure" is preferred over the older term "congestive heart failure". Congestive heart failure is often undiagnosed due to a lack of a universally agreed definition and difficulties in diagnosis, particularly when the condition is considered "mild".

## Causes

Causes and contributing factors to congestive heart failure include (with specific reference to left (L) or right (R) sides):

- Genetic family history of CHF
- Ischaemic heart disease/Myocardial infarction (coronary artery disease)
- Infection
- Alcohol ingestion
- Heartworms
- Anemia
- Thyrotoxicosis (hyperthyroidism)
- Arrhythmia
- Hypertension (L)
- Coarctation of the aorta (L)
- Aortic stenosis/regurgitation (L)
- Mitral regurgitation (L)
- Pulmonary stenosis/Pulmonary hypertension/Pulmonary embolism all leading to cor pulmonale (R)
- Mitral valve disease (L)

The usual heart irritants can make CHF deadly: arterial plaque, stress, smoking, old age, lack of exercise, overworked heart, and obesity. In genetic family history of CHF, the cause is a weak heart having thinner muscle walls than usual, and often weakened further by one or more of the above heart irritants. Arterial plaque (caused by eating fatty or greasy foods) lines the inside of the arteries that supply the heart and the rest of the body, meaning less blood gets to the heart itself, as well as the heart having to work harder to push blood through the thinner systemic arteries. The result is irregular heart beats causing inefficient blood pumping and a tired heart.

[edit]

## Classification



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

- the side of the heart involved, (left heart failure versus right heart failure)
- whether the abnormality is due to contraction or relaxation of the heart (systolic heart failure vs. diastolic heart failure)
- whether the abnormality is due to low cardiac output or low systemic vascular resistance (low-output heart failure vs. high-output heart failure)

The NYHA functional class is a commonly used way to gauge the progression of CHF in a particular patient. This classification is used to determine how much CHF limits their lifestyle, and does not apply to a particular decompensated episode. Depending on symptoms, patients may move in either direction on the NYHA scale.

- Class I: No symptoms at any level of exertion
- Class II: Symptoms with heavy exertion
- Class III: Symptoms with light exertion
- Class IV: Symptoms with no exertion

Heart failure stages from the ACC/AHA guidelines represent a newer classification that complements the NYHA classification.

- Stage A: At risk for developing heart failure without evidence of cardiac dysfunction
- Stage B: Evidence of cardiac dysfunction without symptoms
- Stage C: Evidence of cardiac dysfunction with symptoms
- Stage D: Symptoms of heart failure despite maximal therapy

An important feature of the staging classification is that patients can only progress in one direction: from Stage A to D. This is meant to reflect the progressive nature of heart failure.

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## Signs and Symptoms

**Left Heart Failure:** Symptoms of decompensated heart failure include dyspnea (shortness of breath) on exertion, orthopnea (dyspnea that increases upon lying down), fatigue and paroxysmal nocturnal dyspnea ("cardiac asthma", shortness of breath that occurs hours or minutes after lying down). Nocturnal cough, Confusion and memory impairment (in advanced stages), and diaphoresis and cool extremities at rest.

Signs of decompensated left heart failure include: Displaced apex beat (usually to left due to cardiomegaly), Pathologic S3 Gallop, S4, Crackles at the lung bases due to pulmonary edema (fluid accumulation in the lungs), Dullness to percussion and

tactile fremitus of lower lung fields. Increased intensity of pulmonic component of 2nd heart sound.

**Right Heart Failure:** Symptoms and Signs include: Peripheral edema (fluid build-up in dependent portions of the body), ascites (fluid in the abdominal cavity), nocturia (due to increased venous return with leg elevation), Jugular venous distention, Hepatomegaly, hepatojugular reflux, and right ventricular heave.

Individuals with heart failure are sensitive to small shifts in their intravascular volume status (the amount of fluid in their circulatory system). Increasing the volume in their circulatory system can cause symptoms and signs of decompensated heart failure, while decreasing the volume in the circulatory system can cause hypotension.

Chest X-rays (CXR) are frequently used to aid in the diagnosis of CHF. Signs of CHF on CXR are<sup>[1]</sup>:

- Vascular redistribution
- Peribronchial cuffing/interstitial edema (bat-shaped)
- Kerley B lines
- Consolidation of lower lung fields
- Cardiomegaly

[edit]

## Treatment

The treatment of CHF focuses on treating the symptoms and signs of CHF and preventing the progression of disease. If there is a reversible cause of the heart failure (e.g. infection, alcohol ingestion, anemia, thyrotoxicosis, arrhythmia, or hypertension), that should be addressed as well. Reversible cause treatments can include exercise, eating healthy foods, reduction in salty foods, and abstinence of smoking and drinking alcohol.

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## Non-pharmacological measures

Patients with CHF are educated to undertake various non-pharmacological measures to improve symptoms and prognosis. Such measures include (Smith et al., 2003):

- Moderate physical activity, when symptoms are mild or moderate; or bed rest when symptoms are severe.

- Weight reduction – through physical activity and dietary modification, as obesity is a risk factor for heart failure and ventricular hypertrophy.
- Sodium restriction – excessive sodium intake may precipitate or exacerbate heart failure, thus a "no added salt" diet (60–100 mmol total daily intake) is recommended for patients with CHF. More severe restrictions may be required in severe CHF.
- Fluid restriction – patients with CHF have a diminished ability to excrete free water load. They are also at an increased risk of hyponatremia due to the combination of decreased sodium intake and diuretic therapy. Generally water intake should be limited to 1.5 L daily or less in patients with hyponatremia, though fluid restriction may be beneficial regardless in symptomatic reduction.

[edit]

## Pharmacological management

It has been noted that there is a significant evidence–practice gap in the treatment of CHF, particularly the underuse of ACE inhibitors and β-blockers. (Jackson et al., 2005) Treatment of CHF aims to relieve symptoms, maintain a euvolemic state (normal fluid level in the circulatory system), and to improve prognosis by delaying progression of heart failure and reducing cardiovascular risk. Drugs used include: diuretic agents, vasodilator agents, positive inotropes, ACE inhibitors, beta blockers, and aldosterone antagonists (e.g. spironolactone).

[edit]

## Angiotensin-modulating agents

ACE inhibitor (ACEI) therapy is recommended for *all* patients with systolic heart failure, irrespective of symptomatic severity or blood pressure. (Krum et al., 2001; NICE, 2003; Hunt et al., 2005) ACE inhibitors improve symptoms, decrease mortality and reduce ventricular hypertrophy. Angiotensin II receptor antagonist therapy (also referred to as AT<sub>1</sub>-antagonists or angiotensin receptor blockers), particularly using candesartan, is an acceptable alternative if the patient is unable to tolerate ACEI therapy. (Granger et al., 2003; Pfeffer et al., 2003)

[edit]

## Diuretics

Diuretic therapy is indicated for the relief of congestive symptoms. Several classes are used, with combinations reserved for severe heart failure (Smith et al., 2003):

- Loop diuretics (e.g. furosemide) – most commonly used class in CHF, usually for moderate CHF.

- Thiazide diuretics (e.g. hydrochlorothiazide) – useful for mild CHF.
- Potassium-sparing diuretics (e.g. amiloride) – used first-line use to correct hypokalaemia.
  - Spirolactone is used as add-on therapy to ACEI plus loop diuretic in severe CHF.
  - Eplerenone is specifically indicated for post-MI reduction of cardiovascular risk.

[edit]

## Beta blockers

Until recently, β-blockers were contraindicated in CHF, owing to their negative inotropic effect and ability to produce bradycardia – effects which worsen heart failure. However, current guidelines recommend β-blocker therapy for patients with systolic heart failure due to left ventricular systolic dysfunction after stabilization with diuretic and ACEI therapy, irrespective of symptomatic severity or blood pressure. (NICE, 2003) As with ACEI therapy, the addition of a β-blocker can decrease mortality and improve left ventricular function. Several β-blockers are specifically indicated for CHF including: bisoprolol, carvedilol, and extended-release metoprolol.

[edit]

## Positive inotropes

Digoxin, once used as first-line therapy, is now reserved for control of ventricular rhythm in patients with atrial fibrillation; or where adequate control is not achieved with ACEI plus loop diuretic. There is no evidence that positive inotropes reduce mortality in CHF.

[edit]

## Alternative vasodilators

The combination of isosorbide dinitrate/hydralazine is the only vasodilator regimen, other than ACE inhibitors or angiotensin II receptor antagonists, with proven survival benefits. This combination appears to be particularly beneficial in CHF patients with an African American background, who respond less effectively to ACEI therapy. (Exner et al., 2001; Taylor et al., 2004)

[edit]

## Devices and surgery

Patients with NYHA class III or IV, left ventricular ejection fraction (LVEF) of 35% or less and a QRS interval of 120 ms or more may benefit from cardiac

resynchronization therapy (CRT; pacing both the left and right ventricles), through implantation of an bi-ventricular pacemaker, or surgical remodelling of the heart. These treatment modalities may make the patient symptomatically better, improving quality of life and in some trials have been proven to reduce mortality.

The COMPANION trial demonstrated that CRT improved survival in individuals with NYHA class III or IV heart failure with a widened QRS complex on EKG. (Bristow et al., 2004) The CARE-HF trial showed that patients receiving CRT and optimal medical therapy benefited from a 36% reduction in all cause mortality, and a reduction in cardiovascular-related hospitalization. (Cleland et al., 2005)

Patients with NYHA class II, III or IV, and LVEF of 35% (without a QRS requirement) may also benefit from an implantable cardioverter-defibrillator (ICD), a device that is proven to reduce all cause mortality by 23% compared to placebo. This mortality benefit was observed in patients who were already optimally-managed on drug therapy. (Bardy et al., 2005)

Another current treatment involves the use of left ventricular assist devices (LVADs). LVADs are battery-operated mechanical pump-type devices that are surgically implanted on the upper part of the abdomen. They take blood from the left ventricle and pump it through the aorta. LVADs are becoming more common and are often used by patients who have to wait for heart transplants.

The final option, if other measures have failed, is cardiac transplant surgery (heart transplant) or implantation of an artificial heart.

### **Rheumatic fever**

**rheumatic fever** , a disease that may develop within 1 to 5 weeks after recovery from a sore (strep) throat or from scarlet fever. It most often occurs in young children and may affect the brain, heart, joints, and skin. It is often sudden. Early symptoms are fever, joint pains, nose bleeds, stomach pain, and vomiting. The major effects of this disease are a form of arthritis in many joints. It also causes heart problems, as chest pain, and, in severe cases, symptoms of heart failure. Another disorder (Sydenham's chorea) may develop and is commonly the only, late sign of rheumatic fever. This may at first appear as an increased awkwardness and a habit of dropping objects. Irregular body movements may worsen, and sometimes the tongue and the face muscles are affected. Other problems may be skin disorders, as nodes beneath the skin or red patches with circular sores, a rise in the number of white blood cells, anemia, and protein in the urine. There is no specific diagnostic test for rheumatic fever. Returns of rheumatic fever are common. Except for heart inflammation, all effects of this disease often go away without any permanent problems. Mild cases may last 3 to 4 weeks. Severe cases with arthritis and heart swelling may last 2 to 3 months. Treatment of this disease is bed rest and keeping the patient inactive. Penicillin is often given, even if there is no sign of

bacterial infection. Steroid drugs or aspirin may be used. Large amounts of fluids are given and joint pains are lessened by putting the patient in a comfortable position. **See also rheumatic heart disease.**<sup>1</sup>

**rheumatic heart disease**, damage to heart muscle and heart valves caused by attacks of rheumatic fever. The heart damage may be found during the disease, or it may be discovered long after the disease has gone away. Heart murmurs result from narrowing or poor working of the valves. This causes changes in the size of the chambers of the heart and the thickness of their walls. Abnormal pulse rate and rhythm, heart block, and congestive heart failure are also common. Deaths are often caused by heart failure or infection in the heart. Long-term rheumatic heart disease may require no treatment except for close watching. If signs of poor heart action occur, heart drugs, fluid-releasing drugs (diuretics), and a low-sodium diet are often given. It may be necessary to correct or replace the valves. Patients with a history of rheumatic fever or signs of rheumatic heart disease may get daily doses of penicillin by mouth or monthly injections to protect against streptococcal infections. The antibiotics are given during childhood and adolescence. Patients with signs of deformed heart valves need preventive doses of antibiotics before surgery and dental work to prevent other infections. **See also aortic stenosis, mitral valve stenosis, rheumatic fever.**

2

## Infective endocarditis

As the valves of the heart do not actually receive any blood supply of their own, which may be surprising given their location, defense mechanisms (such as white blood cells) cannot enter. So if an organism (such as bacteria) establish hold on the valves, the body cannot get rid of them.

Normally, blood flows smoothly through these valves. If they have been damaged (for instance in rheumatic fever) bacteria have a chance to take hold.

## Classification

Traditionally, infective endocarditis has been clinically divided into *acute* and *subacute* (between acute and chronic) endocarditis. This classifies both the tempo of progression and severity of disease. Thus subacute bacterial endocarditis (SBE) is often due to streptococci of low virulence and mild to moderate illness which progresses slowly over weeks and months, while acute bacterial endocarditis (ABE) is a fulminant illness over days to weeks, and is more likely due to *Staphylococcus aureus* which has much greater virulence, or disease-producing capacity.

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<sup>2</sup>Excerpted from *Mosby's Medical Encyclopedia*. Copyright (c) 1994-5, 1996, 1997 The Learning Company Inc. All Rights Reserved



This terminology is now discouraged. The terms *short incubation* (meaning less than about six weeks), and *long incubation* (greater than about six weeks) are preferred despite the lack of advantage in meaning.

Infective endocarditis may also be classified as *culture-positive* or *culture-negative*. Culture-negative endocarditis is due to micro-organisms that require a longer period of time to be identified in the laboratory. Such organisms are said to be *fastidious* because they have demanding growth requirements. Some pathogens responsible for culture-negative endocarditis include *Aspergillus species*, *Brucella species*, *Coxiella burnetii*, *Chlamydia species*, and *HACEK* bacteria. Finally, the distinction between *native-valve endocarditis* and *prosthetic-valve endocarditis* is clinically important. The Russian classification includes "endocarditis in narcotic abusers" in addition to above given classification, as this disease is very common in narcotic drug users who inject with non-sterile injections/syringes.

### **Aetiology and pathogenesis**

As previously mentioned, altered blood flow around the valves is a risk factor in obtaining endocarditis. The valves may be damaged congenitally, from surgery, by auto-immune mechanisms, or simply as a consequence of old age. The damaged part of a heart valve becomes covered with a blood clot, a condition known as non-bacterial thrombotic endocarditis (NBTE).

In a healthy individual, a bacteraemia (where bacteria get into the blood stream through a minor cut or wound) would normally be cleared quickly with no adverse consequences. If a heart valve is damaged and covered with a piece of a blood clot, the valve provides a place for the bacteria to attach themselves and an infection can be established.

The bacteraemia is often caused by minor dental procedures, such as a tooth removal. It is important that a dentist is told of any heart problems before commencing.

Another group of causes result from a high number of bacteria getting into the bloodstream. Colorectal cancer, serious urinary tract infections and IV drug use, can all introduce large numbers of bacteria. With a large number of bacteria, even a normal heart valve may be infected. A more virulent organism (such as *Staphylococcus aureus*) is usually responsible for infecting a normal valve.

Intravenous drug users tend to get their right heart valves infected because the veins that are injected enter the right side of the heart. The injured valve is most commonly affected when there is a pre-existing disease. (In rheumatic heart disease this is the aortic and the mitral valves, on the left side of the heart.)

### **Clinical and pathological features**

- Fever (often spiking)
- Continuous presence of micro-organisms in the bloodstream determined by serial collection of blood cultures
- Vegetations on valves on echocardiography
- Septic emboli, causing circulatory problems (stroke, gangrene of fingers)
- Chronic renal failure
- Osler's nodes (painful subcutaneous lesions in the distal fingers)
- Janeway lesions (painless hemorrhagic cutaneous lesions on the palms and soles)
- Roth spots on the retina
- Conjunctival petechiae
- A new or changing heart murmur, particularly murmurs suggestive of valvular incompetence
- Splinter haemorrhages

### Micro-organisms responsible

Many types of organism can cause infective endocarditis. These are generally isolated by blood culture, where the patient's blood is removed, and any growth is noted and identified.

Alpha-haemolytic streptococci, that are present in the mouth will often be the organism isolated if a dental procedure caused the bacteraemia.

If the bacteraemia was introduced through the skin, such as contamination in surgery, during catheterisation, or in an IV drug user, *Staphylococcus aureus* is common.

A third important cause of endocarditis is Enterococci. These bacteria enter the bloodstream as a consequence of abnormalities in the gastrointestinal or urinary tracts. Enterococci are increasingly recognized as causes of nosocomial or hospital-acquired endocarditis. This contrasts with alpha-haemolytic streptococci and Staphylococcus aureus which are causes of community-acquired endocarditis.

Some organisms, when isolated, give valuable clues to the cause, as they tend to be specific.

- Candida albicans, a yeast, is associated with IV drug users and the immunocompromised.
- Pseudomonas species, which are very resilient organisms that thrive in water, may contaminate street drugs that have been contaminated with drinking water.
- Streptococcus bovis, which is part of the natural flora of the bowel, tends to present when the patient has bowel cancer.
- HACEK organisms are a group of bacteria that live on the dental gums, and are associated with IV drug users who contaminate their needles with saliva.

## Treatment

High dose antibiotics are administered by the intravenous route to maximize diffusion of antibiotic molecules into vegetation(s) from the blood filling the chambers of the heart. This is necessary because neither the heart valves nor the vegetations adherent to them are supplied by blood vessels. Antibiotics are continued for a long time, typically two to six weeks. Surgical removal of the valve is necessary in patients who fail to clear micro-organisms from their blood in response to antibiotic therapy, or in patients who develop cardiac failure resulting from destruction of a valve by infection. A removed valve is usually replaced with an artificial valve which may either be mechanical (metallic) or obtained from an animal such as a pig; the latter are termed bioprosthetic valves. Infective endocarditis is associated with a 25% mortality

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## Mitral stenosis

- **Mitral stenosis** is a narrowing of the orifice of the mitral valve of the heart.

## Overview



Mitral stenosis with marked thickening of the leaflets and left atrial hypertrophy. Superior view. Autopsy preparation.

In normal cardiac physiology, the mitral valve opens during left ventricular diastole, to allow blood to flow from the left atrium to the left ventricle. The reason the blood flows in the proper direction is that, during this phase of the cardiac cycle, the pressure in the left ventricle is less than the pressure in the left atrium, and the blood flows down the pressure gradient. In the case of mitral stenosis, the valve does not open completely, so the left atrium has to have a higher pressure than normal to have the blood overcome the increased gradient caused by the mitral valve stenosis.

[Etiology

Most cases of mitral stenosis are due to disease in the heart secondary to rheumatic fever and the consequent rheumatic heart disease. Less common causes of mitral stenosis are calcification of the mitral valve leaflets, and as a form of congenital heart disease.

## **Pathophysiology**

The normal area of the mitral valve orifice is about 4 to 6 cm<sup>2</sup>. Under normal conditions, a normal mitral valve will not impede the flow of blood from the left atrium to the left ventricle during (ventricular) diastole, and the pressures in the left atrium and the left ventricle during diastole will be equal. The result is that the left ventricle gets filled with blood during early diastole, with only a small portion of extra blood contributed by contraction of the left atrium (the "atrial kick") during late ventricular diastole.

When the mitral valve area goes below 2 cm<sup>2</sup>, the valve causes an impediment to the flow of blood into the left ventricle, creating a pressure gradient across the mitral valve. This gradient may be increased by increases in the heart rate or cardiac output. As the gradient across the mitral valve increases, the amount of time necessary to fill the left ventricle with blood increases. Eventually, the left ventricle requires the atrial kick to fill with blood. As the heart rate increases, the amount of time that the ventricle is in diastole and can fill up with blood (called the diastolic filling period) decreases. When the heart rate goes above a certain point, the diastolic filling period is insufficient to fill the ventricle with blood and pressure builds up in the left atrium, leading to pulmonary congestion.

Since the normal left ventricular diastolic pressures is about 5 mmHg, a pressure gradient across the mitral valve of 20 mmHg due to severe mitral stenosis will cause a left atrial pressure of about 25 mmHg. This left atrial pressure is transmitted to the pulmonary vasculature. Pulmonary capillary pressures in this level cause an imbalance between the hydrostatic pressure and the oncotic pressure, leading to extravasation of fluid from the vascular tree and pooling of fluid in the lungs (pulmonary congestion).

Increases in the heart rate will allow less time for the left ventricle to fill, also causing an increase in left atrial pressure and pulmonary congestion.

When the mitral valve area goes less than 1 cm<sup>2</sup>, there will be an increase in the left atrial pressures (required to push blood through the stenotic valve). This increase in left atrial pressures will impede venous return to the left atrium from the lungs, causing pulmonary congestion (congestive heart failure).

The constant pressure overload of the left atrium will cause the left atrium to increase in size. As the left atrium increases in size, it becomes more prone to develop atrial fibrillation. When atrial fibrillation develops, the atrial kick is lost (since it is due to the normal atrial contraction).

In individuals with severe mitral stenosis, the left ventricular filling is dependent on the atrial kick. The loss of the atrial kick due to atrial fibrillation can cause a precipitous decrease in cardiac output and sudden congestive heart failure.

## Diagnosis

In most cases, the diagnosis of mitral stenosis is most easily made by echocardiography, which shows decreased

Severity of mitral stenosis		
Degree of mitral stenosis	Mean gradient	Mitral valve area
Mild mitral stenosis	<5	>1.5 cm <sup>2</sup>
Moderate mitral stenosis	5 - 10	1.0 - 1.5 cm <sup>2</sup>
Severe mitral stenosis	> 10	< 1.0 cm <sup>2</sup>

opening of the mitral valve leaflets, and blunted flow of blood in early diastole.

The trans-mitral gradient as measured by doppler echocardiography is the gold standard in the evaluation of the severity of mitral stenosis.

Another method of measuring the severity of mitral stenosis is the simultaneous left heart catheterization and right heart catheterization. The right heart catheterization (commonly known as Swan-Ganz catheterization) gives the physician the mean pulmonary capillary wedge pressure, which is a reflection of the left atrial pressure. The left heart catheterization, on the other hand, gives the pressure in the left ventricle. By simultaneously taking these pressures, it is possible to determine the gradient between the left atrium and right atrium during ventricular diastole, which is a marker for the severity of mitral stenosis. This method of evaluating mitral stenosis tend to over-estimate the degree of mitral stenosis, however, because of the time lag in the pressure tracings seen on the right heart catheterization and the slow Y descent seen on the wedge tracings. If a trans-septal puncture is made during right heart catheterization, however, the pressure gradient can accurately quantify the severity of mitral stenosis.

## Physical examination

Upon auscultation of an individual with mitral stenosis, an opening snap is heard after the A<sub>2</sub> component of the second heart sound (S<sub>2</sub>). The opening snap correlates to the opening of the mitral valve. The mitral valve opens when the pressure in the left atrium is greater than the pressure in the left ventricle. This happens in ventricular diastole (after closure of the aortic valve), when the pressure in the ventricle precipitously drops. In individuals with mitral stenosis, the pressure in the left atrium correlates with the severity of the mitral stenosis. As the severity of the mitral stenosis increases, the pressure in the left atrium increases, and the mitral valve opens earlier in ventricular diastole. This means that the more severe the mitral stenosis, the shorter the gap between A<sub>2</sub> and the opening snap.

## Natural history

The natural history of mitral stenosis secondary to rheumatic fever (the most common cause) is an asymptomatic latent phase following the initial episode of rheumatic fever. This latent period lasts an average of  $16.3 \pm 5.2$  years. Once symptoms of mitral stenosis begin to develop, progression to severe disability takes  $9.2 \pm 4.3$  years.

In individuals who were offered mitral valve surgery but refused, *survival* with medical therapy alone was  $44 \pm 6\%$  at 5 years, and  $32 \pm 8\%$  at 10 years after they were offered correction.

## Treatment

The treatment options for mitral stenosis include medical management, surgical replacement of the valve, and percutaneous balloon valvuloplasty.

Mitral stenosis typically progresses slowly (over decades) from the initial signs of mitral stenosis to NYHA functional class II symptoms to the development of atrial fibrillation to the development of NYHA functional class III or IV symptoms. Once an individual develops NYHA class III or IV symptoms, the progression of the disease accelerates and the patient's condition deteriorates.

The indication for invasive treatment with either a mitral valve replacement or valvuloplasty is NYHA functional class III or IV symptoms.

To determine which patients would benefit from percutaneous balloon mitral valvuloplasty, a scoring system has been developed.<sup>2</sup> Scoring is based on 4 echocardiographic criteria: leaflet mobility, leaflet thickening, subvalvar thickening, and calcification. Individuals with a score of  $\geq 8$  tended to have suboptimal results.<sup>3</sup> Superb results with valvotomy are seen in individuals with a crisp opening snap, score  $< 8$ , and no calcium in the commissures.

## Mitral regurgitation

**Mitral regurgitation (MR)**, also known as **mitral insufficiency**, is the abnormal leaking of blood through the mitral valve, from the left ventricle into the left atrium of the heart.

## Etiology

The mitral valve is composed of the valve leaflets, the mitral valve annulus (which forms a ring around the valve leaflets), the papillary muscles (which tether the valve leaflets to the left ventricle, preventing them from prolapsing into the left



atrium), and the chordae tendineae (which connect the valve leaflets to the papillary muscles). A dysfunction of any of these portions of the mitral valve apparatus can cause mitral regurgitation.

**Primary mitral regurgitation** is due to any disease process that affects the mitral valve apparatus itself. The causes of primary mitral regurgitation include:

- Myxomatous degeneration of the mitral valve
- Ischemic heart disease / Coronary artery disease
- Infective endocarditis
- Collagen vascular diseases (ie: SLE, Marfan's syndrome)
- Rheumatic heart disease
- Trauma
- Balloon valvulotomy of the mitral valve
- Certain forms of medication (e.g. fenfluramine)

The most common cause of primary mitral regurgitation in the United States (causing about 50% of primary mitral regurgitation) is myxomatous degeneration of the valve. Myxomatous degeneration of the mitral valve is more common in males, and is more common in advancing age. It is due to a genetic abnormality that results in a defect in the collagen that makes up the mitral valve. This causes a stretching out of the leaflets of the valve and the chordae tendineae. The elongation of the valve leaflets and the chordae tendineae prevent the valve leaflets from fully coapting when the valve is closed, causing the valve leaflets to prolapse into the left atrium, thereby causing mitral regurgitation.

Ischemic heart disease causes mitral regurgitation by the combination of ischemic dysfunction of the papillary muscles, and the dilatation of the left ventricle that is present in ischemic heart disease, with the subsequent displacement of the papillary muscles and the dilatation of the mitral valve annulus.

**Secondary mitral regurgitation** is due to the dilatation of the left ventricle, causing stretching of the mitral valve annulus and displacement of the papillary muscles. This dilatation of the left ventricle can be due to any cause of dilated cardiomyopathy, including aortic insufficiency and nonischemic dilated cardiomyopathy.

### **Pathophysiology Acute phase**

Acute mitral regurgitation (as may occur due to the sudden rupture of a chordae tendineae or papillary muscle) causes a sudden volume overload of both the left atrium and the left ventricle. The left ventricle develops volume overload because with every contraction it now has to pump out not only the volume of blood that goes into the aorta (the forward cardiac output or forward stroke volume), but also the blood that regurgitates into the left atrium (the regurgitant volume). The

combination of the forward stroke volume and the regurgitant volume is known as the total stroke volume of the left ventricle.

Comparison of acute and chronic mitral regurgitation		
	Acute mitral regurgitation	Chronic mitral regurgitation
<u>Electrocardiogram</u>	Normal	P mitrale, <u>atrial fibrillation</u> , <u>left ventricular hypertrophy</u>
Heart size	Normal	Cardiomegaly, left atrial enlargement
<u>Systolic murmur</u>	Heard at the base, radiates to the neck, spine, or top of head	Heard at the apex, radiates to the axilla
Apical thrill	May be absent	Present
<u>Jugular venous distension</u>	Present	Absent

The pathophysiology of mitral regurgitation can be broken into three phases of the disease process: the acute phase, the chronic compensated phase, and the chronic decompensated phase.

In the acute setting, the stroke volume of the left ventricle is increased (increased ejection fraction), but the forward cardiac output is decreased. The mechanism by which the total stroke volume is increased is known as the Frank-Starling mechanism.

The regurgitant volume causes a volume overload and a pressure overload of the left atrium. The increased pressures in the left atrium inhibit drainage of blood from the lungs via the pulmonary veins. This causes pulmonary congestion.

### **Chronic compensated phase**

If the mitral regurgitation develops slowly over months to years or if the acute phase can be managed with medical therapy, the individual will enter the chronic compensated phase of the disease. In this phase, the left ventricle develops eccentric hypertrophy in order to better manage the larger than normal stroke volume. The eccentric hypertrophy and the increased diastolic volume combine to increase the stroke volume (to levels well above normal) so that the forward stroke volume (forward cardiac output) approaches the normal levels.

In the left atrium, the volume overload causes enlargement of the chamber of the left atrium, allowing the filling pressure in the left atrium to decrease. This improves the drainage from the pulmonary veins, and signs and symptoms of pulmonary congestion will decrease.

These changes in the left ventricle and left atrium improve the low forward cardiac output state and the pulmonary congestion that occur in the acute phase of the disease. Individuals in the chronic compensated phase may be asymptomatic and have normal exercise tolerances.

### **Chronic decompensated phase**

An individual may be in the compensated phase of mitral regurgitation for years, but will eventually develop left ventricular dysfunction, the hallmark for the chronic decompensated phase of mitral regurgitation. It is currently unclear what causes an individual to enter the decompensated phase of this disease. However, the decompensated phase is characterized by calcium overload within the cardiac myocytes.

In this phase, the ventricular myocardium is no longer able to contract adequately to compensate for the volume overload of mitral regurgitation, and the stroke volume of the left ventricle will decrease. The decreased stroke volume causes a decreased forward cardiac output and an increase in the end-systolic volume. The increased end-systolic volume translates to increased filling pressures of the ventricular and increased pulmonary venous congestion. The individual may again have symptoms of congestive heart failure.

The left ventricle begins to dilate during this phase. This causes a dilatation of the mitral valve annulus, which may worsen the degree of mitral regurgitation. The dilated left ventricle causes an increase in the wall stress of the cardiac chamber as well.

While the ejection fraction is less in the chronic decompensated phase than in the acute phase or the chronic compensated phase of mitral regurgitation, it may still be in the normal range (ie: > 50 percent), and may not decrease until late in the disease course. A decreased ejection fraction in an individual with mitral regurgitation and no other cardiac abnormality should alert the physician that the disease may be in its decompensated phase.

### **[Symptoms]**

The symptoms associated with mitral regurgitation are dependent on which phase of the disease process the individual is in. Individuals with acute mitral regurgitation will have the signs and symptoms of decompensated congestive heart failure (ie: shortness of breath, pulmonary edema, orthopnea, paroxysmal nocturnal dyspnea), as well as symptoms suggestive of a low cardiac output state (ie:

decreased exercise tolerance). Cardiovascular collapse with shock (cardiogenic shock) may be seen in individuals with acute mitral regurgitation due to papillary muscle rupture or rupture of a chordae tendineae.

Individuals with chronic compensated mitral regurgitation may be asymptomatic, with a normal exercise tolerance and no evidence of heart failure. These individuals may be sensitive to small shifts in their intravascular volume status, and are prone to develop volume overload (congestive heart failure).

### **Diagnostic studies**

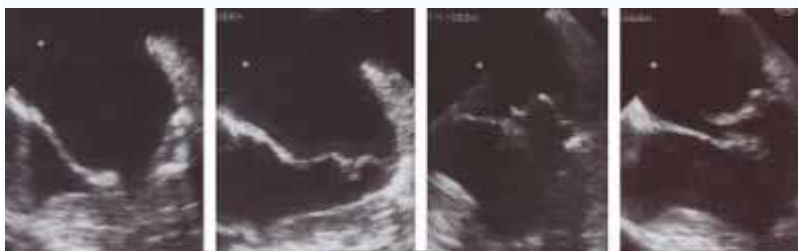
There are many diagnostic tests that have abnormal results in the presence of mitral regurgitation. These tests suggest the diagnosis of mitral regurgitation and may indicate to the physician that further testing is warranted. For instance, the electrocardiogram (ECG) in long standing mitral regurgitation may show evidence of left atrial enlargement and left ventricular hypertrophy. Atrial fibrillation may also be noted on the ECG in individuals with chronic mitral regurgitation. The ECG may not show any of these finding in the setting of acute mitral regurgitation.

The quantification of mitral regurgitation usually employs imaging studies such as echocardiography or magnetic resonance angiography of the heart.

### **Chest x-ray**

The chest x-ray in individuals with chronic mitral regurgitation is characterized by enlargement of the left atrium and the left ventricle. The pulmonary vascular markings are typically normal, since pulmonary venous pressures are usually not significantly elevated.

### **Echocardiography**



transesophageal echocardiogram of mitral valve prolapse

The echocardiogram is commonly used to confirm the diagnosis of mitral regurgitation. Color doppler flow on the transthoracic echocardiogram (TTE) will reveal a jet of blood flowing from the left ventricle into the left atrium during ventricular systole.

Because of the inability in getting accurate images of the left atrium and the pulmonary veins on the transthoracic echocardiogram, a transesophageal echocardiogram may be necessary to determine the severity of the mitral regurgitation in some cases.

Factors that suggest severe mitral regurgitation on echocardiography include systolic reversal of flow in the pulmonary veins and filling of the entire left atrial cavity by the regurgitant jet of MR.

**Quantification of mitral regurgitation**

Determination of the degree of mitral regurgitation		
Degree of mitral regurgitation	Regurgitant fraction	Regurgitant Orifice area
Mild mitral regurgitation	< 20 percent	
Moderate mitral regurgitation	20 - 40 percent	
Moderate to severe mitral regurgitation	40 - 60 percent	
Severe mitral regurgitation	> 60 percent	> 0.3 cm <sup>2</sup>

The degree of severity of mitral regurgitation can be quantified by the percentage of the left ventricular stroke volume that regurgitates into the left atrium (the regurgitant fraction).

Methods that have been used to assess the regurgitant fraction in mitral regurgitation include echocardiography, cardiac catheterization, fast CT scan, and cardiac MRI.

The echocardiographic technique to measure the regurgitant fraction is to determine the forward flow through the mitral valve (from the left atrium to the left ventricle) during ventricular diastole, and comparing it with the flow out of the left ventricle through the aortic valve in ventricular systole. This method assumes that the aortic valve does not suffer from aortic insufficiency. The regurgitant fraction would be described as:

$$\frac{\text{forward flow through the mitral valve} - \text{flow through the aortic valve}}{\text{forward flow through the mitral valve}}$$

Another way to quantify the degree of mitral regurgitation is to determine the area of the regurgitant flow at the level of the valve. This is known as the regurgitant orifice area, and correlates with the size of the defect in the mitral valve. One particular echocardiographic technique used to measure the orifice area is measurement of the proximal isovelocity surface area (PISA). The flaw of using

PISA to determine the mitral valve regurgitant orifice area is that it measures the flow at one moment in time in the cardiac cycle, which may not reflect the average performance of the regurgitant jet.

## Treatment

The treatment of mitral regurgitation depends on the acuteness of the disease and whether there are associated signs of hemodynamic compromise.

In acute mitral regurgitation secondary to a mechanical defect in the heart (ie: rupture of a papillary muscle or chordae tendineae), the treatment of choice is urgent mitral valve replacement. If the patient is hypotensive prior to the surgical procedure, an intra-aortic balloon pump may be placed in order to improve perfusion of the organs and to decrease the degree of mitral regurgitation.

If the individual with acute mitral regurgitation is normotensive, vasodilators may be of use to decrease the afterload seen by the left ventricle and thereby decrease the regurgitant fraction. The vasodilator most commonly used is nitroprusside.

Individuals with chronic mitral regurgitation can be treated with vasodilators as well. In the chronic state, the most commonly used agents are ACE inhibitors and hydralazine. Studies have shown that the use of ACE inhibitors and hydralazine can delay surgical treatment of mitral regurgitation<sup>1,2</sup>. The current guidelines for treatment of mitral regurgitation limit the use of vasodilators to individuals with hypertension, however.

There are two surgical options for the treatment of mitral regurgitation: mitral valve replacement and mitral valve repair.

## Indication for surgery

Indications for surgery for chronic mitral regurgitation include signs of left ventricular dysfunction. These include an ejection fraction of less than 60 percent and a left ventricular end systolic dimension (LVESD) of greater than 45 mm.

Indications for surgery for chronic mitral regurgitation <sup>3</sup>		
Symptoms	LV EF	LVESD
<u>NYHA II - IV</u>	> 60 percent	< 45 mm
Asymptomatic or symptomatic	50 - 60 percent	≥ 45 mm
Asymptomatic or symptomatic	< 50 percent or ≥ 45 mm	
<u>Pulmonary artery</u> systolic pressure ≥ 50 <u>mmHg</u>		



## Aortic valve stenosis

**Aortic valve stenosis (AS)** is a heart condition caused by the incomplete opening of the aortic valve.

The aortic valve controls the direction of blood flow from the left ventricle to the aorta. When in good working order, the aortic valve does not impede the flow of blood between these two spaces. Under some circumstances, the aortic valve becomes narrower than normal, impeding the flow of blood. This is known as aortic valve stenosis, or aortic stenosis, often abbreviated as **AS**.

## Pathophysiology



Severe aortic stenosis due to rheumatic heart disease. Autopsy specimen.

Simultaneous left ventricular and aortic pressure tracings demonstrate a pressure gradient between the left ventricle and aorta, suggesting aortic stenosis. The left ventricle generates higher pressures than what is transmitted to the aorta. The pressure gradient, caused by aortic stenosis, is represented by the green shaded area. (AO = ascending aorta; LV = left ventricle; ECG = electrocardiogram.)

When the aortic valve becomes stenotic, it causes a pressure gradient between the left ventricle (LV) and the aorta. The more constricted the valve, the higher the gradient between the LV and the aorta. For instance, with a mild AS, the gradient may be 20 mmHg. This means that, at peak systole, while the LV may generate a pressure of 140 mmHg, the pressure that is transmitted to the aorta will only be 120 mmHg. So, while a blood pressure cuff may measure a normal systolic blood pressure, the actual pressure generated by the LV would be considerably higher.

In individuals with AS, the left ventricle (LV) has to generate an increased pressure in order to overcome the increased afterload caused by the stenotic aortic valve and eject blood out of the LV. The more severe the aortic stenosis, the higher the gradient is between the left ventricular systolic pressures and the aortic systolic pressures. Due to the increased pressures generated by the left ventricle, the

myocardium (muscle) of the LV undergoes hypertrophy (increase in muscle mass). This is seen as thickening of the walls of the LV. The type of hypertrophy most commonly seen in AS is concentric hypertrophy, meaning that all the walls of the LV are (approximately) equally thickened.

## **Etiology**

Causes of aortic stenosis include acute rheumatic fever, bicuspid aortic valve and congenital anomalies. As individuals age, calcification of the aortic valves may occur and result in stenosis.

## **Physical examination**

It is most often diagnosed when it is asymptomatic. It is found on routine examination of the heart. A fairly loud systolic, crescendo-decrescendo murmur is heard loudest at the upper right sternal border, and radiates to the carotid arteries. The murmur increases with squatting, decreases with standing and isometric muscular contraction, which helps distinguish it from hypertrophic obstructive cardiomyopathy (HOCM). Respiration has no effect on the loudness of the murmur. The more severe the degree of the stenosis, the later the peak occurs in the crescendo-decrescendo of the murmur. Due to increases in left ventricular pressure from the stenotic aortic valve, over time the ventricle may hypertrophy, resulting in a diastolic dysfunction. As a result, one may hear a 4th heart sound due to the stiff ventricle. With continued increases in ventricular pressure, dilatation of the ventricle will occur, and a 3rd heart sound may be manifest.

## **Symptoms and signs of aortic stenosis**

When symptomatic, aortic stenosis can cause syncope, angina and congestive heart failure. More symptoms indicate a worse prognosis. Treatment requires replacement of the diseased valve with either a porcine aortic valve or a cadaveric aortic valve, or an prosthetic aortic valve.

## **Congestive heart failure**

Congestive heart failure (CHF) is a grave prognosis in patients with AS. Patients with CHF that is attributed to AS have a 2 year mortality rate of 50%, if the aortic valve is not replaced.

CHF in the setting of AS is due to a combination of systolic dysfunction (a decrease in the ejection fraction) and diastolic dysfunction (elevated filling pressure of the LV).

## **Syncope**

Syncope in the setting of heart failure increases the risk of death. In patients with syncope, the 3 year mortality rate is 50%, if the aortic valve is not replaced.

While it is unclear why aortic stenosis would cause syncope, the most popular theory is that severe AS produces a nearly fixed cardiac output. When the patient exercises, their peripheral vascular resistance will decrease as the blood vessels of the skeletal muscles dilate to allow the muscles to receive more blood to allow them to do more work. This decrease in peripheral vascular resistance is normally compensated for by an increase in the cardiac output. Since patients with severe AS cannot increase their cardiac output, the blood pressure falls and the patient will syncopize due to decreased blood perfusion to the brain.

A second theory as to why syncope may occur in AS is that during exercise, the high pressures generated in the hypertrophied LV causes a vasodepressor response, which causes a secondary peripheral vasodilatation that will then cause decreased perfusion to the brain.

## **Angina**

Angina in the setting of heart failure also increases the risk of death. In patients with angina, the 5 year mortality rate is 50%, if the aortic valve is not replaced.

Angina in the setting of AS is secondary to the left ventricular hypertrophy (LVH) that is caused by the constant production of increased pressure required to overcome the pressure gradient caused by the AS. While the myocardium of the LV gets thicker, the arteries that supply the muscle does not get significantly longer or bigger, so the muscle may become ischemic. The ischemia may first be evident during exercise, when the muscle requires increased blood supply to compensate for the increased workload. The individual may complain of exertional angina. At this stage, a stress test with imaging may be suggestive of ischemia.

Eventually, however, the muscle will require more blood supply at rest than can be supplied by the coronary artery branches. At this point there may be signs of *ventricular strain pattern* on the EKG, suggesting subendocardial ischemia. The subendocardium is the region that becomes ischemic because it is the most distant from the epicardial coronary arteries.

## **Associated symptoms**

In Heyde's syndrome, aortic stenosis is associated with angiodysplasia of the colon. Recent research has shown that the stenosis causes a form of von Willebrand disease by breaking down its associated coagulation factor (factor VIII-associated antigen, also called von Willebrand factor), due to increased turbulence around the stenosed valve.

## Aortic insufficiency

### Etiology

About half of the cases of aortic insufficiency are due to the aortic root dilatation (*annuloaortic ectasia*), which is idiopathic in over 80% of cases, but otherwise occurs with aging and hypertension, Marfan syndrome, aortic dissection, and syphilis. In about 15% the cause is innate bicuspidal aortic valve, while another 15% cases are due to retraction of the cusps as part of postinflammatory processes of endocarditis in rheumatic fever and various collagen vascular diseases.

[edit]

### Physiology

In individuals with a normally functioning aortic valve, the valve is only open when the pressure in the left ventricle is higher than the pressure in the aorta. This allows the blood to be ejected from the left ventricle into the aorta during ventricular systole. After ventricular systole, the pressure in the ventricle decreases, as the ventricle relaxes and gets ready to fill up with blood from the left atrium. This relaxation of the left ventricle (early ventricular diastole) causes a fall in the pressure in the left ventricle. When the pressure in the left ventricle falls below the pressure in the aorta, the aortic valve will close, preventing blood from going from the aorta back into the left ventricle. The amount of blood that is ejected by the heart is known as the **stroke volume** or **stroke work**. Under normal conditions, the entire stroke volume delivers oxygenated blood to the body.

### Hemodynamics

The hemodynamic sequelae of AI are dependent on the rate of onset of AI. Acute AI and chronic AI will have different hemodynamics and individuals will have different signs and symptoms.

### Acute aortic insufficiency

In acute AI, as may be seen with acute perforation of the aortic valve due to endocarditis, there will be a sudden increase in the volume of blood in the left ventricle. The ventricle, unable to deal with the sudden change in volume, decompensates. The filling pressure of the left ventricle will increase. This causes pressure in the left atrium to rise, and the individual will develop congestive heart failure.

Severe acute aortic insufficiency is considered a medical emergency. There is a high mortality rate if the individual does not undergo immediate surgery for aortic

valve replacement. If the acute AI is due to aortic valve endocarditis, there is a risk that the new valve may become seeded with bacteria. However, this risk is small.<sup>1</sup>

Acute AI may be difficult to diagnose clinically, since the left ventricle had not yet developed the eccentric hypertrophy and dilatation that allow an increased stroke volume and bounding peripheral pulses that are common in chronic AI. On auscultation, there may be a short diastolic murmur and a soft S<sub>1</sub>. S<sub>1</sub> is soft because the elevated filling pressures close the mitral valve in diastole (rather than the mitral valve being closed at the beginning of systole).

### **Chronic aortic insufficiency**

If the individual survives the initial hemodynamic derailment that acute AI presents as, the left ventricle adapts by eccentric hypertrophy and dilatation of the left ventricle, and the volume overload is compensated for. The left ventricular filling pressures will revert to normal and the individual will no longer have overt heart failure.

In this compensated phase, the individual may be totally asymptomatic and may have normal exercise tolerance.

Eventually (typically after a latency period) the left ventricle will become decompensated, and filling pressures will increase. While most individuals would complain of symptoms of congestive heart failure to their physicians, some enter this decompensated phase asymptotically. Proper treatment for AI involves aortic valve replacement prior to this decompensation phase.

### **Physical examination**

The physical examination of an individual with aortic insufficiency involves auscultation of the heart to listen for the murmur of aortic insufficiency and related heart sounds. The murmur of chronic aortic insufficiency is a holodiastolic (lasts all of diastole) decrescendo murmur (starts off loud and becomes soft). The murmur of chronic aortic insufficiency has the following characteristics:

- Systolic ejection click
- Ejection murmur
- S<sub>3</sub> present
- Holodiastolic decrescendo murmur - best heard with patient sitting and leaning forward (If radiation to the right parasternal region, consider ascending aortic aneurysm)
- Austin flint murmur (an apical diastolic rumble due to mitral regurgitation)

Physical signs of aortic insufficiency are related to the high pulse pressure and the rapid decrease in blood pressure during diastole due to the AI:

- Lighthouse sign (blanching & flushing of forehead)
- de Musset's sign (head nodding in time with the heart beat)
- Ladolfi's sign (alternating constriction & dilatation of pupil)
- Becker's sign (pulsations of retinal vessels)
- Müller's sign (pulsations of uvula)
- Corrigan's pulse (rapid upstroke and collapse of the carotid artery pulse)
- (Watson's) Water-hammer pulse
- Quincke's sign (pulsation of the capillary bed in the nail)
- Mayen's sign (diastolic drop of BP > 15 mm Hg with arm raised)
- Rosenbach's sign (pulsatile liver)
- Gerhardt's sign (enlarged spleen)
- Duroziez's sign (systolic and diastolic murmurs heard over the femoral artery when it is gradually compressed)
- Hill's sign ( $A \geq 20$  mmHg difference in popliteal and brachial systolic cuff pressures, seen in chronic severe AI)
- Traube's sign (a double sound heard over the femoral artery when it is compressed distally)
- Lincoln sign (pulsatile popliteal)
- Sherman sign (dorsalis pedis pulse is quickly located & unexpectedly prominent in age > 75 yr)

#### [edit] Diagnostic evaluation

The most common test used for the evaluation of the severity of aortic insufficiency is the echocardiogram, which can provide two-dimensional views of the regurgitant jet, and allow measurement of the velocity and volume of the jet.

The echocardiographic findings in severe aortic regurgitation include:

- An AI color jet dimension > 60 percent of the left ventricular outflow tract (LVOT) diameter (may not be true if the jet is eccentric)
- The pressure half-time of the regurgitant jet is < 250 msec
- Early termination of the mitral inflow (due to increase in LV pressure due to the AI.)
- Early diastolic flow reversal in the descending aorta.
- Regurgitant volume > 60 ml
- Regurgitant fraction > 55 percent

#### Prognosis

The risk of death in individuals with aortic insufficiency, dilated ventricle, normal ejection fraction who are asymptomatic is about 0.2 percent per year. Risk increases if the ejection fraction decreases or if the individual develops symptoms.

#### Treatment



Indications for surgery for chronic severe aortic insufficiency <sup>2</sup>		
Symptoms	Ejection fraction	Other information
<u>NYHA class III - IV</u>	$\geq 50 \%$	
NYHA class II	$\geq 50 \%$	Progression of symptoms or worsening parameters on echocardiography
<u>CHA class <math>\geq</math> II angina</u>	$\geq 50 \%$	
Regardless of symptoms	25 - 49 %	
Cardiac surgery for other cause (ie: <u>CAD</u> , other valvular disease, ascending aortic aneurysm)		

Aortic insufficiency can be treated either medically or surgically, depending on the acuteness of presentation, the symptoms and signs associated with the disease process, and the degree of left ventricular dysfunction.

Surgical treatment is typically warranted prior to the ejection fraction falling below 55% or the left ventricular end-systolic dimension falling below 55mm, regardless of symptoms. If either of these thresholds is passed, the prognosis worsens.

### Medical treatment

Medical therapy of chronic aortic insufficiency involves the use of vasodilators. Small trials have shown a short term benefit in the use of ACE inhibitors, nifedipine, and hydralazine in improving left ventricular wall stress, ejection fraction, and mass. The use of these vasodilators is only indicated in individuals who suffer from hypertension in addition to AI. The goal in using the use of these pharmacologic agents is to decrease the afterload so that the left ventricle is spared somewhat. The regurgitant fraction may not change significantly, since the gradient between the aortic and left ventricular pressures is usually fairly low at the initiation of treatment.

### Surgical treatment

The surgical treatment of choice at this time is an aortic valve replacement. This is currently an open-heart procedure, requiring the individual to be placed on cardiopulmonary bypass.

In the case of severe acute aortic insufficiency, all individuals should undergo surgery if there are no absolute contraindications for surgery. Individuals with bacteremia with aortic valve endocarditis should not wait for treatment with

antibiotics to take effect, given the high mortality associated with the acute AI. Instead, replacement with an aortic valve homograft should be performed if feasible.

In the future, it is believed that a percutaneous approach to aortic valve replacement will be feasible.