The Crux

BIMONTHLY FORUM FOR THE LABORATORIANS

CONTENTS

Editorial

A **myocardial infarction (MI)**, commonly known as a **heart attack** occurs when blood flow decreases or stops to the coronary artery of the heart, causing damage to the heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck or jaw. Often it occurs in the center or left side of the chest and lasts for more than a few minutes. The discomfort may occasionally feel like heartburn. Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat or feeling tired. About 30% of people have atypical symptoms. Women more often present without chest pain and instead have neck pain, arm pain or feel tired. Among those over 75 years old, about 5% have had an MI with little or no history of symptoms. An MI may cause heart failure, an irregular heartbeat, cardiogenic shock or cardiac arrest.

Most MIs occur due to coronary artery disease. Risk factors include high blood pressure, smoking, diabetes, lack of exercise, obesity, high blood cholesterol, poor diet and excessive alcohol intake. The complete blockage of a coronary artery caused by a rupture of an atherosclerotic plaque is usually the underlying mechanism of an MI. MIs are less commonly caused by coronary artery spasms, which may be due to cocaine, significant emotional stress (commonly known as Takotsubo syndrome or broken heart syndrome) and extreme cold, among others. A number of tests are useful to help with diagnosis, including electrocardiograms (ECGs), blood tests and coronary angiography. An ECG, which is a recording of the heart's electrical activity, may confirm an **ST elevation MI** (STEMI), if ST elevation is present. Commonly used blood tests include troponin and less often creatine kinase MB. The "**DISEASE DIAGNOSIS**" segment succinctly highlights all aspects as related to MI.

"**INTERPRETATION**" talks about a very important marker related to Heart Failure – BNP. All related information is discretely given.

While "**TROUBLE SHOOTING**" portion removes your doubts about at what stage which cardiac marker to request for. In medical parlance it is called Triaging.

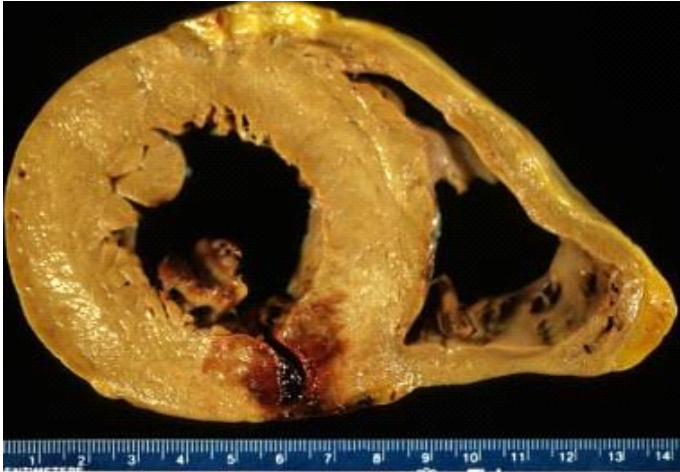Well, that's not all, take a peep inside!

DISEASE DIAGNOSIS
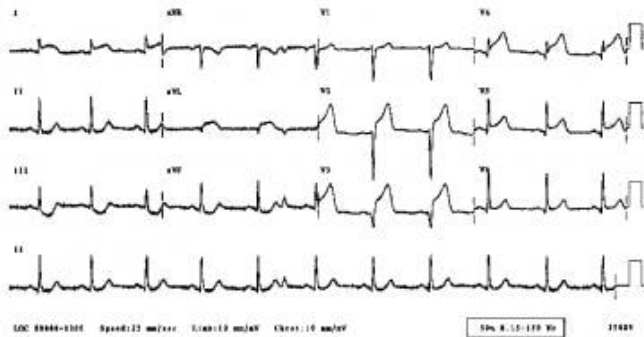
MYOCARDIAL INFARCTION

Practice Essentials

Myocardial infarction (MI) (ie, heart attack) is the irreversible necrosis of heart muscle secondary to prolonged ischemia.


Acute myocardial infarction, reperfusion type. In this case, the infarct is diffusely hemorrhagic. There is a rupture track through the center of this posterior left ventricular transmural infarct. The mechanism of death was hemopericardium.
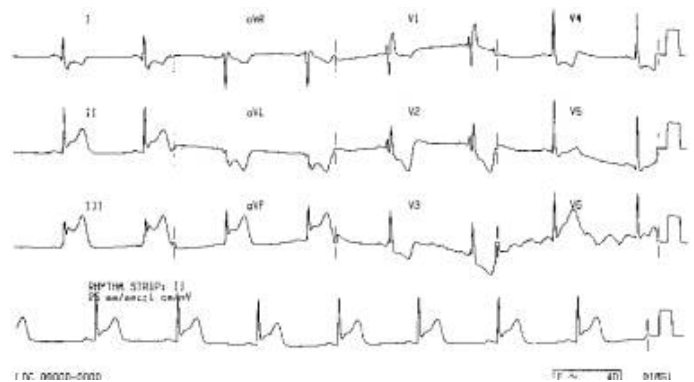

Acute anterior myocardial infarction.

Background

Myocardial infarction, commonly known as a heart attack, is the irreversible necrosis of heart muscle secondary to prolonged ischemia. This usually results from an imbalance in oxygen supply and demand, which is most often caused by plaque rupture with thrombus formation in a coronary vessel, resulting in an acute reduction of blood supply to a portion of the myocardium. (See Etiology.) The electrocardiographic results of an acute myocardial infarction are seen below.
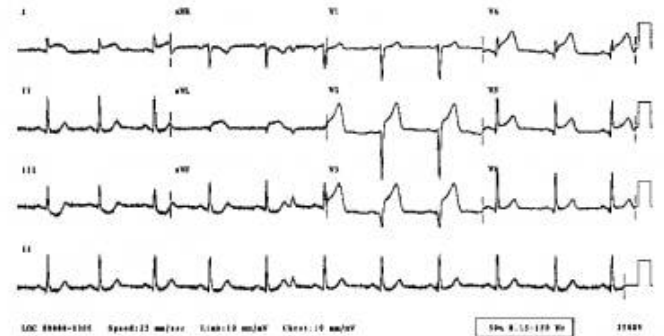
Acute anterior myocardial infarction.

Acute inferior myocardial infarction.

Although the clinical presentation of a patient is a key component in the overall evaluation of the patient with myocardial infarction, many events are either "silent" or are clinically unrecognized, evidencing that patients, families, and health care providers often do not recognize symptoms of a myocardial infarction. The appearance of cardiac markers in the circulation generally indicates myocardial necrosis and is a useful adjunct to diagnosis. Myocardial infarction is considered part of a spectrum referred to as acute coronary syndrome (ACS). The ACS continuum representing ongoing myocardial ischemia or injury consists of unstable angina, non–ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Patients with ischemic discomfort may or may not have ST-segment or T-wave changes denoted on the electrocardiogram (ECG). ST elevations seen on the ECG reflect active and ongoing transmural myocardial injury. Without immediate reperfusion therapy, most persons with STEMI develop Q waves, reflecting a dead zone of myocardium that has undergone irreversible damage and death. Those without ST elevations are diagnosed either with unstable angina or NSTEMI—differentiated by the presence of cardiac enzymes. Both these conditions may or may not have changes on the surface ECG, including ST-segment depression or T-wave morphological changes. Myocardial infarction may lead to impairment of systolic or diastolic function and to increased predisposition to arrhythmias and other long-term complications. Coronary thrombolysis and mechanical revascularization have revolutionized the primary treatment of acute myocardial infarction,

largely because they allow salvage of the myocardium when implemented early after the onset of ischemia. (See Treatment Strategies and Management.) The modest prognostic benefit of an opened infarct-related artery may be realized even when recanalization is induced only 6 hours or more after the onset of symptoms, that is, when the salvaging of substantial amounts of jeopardized ischemic myocardium is no longer likely. The opening of an infarct-related artery may improve ventricular function, collateral blood flow, and ventricular remodeling, and it may decrease infarct expansion, ventricular aneurysm formation, left ventricular dilatation, late arrhythmia associated with ventricular aneurysms, and mortality. Evidence suggests a benefit from the use of beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, and statins.

Anatomy

The right and left coronary arteries most often arise independently from individual ostia in association with the right and left aortic valve cusps. The left anterior descending (LAD) and left circumflex (LCX) coronary arteries arise at the left main coronary artery bifurcation; they supply the anterior LV, the bulk of the interventricular septum (anterior two thirds), the apex, and the lateral and posterior LV walls. The right coronary artery (RCA) generally supplies the right ventricle (RV), the posterior third of the interventricular septum, the inferior wall (diaphragmatic surface) of the left ventricle (LV), and a portion of the posterior wall of the LV (by means of the posterior descending branch). When the posterior descending coronary artery (PDA), which supplies the posterior interventricular septum, arises from the LCX artery, the circulation is called left dominant. Most often, the PDA arises from the RCA; this anatomy is called right-dominant circulation. In two thirds of patients, the first branch of the RCA is the conus artery, which supplies the conus arteriosus (RV outflow tract); occasionally the conus arteriosus arises from a separate orifice. In 60% of patients, the sinus node artery arises from the proximal RCA, and in 40% of patients, it arises from the LCX artery. The anterior branches supply the free wall of the RV, and the acute marginal branches supply the RV. When the RCA extends to the crux (the origin of the PDA), it supplies the atrioventricular (AV) node (90%); otherwise, the AV node is supplied by the LCX. Therefore, obstruction of the RCA commonly affects the sinus node and the AV node, resulting in bradycardia, with or without heart block. Not surprisingly, RCA occlusion frequently manifests with sinus bradycardia, AV block, RV myocardial infarction, and/or inferoposterior myocardial infarction (of the LV).

Pathophysiology

The spectrum of myocardial injury depends not only on the intensity of impaired myocardial perfusion but also on the duration and the level of metabolic demand at the time of the event. The damage in the myocardium is essentially the result of a tissue response that includes apoptosis (cell death) and inflammatory changes. Therefore, the hearts of patients who suddenly die from an acute coronary event may show little or no evidence of damage response to the myocardium at autopsy. The typical myocardial infarction initially manifests as coagulation necrosis that is ultimately followed by myocardial fibrosis. Contraction-band necrosis is also seen in many patients with ischemia. This is followed by reperfusion, or it is accompanied by massive adrenergic stimulation, often with concomitant myocytolysis. The left coronary artery system covers more territory than does the right system; therefore, a myocardial infarction in this system is most likely to produce extensive injury, with impairment of function, pulmonary congestion, and

low output. Occlusion of the left coronary artery may also cause a left anterior hemiblock or a left posterosuperior hemiblock conduction abnormality; these effects are evidenced by a change of frontal axis on the electrocardiogram (ECG

Inferior-wall myocardial infarction and right ventricular myocardial infarction

In severe cases of acute inferior-wall myocardial infarction with RV involvement, the forward delivery of blood from the RV to the LV may be insufficient to fill the LV, resulting in low blood pressure even if the LV is intact. (See Physical Examination.) Chemoreceptor activation in the myocardium actuates vagal (parasympathetic) efferent discharge, known as the Bezold-Jarisch reflex, which causes bradycardia and vessel dilation that may further lower blood pressure. Adenosine may accumulate in the infarct zone secondary to a local inhibition of adenosine deaminase, for which aminophylline may act pharmacologically as an antagonist. The hemodynamic changes resemble many of those seen with pericardial constriction or tamponade. Patients with this condition respond well to an infusion of normal sodium chloride solution. Improvement with such infusion compensates for failure of the pumping action of the RV; it reduces vagal tone, and it deactivates the pressure sensors that were sending a hormonal signal to the kidneys to retain salt.

Arrhythmogenesis

In addition to the direct effects of ischemia and tissue hypoxia, decreased removal of noxious metabolites, including potassium, calcium, amphophilic lipids, and oxygen-centered free radicals, also impair ventricular performance. These abnormalities promote potentially lethal arrhythmias.

Pericarditis

Epicardial inflammation may initiate pericarditis, which is seen in more than 20% of patients presenting with Q-wave infarctions.

Reduced systolic function

Lack of adequate oxygen and insufficient metabolite delivery to the myocardium diminish the force of muscular contraction and decrease systolic wall motion in the affected territory.

Abnormal regional wall motion

Even brief deprivation of oxygen and the requisite metabolites to the myocardium diminishes diastolic relaxation and causes abnormal regional systolic contractile function, wall thickening, and abnormal wall motion. If the area affected is extensive, diminished stroke volume and cardiac output may result.

Hypokinesis and akinesis

In general, regions of hypokinesis and akinesis of the ventricular myocardium reflect the location and extent of myocardial injury.

Myocardial infarction expansion

In general, expansion of infarcted myocardium and resultant ventricular dilatation (ie, ventricular remodeling) ensues within a few hours after the onset of a myocardial infarction. An expanding myocardial infarction leads to thinning of the infarct zone and realignment of layers of tissue in and adjacent to it, causing ventricular dilatation.

Myocardial rupture

Myocardial rupture was seen in as many as 10% of fatal myocardial infarctions before the era of thrombolytic agents, but it is now encountered much less often. When rupture occurs, it may be associated with large infarctions; indications include cardiogenic shock or hemodynamically significant arrhythmia. Patients may have a history of hypertension with ventricular hypertrophy.

Ventricular aneurysm

A ventricular aneurysm is an outward bulging of a noncontracting

segment. In the early days of cardiac imaging, ventricular aneurysms were seen in as many as 20% of patients with Q-wave myocardial infarction, but now it is seen in less than 8%.

Cardiogenic shock

In patients with extensive myocardial injury, coronary blood flow diminishes as cardiac output declines and heart rate accelerates. Because coronary artery disease is usually generalized or diffuse, ischemia that occurs at a distance from the infracted segment may result in a vicious cycle in which a stuttering and expanding myocardial infarction ultimately leads to profound LV failure, hypotension, and cardiogenic shock.

Effect on diastolic function

Immediately after the onset of myocardial infarction, the ability of ischemic myocardium to relax declines. Relaxation is an active process that uses ATP. Impaired relaxation increases LV end-diastolic volume (LVEDV) and LV end-diastolic pressure (LVEDP). The increased LVEDP results in ventricular dilation, increased pulmonary venous pressure, decreased pulmonary compliance, and interstitial and (ultimately) alveolar pulmonary edema. These effects lead to increased hypoxemia, which may worsen ischemic injury to the myocardium.

Etiology

Atherosclerosis is the disease primarily responsible for most acute coronary syndrome (ACS) cases. Approximately 90% of myocardial infarctions result from an acute thrombus that obstructs an atherosclerotic coronary artery. Plaque rupture and erosion are considered to be the major triggers for coronary thrombosis. Following plaque erosion or rupture, platelet activation and aggregation, coagulation pathway activation, and endothelial vasoconstriction occur, leading to coronary thrombosis and occlusion. Within the coronary vasculature, flow dynamics and endothelial shear stress are implicated in the pathogenesis of vulnerable plaque formation. Evidence indicates that in numerous cases, culprit lesions are stenoses of less than 70% and are located proximally within the coronary tree. Coronary atherosclerosis is especially prominent near branching points of vessels. Culprit lesions that are particularly prone to rupture are atheromas containing abundant macrophages, a large lipid-rich core surrounded by a thinned fibrous cap.

Nonmodifiable risk factors for atherosclerosis include the following:

- Age
- Sex
- Family history of premature coronary heart disease
- Male-pattern baldness

Modifiable risk factors for atherosclerosis include the following:

- Smoking or other tobacco use
- Diabetes mellitus
- Hypertension
- Hypercholesterolemia and hypertriglyceridemia, including inherited lipoprotein disorders
- Dyslipidemia
- Obesity
- Sedentary lifestyle and/or lack of exercise
- Psychosocial stress
- Poor oral hygiene
- Type A personality

Elevated homocysteine levels and the presence of peripheral vascular disease are also risk factors for atherosclerosis.

Intramural thrombus development

Inflammation of the endocardial surfaces and stasis of blood flow associated with regional akinesis (no wall motion) or dyskinesis (abnormal, passively reversed wall motion) may lead to the formation of ventricular mural thrombi, which have the potential to embolize. Patients with acute myocardial infarction are prone to cerebrovascular injury as a result of emboli from ventricular mural thrombi; the rate is approximately 1%.

Causes of myocardial infarction other than atherosclerosis

Nonatherosclerotic causes of myocardial infarction include the following:

- Coronary occlusion secondary to vasculitis
- Ventricular hypertrophy (eg, left ventricular hypertrophy, idiopathic hypertrophic subaortic stenosis [IHSS], underlying valve disease)
- Coronary artery emboli, secondary to cholesterol, air, or the products of sepsis
- Congenital coronary anomalies
- Coronary trauma
- Primary coronary vasospasm (variant angina)
- Drug use (eg, cocaine, amphetamines, ephedrine)
- Arteritis
- Coronary anomalies, including aneurysms of coronary arteries
- Factors that increase oxygen requirement, such as heavy exertion, fever, or hyperthyroidism
- Factors that decrease oxygen delivery, such as hypoxemia of severe anemia
- Aortic dissection, with retrograde involvement of the coronary arteries
- Infected cardiac valve through a patent foramen ovale (PFO)
- Significant gastrointestinal bleed

In addition, myocardial infarction can result from hypoxia due to carbon monoxide poisoning or acute pulmonary disorders. Infarcts due to pulmonary disease usually occur when demand on the myocardium dramatically increases relative to the available blood supply. Although rare, pediatric coronary artery disease may be seen with Marfan syndrome, Kawasaki disease, Takayasu arteritis, progeria, and cystic medial necrosis. Imaging studies, such as contrast chest CT scans or transesophageal echocardiograms, should be used to differentiate myocardial infarction from aortic dissection in patients in whom the diagnosis is in doubt. Stanford type A aortic dissections may dissect in a retrograde fashion causing coronary blockage and dissection, which may result in myocardial infarction. In one study, 8% of patients with Stanford type A dissections had ST elevation on ECG. Myocardial infarction induced by chest trauma has also been reported, usually following severe chest trauma such as motor vehicle accidents and sports injuries.

Acute myocardial infarction in childhood

Acute myocardial infarction is rare in childhood and adolescence (See Epidemiology). Although adults acquire coronary artery disease from lifelong deposition of atheroma and plaque, which causes coronary artery spasm and thrombosis, children with acute myocardial infarction usually have either an acute inflammatory condition of the coronary arteries or an anomalous origin of the left coronary artery. Intrauterine myocardial infarction also does occur, often in association with coronary artery stenosis.

Epidemiology

Cardiovascular disease in industrialized and developing nations

Ischemic heart disease is the leading cause of death worldwide. Cardiovascular diseases cause 12 million deaths throughout the world each year, according to the third monitoring report of the World Health

Organization, 1991-93. They cause half of all deaths in several industrialized countries and are one of the main causes of death in many developing countries; they are the major cause of death in adults everywhere. Of particular concern are projections from the World Heart Federation that the burden of atherosclerotic cardiovascular disease in developing countries will increasingly become commensurate with that seen in industrialized countries. With a decline in infectious disease-related deaths, in conjunction with accelerated economic development and life-style changes that promote atherosclerosis, rates of ischemic heart disease and myocardial infarction are expected to sharply increase in developing countries, especially such countries in Eastern Europe, Asia, and parts of Latin America.

Sex predilection in cardiovascular disease
A male predominance in the incidence of cardiovascular disease exists up to approximately age 70 years, when the sexes converge to equal incidence. Premenopausal women appear to be somewhat protected from atherosclerosis, possibly owing to the effects of estrogen.

Age predilection in cardiovascular disease
The incidence of cardiovascular disease increases with age, with acute myocardial infarction being rare in childhood and adolescence. Most patients who develop an acute myocardial infarction are older than 60 years. Elderly people also tend to have higher rates of morbidity and mortality from their infarcts. Age (≥75 y) is the strongest predictor of 90-day mortality in patients with STEMI undergoing percutaneous coronary intervention. A continued focus on improving outcomes for these high-risk patients is needed.

Prognosis
One third of patients who experience STEMI die within 24 hours of the onset of ischemia, and many of the survivors experience significant morbidity. However, a steady decline has occurred in the mortality rate from STEMI over the last several decades. Acute myocardial infarction is associated with a 30% mortality rate; half of the deaths occur prior to arrival at the hospital. An additional 5-10% of survivors die within the first year after their myocardial infarction. Approximately half of all patients with a myocardial infarction are rehospitalized within 1 year of their index event. In a study that assessed the impact of prehospital time on STEMI outcome, Chughatai et al suggest that "total time to treatment" should be used as a core measure instead of "door-to-balloon time." This is because on-scene time was the biggest fraction of "prehospital time." The study compared groups with total time to treatment of more than 120 minutes compared with 120 minutes or less and found mortalities were 4 compared with 0 and transfers to a tertiary care facility were 3 compared with 1, respectively. Overall, prognosis is highly variable and depends largely on the extent of the infarct, the residual left ventricular function, and whether the patient underwent revascularization.

Better prognosis is associated with the following factors:
- Successful early reperfusion (STEMI goals: patient arrival to fibrinolysis infusion within 30 minutes OR patient arrival to percutaneous coronary intervention within 90 minutes)
- Preserved left ventricular function
- Short-term and long-term treatment with beta-blockers, aspirin, and ACE inhibitors

Poorer prognosis is associated with the following factors:
- Increasing age
- Diabetes
- Previous vascular disease (ie, cerebrovascular disease or peripheral vascular disease)
- Elevated Thrombolysis in Myocardial Infarction (TIMI) risk score for unstable angina/NSTEMI (7 factors: Age ≥65 y, ≥3 risk factors for cardiac disease, previous coronary disease, ST segment deviation ≥0.5 mm, ≥2 episodes of angina in last 24 h, aspirin use within prior wk, and elevated cardiac enzyme levels)
- Delayed or unsuccessful reperfusion
- Poorly preserved left ventricular function (the strongest predictor of outcome)
- Evidence of congestive heart failure (Killip classification ≥II) or frank pulmonary edema (Killip classification ≥III)
- Elevated B-type natriuretic peptide (BNP) levels
- Elevated high sensitive C-reactive protein (hs-CRP), a nonspecific inflammatory marker
- Secretory-associated phospholipase A2 activity is related to atherosclerosis and predicts all-cause mortality in elderly patients; it also predicts mortality or MI in post-MI patients.

A study by Alherbish et al found that in patients with STEMI, the presence of ST deviation in ECG lead aVR indicates an increased mortality risk. Data from the APEX-AMI (Pexelizumab in Conjunction With Angioplasty in Acute Myocardial Infarction) trial were examined to determine the incidence and prognostic value of aVR ST deviation in STEMI patients undergoing primary percutaneous coronary intervention within 6 hours of symptom onset; the investigators determined that aVR ST deviation was associated with a 50% relative increase in the risk of death within 90 days in patients with noninferior MI, whereas aVR ST elevation in patients with inferior MI was associated with a nearly 6-fold increase in such risk.

Blood glucose
Beck et al found that elevated blood glucose level on admission is associated with increased short-term mortality in nondiabetic patients presenting with a first acute myocardial infarction.

Psychological depression
The combination of acute myocardial infarction and psychological depression appears to worsen the patient's prognosis. Acute myocardial infarction may precipitate reactive depression whether or not beta-adrenergic blocking agents or other CNS-active agents are administered.

Myocardial hibernation and stunning
After the occurrence of 1 or more ischemic insults, impaired wall motion is often transient (myocardial stunning) or prolonged (myocardial hibernation). These phenomena occur because of the loss of essential metabolites such as adenosine, which is needed for adenosine triphosphate (ATP)–dependent contraction. Hibernation, a persisting wall-motion abnormality that is curable with revascularization, must be differentiated from permanent, irreversible damage or completed infarct.

Scar tissue and prognosis
Scars involving less than one third of the thickness of the wall, as shown on contrast-enhanced MRI, likely correspond to a recovery of myocardial function, whereas with scars measuring more than one third the thickness of the wall, the potential for recovery with therapy is limited (except in cases involving research cell therapies or surgical scar revision). Other findings associated with recovery are activity on 2-[Fluorine 18]-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) scanning and a monophasic or biphasic contractile response to dobutamine infusion, caused by the induction of ischemia.

CLINICAL PRESENTATION
History
The patient's history is critical in diagnosing myocardial infarction and sometimes may provide the only clues that lead to the diagnosis in the

initial phases of the patient presentation. Patients with typical myocardial Infarction may have prodromal symptoms of fatigue, chest discomfort, or malaise in the days preceding the event; alternatively, typical STEMI may occur suddenly, without warning. Myocardial infarction occurs most often in the early morning hours, perhaps partly because of the increase in catecholamine-induced platelet aggregation and increased serum concentrations of plasminogen activator inhibitor-1 (PAI-1) that occur after awakening. In general, the onset is not directly associated with severe exertion. Instead, it is concomitant with exertion. The immediate risk of myocardial infarction increases 6-fold on average and by as much as 30-fold in sedentary people. Takotsubo cardiomyopathy (TTC) is an acute reversible cardiac condition often triggered by stressful events, which is often confused with acute coronary syndrome. In a 2012 report, TTC events occurred in a circadian pattern with a peak in the afternoon hours, as opposed to the the predilection of STEMI for occurring in the morning hours. This timing is consistent with mechanisms underlying stressful life events that usually trigger TTC. A high index of suspicion should be maintained for myocardial infarction especially when evaluating women, patients with diabetes, older patients, patients with dementia, patients with a history of heart failure, cocaine users, patients with hypercholesterolemia, and patients with a positive family history for early coronary disease (See Etiology). A positive family history includes any first-degree male relative aged 45 years or younger or any first-degree female relative aged 55 years or younger who experienced a myocardial infarction.

Other symptoms of myocardial infarction include the following:
- Anxiety
- Light-headedness with or without syncope
- Cough
- Nausea with or without vomiting
- Diaphoresis
- Wheezing

The patient may recall only an episode of indigestion as an indication of myocardial infarction (see Physical Examination). In some cases, patients do not recognize chest pain, possibly because they have a stoic outlook, have an unusually high pain threshold, have a disorder that impairs function of the nervous system and that results in a defective anginal warning system (eg, diabetes mellitus), or have obtundation caused by medication or impaired cerebral perfusion. Elderly patients with preexisting altered mental status or dementia may have no recollection of recent symptoms and may have no complaints whatsoever.

Physical Examination

For many patients, the first manifestation of coronary artery disease is sudden death likely from malignant ventricular dysrhythmia. Physical examination findings for myocardial infarction can vary; one patient may be comfortable in bed, with normal examination results, while another may be in severe pain, with significant respiratory distress and a need for ventilatory support. Patients with ongoing symptoms usually lie quietly in bed and appear pale and diaphoretic. Hypertension may precipitate myocardial infarction, or it may reflect elevated catecholamine levels due to anxiety, pain, or exogenous sympathomimetics. Hypotension may indicate ventricular dysfunction due to ischemia. Hypotension in the setting of myocardial infarction usually indicates a large infarct secondary to either decreased global cardiac contractility or a right ventricular infarct. Acute valvular dysfunction may be present. Valvular dysfunction usually results from infarction that involves the papillary muscle. Mitral regurgitation due to papillary muscle ischemia or necrosis

may be present. The typical chest pain of acute myocardial infarction is intense and unremitting for 30-60 minutes. It is retrosternal and often radiates up to the neck, shoulder, and jaw and down to the ulnar aspect of the left arm. Chest pain is usually described as a substernal pressure sensation that also may be described as squeezing, aching, burning, or even sharp. In some patients, the symptom is epigastric, with a feeling of indigestion or of fullness and gas. Atypical presentations are common and frequently lead to misdiagnoses. Moreover, any patient may present with atypical symptoms, which are considered the anginal equivalent for that patient. A patient, for example, may present with abdominal discomfort or jaw pain as his or her anginal equivalent. An elderly patient may present with altered mental status. Atypical chest pain is common, especially in elderly patients and patients with diabetes. A low threshold should be maintained when evaluating high- and moderate-risk patients, as their anginal equivalents may mimic other presentations. Women tend to present more commonly with atypical symptoms such as sharp pain, fatigue, weakness, and other nonspecific complaints. Diaphoresis, weakness, a sense of impending doom, profound restlessness, confusion, presyncope, hiccupping (which presumably reflects irritation of the phrenic nerve or diaphragm), nausea and vomiting, and palpitations may be present. (Nausea and/or abdominal pain often are present in infarcts involving the inferior or posterior wall.) Decreased systolic ventricular performance may lead to impaired perfusion of vital organs and reflex-mediated compensatory responses, such as restlessness, impaired mentation, pallor, peripheral vasoconstriction and sweating, tachycardia, and prerenal failure. By contrast, impaired left ventricular diastolic function leads to pulmonary vascular congestion with shortness of breath and tachypnea and, eventually, pulmonary edema with orthopnea. Shortness of breath may be the patient's anginal equivalent or a symptom of heart failure. In an elderly person or a patient with diabetes, shortness of breath may be the only complaint. In patients with acute inferior-wall myocardial infarction with right ventricular involvement, distention of neck veins is commonly described as a sign of failure of the RV. (Central venous pressure is most properly estimated independently of venous distension on the basis of the height of the meniscus of venous pulsation above the mid atrium.) Impaired right ventricular diastolic function also leads to systemic venous hypertension, edema, and hepatomegaly with abdominojugular reflux, which may result in saline-response underfilling of the LV and a concomitant reduction in cardiac output. Elderly patients and those with diabetes may have particularly subtle presentations and may complain of fatigue, syncope, or weakness. The elderly may also present with only altered mental status. As many as half of myocardial infarctions are clinically silent in that they do not cause the classic symptoms described above and consequently go unrecognized by the patient. Myocardial infarction is clinically silent in as many as 25% of elderly patients, a population in whom 50% of myocardial infarctions occur; in such patients, the diagnosis is often established only retrospectively, by applying electrocardiographic criteria or by scanning the patients using 2-dimensional (2D) echocardiography or magnetic resonance imaging (MRI). On clinical evaluation, ventricular aneurysms may be recognized late, with symptoms and signs of heart failure, recurrent ventricular arrhythmia, or recurrent embolization.

Vital signs

The patient's heart rate is often increased secondary to sympathoadrenal discharge. The pulse may be irregular because of ventricular ectopy, an accelerated idioventricular rhythm, ventricular tachycardia, atrial fibrillation or flutter, or other supraventricular arrhythmias. Bradyarrhythmias may be present; bradyarrhythmias may

be attributable to impaired function of the sinus node. An AV nodal block or infranodal block may be evident. In general, the patient's blood pressure is initially elevated because of peripheral arterial vasoconstriction resulting from an adrenergic response to pain and ventricular dysfunction. However, with right ventricular myocardial infarction or severe left ventricular dysfunction, hypotension is seen. The respiratory rate may be increased in response to pulmonary congestion or anxiety. Coughing, wheezing, and the production of frothy sputum may occur. Fever is usually present within 24-48 hours, with the temperature curve generally parallel to the time course of elevations of creatine kinase (CK) levels in the blood. Body temperature may occasionally exceed 102°F.

Funduscopic examination

Manifestations of atherosclerotic vascular disease include copper wiring, or narrowing, of arterioles. Hypertension may manifest with arteriovenous nicking, which is a pinching of the veins by small arteries where they cross. Extreme hypertension may cause cupping or loss of the margins of the optical disk. Antecedent long-standing hypertension may be reflected by arterial narrowing and hemorrhages.

Arterial pulsations

Arterial pulsations may exhibit pulsus alternans, which reflects impaired left ventricular function and is characterized by strong and weak alternating pulse waves (the variation in systolic pressure is >20 mm Hg). Carotid pulsation may be thin (pulsus parvus) because of decreased amplitude and length of the pulse secondary to decreased stroke volume. Pulsus bisferiens consists of 2 systolic peaks; it may be palpated in association with hypertrophic obstructive cardiomyopathy (HOCM) or mixed aortic stenosis and regurgitation. A dicrotic pulse is encountered in cases involving hypovolemic shock, severe heart failure, or cardiac tamponade. It manifests as a double pulse, produced by a combination of the systolic wave followed by an exaggerated dicrotic (diastolic) wave. A bigeminal pulse is observed in the presence of ectopic beats or Wenckebach heart block; it is characterized by regular coupling of 2 beats with the interval between a pair of beats greater than that between the coupled beats themselves. Pulsus paradoxus is defined as a decline in systolic blood pressure of 10 mm Hg or more on inspiration; it is seen in cases involving cardiac tamponade, constrictive pericarditis, restrictive cardiomyopathy, hypotensive shock, severe chronic lung disease, or pulmonary embolism. In patients with associated aortic regurgitation, a pulse with sharp descent, or a water-hammer pulse, may be observed.

Venous pulsations

Jugular venous distention may accompany right ventricular myocardial infarction or right ventricular failure secondary to profound left ventricular dysfunction and pulmonary hypertension. It may also be elevated as a result of an increase in right atrial pressure in patients with heart failure, decreased right ventricular compliance, pericardial disease, fluid overload, or tricuspid or superior vena cava obstruction. The Kussmaul sign, characterized by a paradoxical increase in jugular venous pressure during inspiration, may occur in patients with constrictive pericarditis, congestive HF (CHF), or tricuspid stenosis.

Chest

Rales or wheezes may be auscultated; these occur secondary to pulmonary venous hypertension, which is associated with extensive acute left ventricular myocardial infarction. Unilateral or bilateral pleural effusions may produce egophony at the lung bases. On chest radiographs, they are evidenced by blunted costophrenic angles; on MRI, they are evidenced by dependent fluid signal intensity; on echocardiography, they are evidenced by echolucent zones adjacent to the heart.

Heart

On palpation, lateral displacement of the apical impulse, dyskinesis, a palpable S4 gallop, and a soft S1 sound may be found. These indicate diminished contractility of the compromised LV. Paradoxical splitting of S2 may reflect the presence of left bundle-branch block or prolongation of the preejection period with delayed closure of the aortic valve, despite decreased stroke volume. Increased S4 and S3 gallops may suggest increased LV stiffness; they represent the rapid filling phase (S3) or atrial contraction (S4). A mitral regurgitation murmur (typically holosystolic near the apex) indicates papillary muscle dysfunction or rupture or mitral annular dilatation; it may be audible even when cardiac output is substantially decreased. A holosystolic systolic murmur that radiates to the midsternal border and not to the back, possibly with a palpable thrill, suggests a ventricular septal rupture; such a rupture may occur as a complication in some patients with full-thickness (or Q-wave) myocardial infarctions. With resistive flow and an enlarged pressure difference, the ventricular septal defect murmur becomes harsher, louder, and higher in pitch than before. A pericardial friction rub may be audible as a to-and-fro rasping sound with 1-3 components; it is produced through sliding contact of inflammation-roughened surfaces. Neck vein and pulse patterns, splitting of S2, or ECG findings may suggest premature ventricular beats, brief runs of ventricular tachycardia, accelerated idioventricular rhythm, atrial flutter or atrial fibrillation, or conduction delays.

Abdomen

Patients frequently develop tricuspid incompetence; hepatojugular reflux may be elicited even when hepatomegaly is not marked.

Extremities

Peripheral cyanosis, edema, pallor, diminished pulse volume, delayed rise, and delayed capillary refill may indicate vasoconstriction, diminished cardiac output, and right ventricular dysfunction or failure. Pulse and neck-vein patterns may reveal other associated abnormalities, as previously discussed. Dependent edema may be graded 0-4 by assessing the depth of persistent pitting after thumb pressure is applied to the patient's inner shin for more than 10 seconds or by evaluating the lower back if the patient has had his or her legs elevated.

Differential Diagnoses
Diagnostic Considerations

Epigastric or chest symptoms from myocardial ischemia may incorrectly be attributed to a GI source. Often, this occurs despite the presence of dyspnea or diaphoresis, symptoms that are difficult to attribute to the GI system. Additionally, patients with myocardial ischemia may report relief or improvement with GI remedies (eg, antacids). Remember that even myocardial ischemia can worsen with recumbency (eg, angina decubitus) because of an increase in venous return and a temporary greater workload. The discomfort of myocardial ischemia may erroneously be attributed to a musculoskeletal etiology. Tenderness of the chest wall is reported in as many as 5% of patients who prove to have an MI. If no injury or event is defined that could have led to a soft tissue injury, the clinician should be reluctant to render a diagnosis of musculoskeletal chest pain. Younger patients are overly represented in cases of missed MI. Most likely, this is because of the inherent bias that this is a disease of those who are late middle-aged and older. Approach each patient with chest symptoms as an individual who could have the disease. Unfortunately, in a series of missed MI, the failure to recognize ischemic changes is frequent. The inferior leads, in particular, must be

scrutinized carefully for any evidence of ST-segment elevation by using a straight edge across the T-P segments. Another common error is to recognize ischemic changes and then discharge the patient without definitively proving that the changes were pre-existent. Nonischemic causes of ST-segment elevation include LVH, pericarditis, ventricular-paced rhythms, hypothermia, hyperkalemia, and LV aneurysm. Nonischemic causes may lead to overtreatment. The diagnosis of an MI may be missed in the setting of a left bundle-branch block, and there may be delays in, or a failure of, administering thrombolytic agents or initiating PCI. This is usually because of delays in ECG performance, interpretation, and decision-making, and it is also affected by the availability of thrombolytics in the ED. Excluding patients based on age alone will deny some the significant benefit of thrombolysis.

Differential Diagnoses

- Abdominal Compartment Syndrome
- Acute Aortic Dissection
- Acute Cholecystitis and Biliary Colic
- Acute Coronary Syndrome
- Acute Gastritis
- Acute Mitral Regurgitation
- Acute Pericarditis
- Angina Pectoris
- Anxiety Disorders
- Aortic Dissection
- Aortic Regurgitation
- Aortic Stenosis Imaging
- Asthma
- Biliary Disease
- Cardiogenic Shock
- Acute Cholecystitis
- Chronic Obstructive Pulmonary Disease (COPD) and Emphysema in Emergency Medicine
- Contusions
- Depression
- Dyspepsia
- Emergent Management of Pancreatitis
- Emergent Treatment of Gastroenteritis
- Esophageal Reflux
- Esophageal Spasm
- Esophagitis
- Gallstones (Cholelithiasis)
- Gastroesophageal Reflux Disease
- Heart Arrhythmias
- Heart rupture
- Herpes Zoster
- Hypotension
- Infective Endocarditis
- Mitral Valve Prolapse in Emergency Medicine
- Myocarditis
- Myopericarditis
- Pediatric Pneumonia
- Pleurodynia
- Pneumothorax
- Pneumothorax Imaging
- Idiopathic Pulmonary Arterial Hypertension
- Pulmonary Embolism (PE)
- Radicular Pain
- Stroke Imaging
- Tachycardia Myopathy

- Unstable Angina
- Ventricular Septal Defect Surgery in the Pediatric Patient

Workup

Approach Considerations

The objectives of laboratory testing and imaging include the following:

- To determine the presence or absence of myocardial infarction for diagnosis and differential diagnosis (point–of-care testing and testing in central laboratory of cardiac biomarkers)
- To characterize the locus, nature (STEMI or NSTEMI), and extent of myocardial infarction (ie, to estimate infarct size)
- To detect recurrent ischemia or myocardial infarction (extension of myocardial infarction)
- To detect early and late complications of myocardial infarction
- To estimate the patient's prognosis

Laboratory evaluation is particularly helpful in the presence of comorbid conditions that may affect the patient's prognosis and influence his or her care. Such comorbidities include the following:

- Diabetes
- Renal or hepatic failure
- Anemia
- Bleeding disorders
- Respiratory failure

Cardiac imaging

The role of imaging in ACSs is broad, but the procedures are primarily used to confirm or rule out coronary disease. Furthermore, it may help define the anatomy and degree of myocardial perfusion abnormalities. In lower-risk individuals in whom ACS is suspected and who do not have serial ECG changes or positive serial cardiac biomarker findings, the ACC/AHA guidelines recommend some form of stress testing to help confirm the diagnosis and guide therapy. For individuals with highly probable or confirmed ACS, consultation with a cardiologist is carried out so that coronary angiography can be performed; this procedure can be used to definitively diagnose or rule out coronary artery disease. Based on the angiographic result and patient comorbidities, subsequent treatment recommendations can be made, which may include medical therapy, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) surgery. High-risk coronary plaque may independently predict ACS in patients with acute chest pain in the emergency department (ED). Coronary computed-tomography angiography (CCTA) may detect high-risk coronary plaque features in patients with acute chest pain and a negative initial ECG or troponin test in the ED; such plaques may predict which patients are at higher risk of imminent ACS (MI or unstable angina). In addition, high-risk plaque appears to be an independent risk factor for an increased risk of ACS. The data were derived from 472 patients in the CCTA arm of the Rule Out Myocardial Infarction With Computer Assisted Tomography II (ROMICAT II) study which showed that, after adjustment for stenosis (>50%) and other cardiovascular risk factors, patients with high-risk plaques were significantly more likely to have ACS during their index hospitalization. In a separate study, automated software that quantified plaque features in 56 coronary lesions improved the ability to predict lesion-specific ischemia. The investigators believe that this technique has the potential to noninvasively identify hemodynamically significant coronary lesions.

Cardiac Biomarkers/Enzymes

The American College of Cardiology/American Heart Association (ACC/AHA) guidelines on unstable angina/NSTEMI recommend that in patients with suspected myocardial infarction, cardiac biomarkers

should be measured at presentation. The guidelines recommend a total turnaround time of less than 1 hour and preferably less than 30 minutes for the cardiac biomarker measurements. Several studies have shown that implementation of point-of-care testing (POCT) for cardiac biomarkers may improve early diagnosis as well as decrease patient length of stay. Additional studies are needed to determine the relative analytic performance of different POCT assays for troponins, creatine phosphokinase–myocardial band (CPK-MB) and myoglobin alone or in combination in the current state of analytical technologies. If initial markers are negative and have been measured within 6 hours of symptom onset, the biomarkers should be remeasured within 8-12 hours after symptom onset. Remeasuring cardiac enzyme levels at regular intervals for the first 24 hours is a reasonable approach to improving the sensitivity of detection of myocardial necrosis, and the degree of positivity can be important for prognostication. Note the graph below.
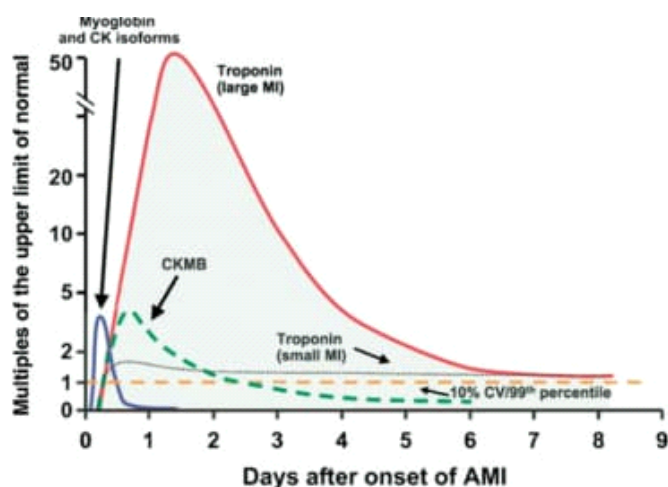
Timing of release of various cardiac biomarker peaks after the onset of myocardial infarction

In addition, biomarkers alone or as part of accelerated diagnostic protocols (ADP) can reduce the number of patients with a missed diagnosis of NSTEMI who are at increased risk of major adverse cardiac events. Furthermore, such approaches can facilitate early discharge from the ED in patients who a have a low short-term risk of a major cardiac event as reported in The Asia-Pacific Evaluation of Chest Pain Trial (ASPECT).

Troponin Levels

Troponin is a contractile protein that normally is not found in serum. It is released only when myocardial necrosis occurs. Troponin levels are now considered to be the criterion standard for defining and diagnosing myocardial infarction, according to the American College of Cardiology (ACC)/American Heart Association (AHA) consensus statement on myocardial infarction. Positive troponin levels are considered virtually diagnostic of myocardial infarction, according to a revised version of the ACC/AHA consensus statement, as they are without equal in combined specificity and sensitivity in this diagnosis. Reichlan et al suggest that absolute changes in troponin levels have a significantly higher diagnostic accuracy for acute myocardial infarction than relative changes. Serum levels increase within 3-12 hours from the onset of chest pain, peak at 24-48 hours, and return to baseline over 5-14 days. Improved cardiac troponin assays offer even greater diagnostic

accuracy than the standard assays do, according to a study by Reichlin et al. This is especially true for the early diagnosis of acute myocardial infarction, particularly in patients with a recent onset of chest pain, according to the investigators. Keller et al suggest that among patients with suspected acute coronary syndrome, highly sensitive troponin I assay (hsTnI) or contemporary troponin I assay (cTnI) determination 3 hours after admission for chest pain may facilitate early rule-out of acute myocardial infarction. A serial change in hsTnI or cTnI levels from admission (using the 99th percentile diagnostic cutoff value) to 3 hours postadmission may aid in early diagnosis of acute myocardial infarction. According to Hubbard et al, in patients without heart failure with marginally increased troponin levels, a low BNP level (BNP ≤80 pg/mL) cannot identify patients at low-risk for 30-day acute MI or death. MI is a strong trigger of N-terminal pro-B-type natriuretic peptide (NT-proBNP) release, and checking these levels may improve the early diagnosis and risk stratification of patients with suspected acute MI.

Creatine Kinase Levels

The 3 CK isoenzymes are as follows:
- CK with muscle subunits (CK-MM), which is found mainly in skeletal muscle
- CK with brain subunits (CK-BB), which is found predominantly in the brain
- CK-MB, which is found mainly in the heart

Serial measurements of CK-MB isoenzyme levels were previously the standard criterion for the diagnosis of myocardial infarction. CK-MB levels increase within 3-12 hours of the onset of chest pain, reach peak values within 24 hours, and return to baseline after 48-72 hours. levels peak earlier (wash out) if reperfusion occurs. Sensitivity is approximately 95%, with high specificity. However, sensitivity and specificity are not as high as they are for troponin levels, and, as mentioned above, the trend has favored using troponins for the diagnosis of myocardial infarction.

Myoglobin levels

Myoglobin, a low-molecular-weight heme protein found in cardiac and skeletal muscle, is released more rapidly from infarcted myocardium than is troponin. Urine myoglobin levels rise within 1-4 hours from the onset of chest pain. Myoglobin levels are highly sensitive but not specific; they may be useful within the context of other studies and in the early detection of myocardial infarction in the emergency department (ED).

Other Significant Laboratory Studies
Complete blood cell count

Obtain a complete blood cell (CBC) count if myocardial infarction is suspected in order to rule out anemia as a cause of decreased oxygen supply and prior to giving thrombolytic agents. Leukocytosis is also common, but not universal, in the setting of acute myocardial infarction. A platelet count is necessary if a IIb/IIIa agent is considered; furthermore, the patient's white blood cell (WBC) count may be modestly elevated in the setting of myocardial infarction, signifying an acute inflammatory state. The platelet count may become dangerously low after the use of heparin because of heparin-induced thrombocytopenia (HIT). The leukocyte count may be normal initially, but it generally increases within 2 hours and peaks in 2-4 days, with predominance of polymorphonuclear leukocytes and a shift to the left. Elevations generally persist for 1-2 weeks.

Chemistry profile

In the setting of myocardial infarction, closely monitor potassium and

magnesium levels. The creatinine level is also needed, prior to initiating treatment with an ACE inhibitor. The erythrocyte sedimentation rate (ESR) rises above reference range values within 3 days and may remain elevated for weeks. The serum lactate dehydrogenase (LDH) level rises above the reference range within 24 hours of myocardial infarction, reaches a peak within 3-6 days, and returns to the baseline within 8-12 days. Blood oxygenation should be checked and repeatedly corrected if any clinical findings suggest hypoxemia; hypoxemia may result from pulmonary congestion, atelectasis, or ventilatory impairment secondary to complications of myocardial infarction or excessive sedation or analgesia. Fingertip oximetry may be adequate in the absence of carbon dioxide retention and may obviate puncture to assess arterial blood gases (ABGs). Such puncturing may lead to bleeding in patients being treated with thrombolytic drugs. However, normal oxygen saturation does not exclude impending respiratory failure.

Lipid profile

This may be helpful if obtained upon presentation, because levels can change after 12-24 hours of an acute illness.

C-reactive protein and other inflammation markers

Consider measuring C-reactive protein (CRP) levels and other inflammation markers upon presentation if an ACS is suspected.

Electrocardiogram

As recommended by the most recent ACC/AHA guidelines for the management of unstable angina/NSTEMI, last updated in 2007, patients with active ongoing symptoms suggestive of an acute coronary syndrome should have early risk stratification by checking cardiac enzyme levels and undergoing a 12-lead ECG within 10 minutes of presentation of the emergency department. For patients with ongoing symptoms, serial ECGs should be performed to look for dynamic changes in the ST segment. The ECG is the most important tool in the initial evaluation and triage of patients in whom an ACS is suspected. It is confirmatory of the diagnosis in approximately 80% of cases. The electrocardiographic evidence of myocardial infarction is seen in the images below.
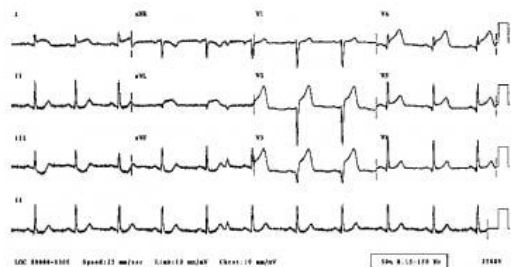
Acute anterior myocardial infarction.
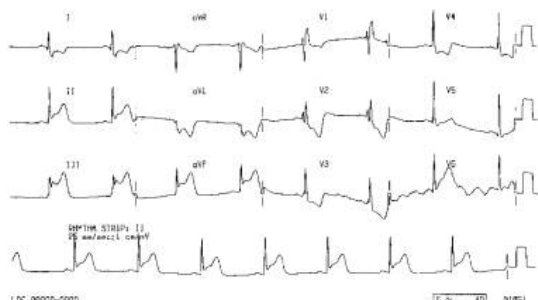
Acute inferior myocardial infarction.
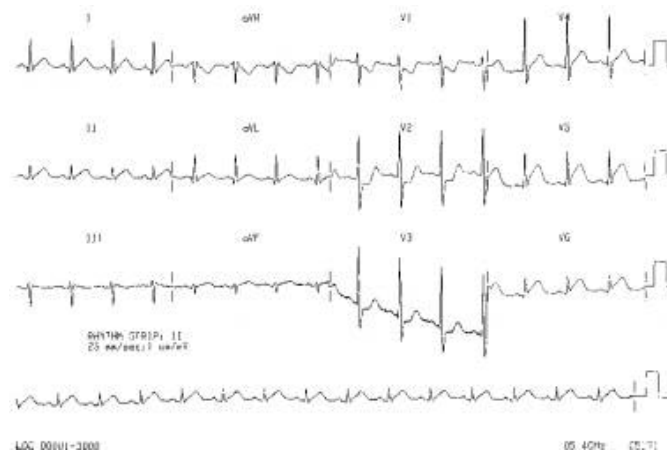

Acute posterolateral myocardial infarction.

Obtain an ECG immediately if myocardial infarction is considered or suspected. In patients with inferior myocardial infarction, record a right-sided ECG to rule out right ventricular infarct. Qualified personnel should review the ECG as soon as possible. Electrocardiography should be performed serially upon presentation to evaluate progression and assess changes with and without pain. Obtain daily serial ECGs for the first 2-3 days and additionally as needed. Because the symptoms of acute myocardial infarction can be subtle or protean, electrocardiography should be performed on any patient who is older than age 45 years and is experiencing any form of thoracoabdominal discomfort, including new epigastric pain or nausea. In younger patients, an ECG should be considered when suggestive symptoms are present or when risk factors exist for early coronary artery disease. Younger patients are disproportionately represented in missed cases. An ECG is a rapid, low-risk, relatively low-cost measure.

Electrocardiographic abnormalities

The diagnosis may be established with certainty when typical ST-segment elevation persists for hours and is followed by inversion of T waves during the first few days and by the development of Q waves. However, initial ST depression or T-wave inversion associated with myocardial infarction is difficult to differentiate from that seen in the presence of ischemia without myocardial infarction or in unrelated conditions. ST-segment depression followed by T-wave inversion without the evolution of Q waves may result from non–Q-wave myocardial infarction or from subendocardial ischemia without myocardial infarction. True posterior-wall myocardial infarctions may cause precordial ST depression, inverted and hyperacute T waves, or both. ST-segment elevation and upright hyperacute T waves may be evident with the use of right-sided chest leads. High probability of myocardial infarction is indicated either by ST-segment elevation greater than 1 mm in 2 anatomically contiguous leads or by the presence of new Q waves. Results that indicate intermediate probability of myocardial infarction are ST-segment depression, T-wave inversion, and other nonspecific ST-T wave abnormalities. Results that indicate low probability of myocardial infarction are normal findings on ECGs; however, normal or nonspecific findings on ECGs do not exclude the possibility of myocardial infarction.

Localization based on distribution of electrocardiographic abnormalities is as follows:

· Inferior wall - II, III, aVF (See the image below.)
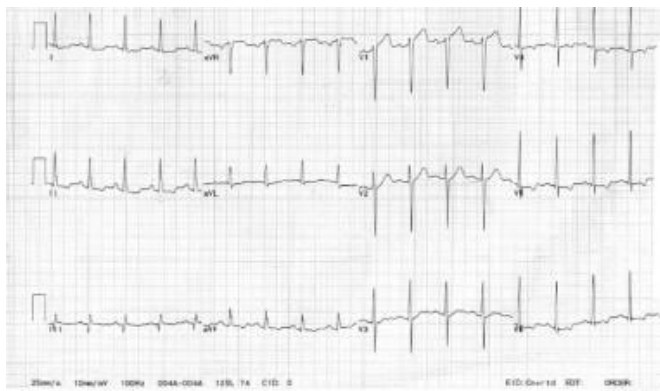
The right-sided leads indicate ST-segment elevations in RV$_3$ to RV$_5$, which are consistent with a right ventricular infarct.

· Lateral wall - I, aVL, V4 through V6
· Anteroseptal - V1 through V3
· Anterolateral - V1 through V6
· Right ventricular - RV4, RV5
· Posterior wall - R/S ratio greater than 1 in V1 and V2; T-wave changes (ie, upright) in V1, V8, and V9

Right ventricular myocardial infarction commonly is manifested by ST-segment elevation or Q waves detectable in right-sided precordial leads. The appearance of abnormalities in a large number of ECG leads often indicates extensive injury or concomitant pericarditis. Anterior and anterolateral myocardial infarctions tend to involve more left ventricular myocardium than do inferior or true posterior myocardial infarctions. Hyperacute (symmetrical and often but not necessarily pointed) T waves are frequently an early sign of myocardial infarction at any locus. The characteristic electrocardiographic changes may be seen in conditions other than acute myocardial infarction. For example, patients with previous myocardial infarction and left ventricular aneurysm may have persistent ST elevation resulting from dyskinetic wall motion, rather than from acute ischemic injury. ST-segment changes may also be the result of misplaced precordial leads, hypothermia (elevated J point or Osborne waves), or hypothyroidism. False q waves may be seen in septal leads in hypertrophic-obstructive cardiomyopathy (HOCM). They may also result from cardiac rotation. Substantial T-wave inversion may be seen in some forms of left ventricular hypertrophy with secondary changes. The Q-T segment may be prolonged because of ischemia or hypomagnesemia. Saddleback ST-segment elevation (Brugada epsilon waves) may be seen in leads V1 -V3 in patients with a congenital predisposition to life-threatening arrhythmias. This elevation may be confused with that observed in acute anterior myocardial infarction. Brugada electrocardiographic changes may be seen during the administration of procainamide or a beta-blocker in patients whose ECG was previously normal. Brain injuries also may trigger changes in T waves. Convex ST-segment elevation with upright or inverted T waves is generally indicative of myocardial infarction in the appropriate clinical setting. ST depression and T-wave changes may also indicate evolution of NSTEMI. Unfortunately, in a series of missed myocardial infarction, the failure to recognize ischemic changes is frequent. The inferior leads, in particular, must be scrutinized carefully for any evidence of ST-segment elevation by using a straight edge across the T-P segments. Another common error is to recognize ischemic changes and then discharge the patient

without definitively proving that the changes were preexistent. Nonischemic causes of ST-segment elevation include left ventricular hypertrophy, pericarditis, ventricular-paced rhythms, hypothermia, hyperkalemia, and left ventricular aneurysm. Nonischemic causes may lead to overtreatment. Patients with a permanent pacemaker in place may confound recognition of STEMI by 12-lead ECG due to the presence of paced ventricular contractions.

Cardiac Imaging

The roles and appropriateness of imaging in acute coronary syndromes (ACSs) are broad but primarily are used to confirm or rule out coronary disease. Furthermore, it may help define the anatomy and degree of myocardial perfusion abnormalities. In lower-risk individuals in whom ACS is suspected, serial ECG changes are not present, and serial cardiac biomarkers are negative, the ACC/AHA guidelines recommend for some form of stress testing to help confirm diagnosis and guide therapy. In individuals with highly probable or confirmed ACS, consultation to a cardiologist is made to perform a coronary angiogram to definitively diagnose or rule out coronary artery disease. Based on the angiographic result and patient comorbidities, subsequent treatment recommendations can be made: medical therapy, percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) surgery. High-risk coronary plaque may independently predict ACS in patients with acute chest pain in the emergency department (ED). Coronary computed-tomography angiography (CCTA) may detect high-risk coronary plaque features in patients with acute chest pain and a negative initial ECG or troponin test in the ED; such plaques may predict which patients are at higher risk of imminent ACS (MI or unstable angina). In addition, high-risk plaque appears to be an independent risk factor for an increased risk of ACS. The data were derived from 472 patients in the CCTA arm of the Rule Out Myocardial Infarction With Computer Assisted Tomography II (ROMICAT II) study which showed that, after adjustment for stenosis (>50%) and other cardiovascular risk factors, patients with high-risk plaques were significantly more likely to have ACS during their index hospitalization. In a separate study, automated software that quantified plaque features in 56 coronary lesions improved the ability to predict lesion-specific ischemia. The investigators believe that this technique has the potential to noninvasively identify hemodynamically significant coronary lesions.

Stress echocardiography

Stress echocardiography can be used to rule out myocardial ischemia in patients who come to the emergency department with chest pain, according to a retrospective study of 474 unselected consecutive patients who presented with spontaneous chest pain, a nondiagnostic ECG, and negative cardiac enzymes at baseline and after 6 and 12 hours. Exercise stress echocardiography was performed in 270 patients, showing inducible ischemia in 41; dobutamine stress echocardiography was performed in 218, showing inducible ischemia in 72. Of the 113 patients with inducible ischemia, 98 underwent angiography, which revealed significant coronary artery disease in 78. The 2 types of stress echocardiography yielded statistically similar sensitivities (88% and 90%, respectively), positive predictive values (90% and 70%), and negative predictive values (98% and 95%); exercise stress echocardiography was significantly more specific (98% vs 83%).

Coronary Artery Calcium Scoring

Coronary artery calcium scoring is an emerging technique that appears to add some predictive value in identifying patients at low risk for

coronary artery disease. However, in high-risk patients or in those who have established coronary artery disease, the test does not appear to be helpful at this time.

Treatment & Management
Approach Considerations

Morbidity and mortality from myocardial infarction are significantly reduced if patients and bystanders recognize symptoms early, activate the emergency medical service (EMS) system, and thereby shorten the time to definitive treatment. Trained prehospital personnel can provide life-saving interventions if the patient develops cardiac arrest. The key to improved survival is the availability of early defibrillation. Approximately 1 in every 300 patients with chest pain transported to the ED by private vehicle goes into cardiac arrest en route. Several studies have confirmed that patients with STEMI usually do not call 911; in one study, only 23% of patients with a confirmed coronary event used EMS. The first goal for healthcare professionals is to diagnose in a very rapid manner whether the patient is having an STEMI or NSTEMI because therapy differs between the 2 types of myocardial infarction. Particular considerations and differences involve the urgency of therapy and degree of evidence regarding different pharmacological options. As a general rule, initial therapy for acute myocardial infarction is directed toward restoration of perfusion as soon as possible to salvage as much of the jeopardized myocardium as possible. This may be accomplished through medical or mechanical means, such as PCI or CABG.

Further treatment is based on the following:

- Restoration of the balance between the oxygen supply and demand to prevent further ischemia
- Pain relief
- Prevention and treatment of any complications that may arise.

Coronary collateral circulation

The coronary collateral circulation is an important factor in terms of the amount of damage to the myocardium that results from coronary occlusion. Well-developed collaterals may greatly limit or even completely eliminate myocardial infarction despite complete occlusion

of a coronary artery. Reports vary as to the number of patients who have collaterals at the time of a myocardial infarction; many patients develop collaterals in the hours and days after an occlusion occurs. When the patient is at rest, blood flow through collaterals is normal, a fact that accounts for the absence of resting ischemia. However, blood flow through collaterals does not increase with exercise; this inability accounts for the occurrence of ischemia during periods of stress.

Management
Prehospital care

For patients with chest pain, prehospital care includes the following:

- Intravenous access, supplemental oxygen, pulse oximetry
- Immediate administration of aspirin en route
- Nitroglycerin for active chest pain, given sublingually or by spray
- Telemetry and prehospital ECG, if available.

Emergency department and inpatient care

Initial stabilization of patients with suspected myocardial infarction and ongoing acute chest pain should include administration of sublingual nitroglycerin if patients have no contraindications to it. The American Heart Association (AHA) recommends the initiation of beta blockers to all patients with STEMI (unless beta blockers are contraindicated). If STEMI is present, the decision must be made quickly as to whether the patient should be treated with thrombolysis or with primary percutaneous coronary intervention (PCI). Although patients presenting with no ST-segment elevation are not candidates for immediate administration of thrombolytic agents, they should receive anti-ischemic therapy and may be candidates for PCI urgently or during admission. Critical care units have reduced early mortality rates from acute myocardial infarction by approximately 50% by providing immediate defibrillation and by facilitating the implementation of beneficial interventions. These interventions include the administration of IV medications and therapy designed to do the following:

- Limit the extent of myocardial infarction
- Salvage jeopardized ischemic myocardium
- Recanalize infarct-related arteries

INTERPRETATION

Brain natriuretic peptide

Brain natriuretic peptide 32 (BNP), also known as **B-type natriuretic peptide**, is a hormone secreted by cardiomyocytes in the heart ventricles in response to stretching caused by increased ventricular blood volume. BNP is one of two natriuretic peptides. The 32-amino acid polypeptide BNP is secreted attached to a 76–amino acid N-terminal fragment in the prohormone called NT-proBNP (BNPT), which is biologically inactive. Once released, BNP binds to and activates the atrial natriuretic factor receptor NPRA, and to a lesser extent NPRB, in a fashion similar to atrial natriuretic peptide (ANP) but with 10-fold lower affinity. The biological half-life of BNP, however, is twice as long as that of ANP, and that of NT-proBNP is even longer, making these peptides better targets than ANP for diagnostic blood testing. The physiologic actions of BNP are similar to those of ANP and include decrease in systemic vascular resistance and central venous pressure as well as an increase in natriuresis. The net effect of these peptides is a decrease in blood pressure due to the decrease in systemic vascular resistance and, thus, afterload. Additionally, the actions of both BNP and ANP result in a decrease in cardiac output due to an overall decrease in central venous pressure and preload as a result of the reduction in blood volume that follows natriuresis and diuresis.

Biosynthesis

BNP is synthesized as a 134-amino acid preprohormone (preproBNP), encoded by the human gene NPPB. Removal of the 25-residue N-terminal signal peptide generates the prohormone, proBNP, which is stored intracellularly as an O-linked glycoprotein; proBNP is subsequently cleaved between arginine-102 and serine-103 by a specific convertase (probably furin or corin) into NT-proBNP and the biologically active 32-amino acid polypeptide BNP-32, which are secreted into the blood in equimolar amounts. Cleavage at other sites produces shorter BNP peptides with unknown biological activity. Processing of proBNP may be regulated by O-glycosylation of residues near the cleavage sites.

Physiologic effects

Since the actions of BNP are mediated via the ANP receptors, the physiologic effects of BNP are identical to those of ANP, those will be reviewed here. Receptor-agonist binding causes a reduction in renal sodium reabsorption, which results in a decreased blood volume. Secondary effects may be an improvement in cardiac ejection fraction and reduction of systemic blood pressure. Lipolysis is also increased.

Renal

- Dilates the afferent glomerular arteriole, constricts the efferent glomerular arteriole, and relaxes the mesangial cells. This increases pressure in the glomerular capillaries, thus increasing the glomerular filtration rate (GFR), resulting in greater filter load of sodium and water.
- Increases blood flow through the vasa recta, which will wash the solutes (NaCl and urea) out of the medullary interstitium. The lower osmolarity of the medullary interstitium leads to less reabsorption of tubular fluid and increased excretion.
- Decreases sodium reabsorption in the distal convoluted tubule (interaction with NCC) and cortical collecting duct of the nephron via

guanosine 3',5'-cyclic monophosphate (cGMP) dependent phosphorylation of ENaC.
- Inhibits renin secretion, thereby inhibiting the renin–angiotensin–aldosterone system.

Adrenal

- Reduces aldosterone secretion by the zona glomerulosa of the adrenal cortex.

Vascular

Relaxes vascular smooth muscle in arterioles and venules by:
- Membrane Receptor-mediated elevation of vascular smooth muscle cGMP
- Inhibition of the effects of catecholamines
  Promotes uterine spiral artery remodeling, which is important for preventing pregnancy-induced hypertension.

Cardiac

- Inhibits maladaptive cardiac hypertrophy
- Mice lacking cardiac NPRA develop increased cardiac mass and severe fibrosis and die suddenly
- Re-expression of NPRA rescues the phenotype.

Adipose tissue

- Increases the release of free fatty acids from adipose tissue. Plasma concentrations of glycerol and nonesterified fatty acids are increased by i.v. infusion of ANP in humans.
- Activates adipocyte plasma membrane type A guanylyl cyclase receptors NPR-A
- Increases intracellular cGMP levels that induce the phosphorylation of a hormone-sensitive lipase and perilipin A via the activation of a cGMP-dependent protein kinase-I (cGK-I)
- Does not modulate cAMP production or PKA activity

Measurement

BNP and NT-proBNP are measured by immunoassay.

Interpretation of BNP

- The main clinical utility of either BNP or NT-proBNP is that a normal level helps to rule out chronic heart failure in the emergency setting. An elevated BNP or NT-proBNP should never be used exclusively to "rule in" acute or chronic heart failure in the emergency setting due to lack of specificity   .
- Either BNP or NT-proBNP can also be used for screening and prognosis of heart failure.
- BNP and NT-proBNP are also typically increased in patients with left ventricular dysfunction, with or without symptoms (BNP accurately reflects current ventricular status, as its half-life is 20 minutes, as opposed to 1–2 hours for NT-proBNP).

A preoperative BNP can be predictive of a risk of an acute cardiac event during vascular surgery. A cutoff of 100 pg/ml has a sensitivity of approximately 100%, a negative predictive value of approximately 100%, a specificity of 90%, and a positive predictive value of 78% according to data from the United Kingdom. BNP is cleared by binding to natriuretic peptide receptors (NPRs) and neutral endopeptidase (NEP). Less than 5% of BNP is cleared renally. NT-proBNP is the inactive molecule resulting from cleavage of the prohormone Pro-BNP and is reliant solely on the kidney for excretion. The achilles heel of the NT-proBNP molecule is the overlap in kidney disease in the heart failure patient population. Some laboratories report in units ng per Litre (ng/L), which is equivalent to pg/mL. There is a diagnostic 'gray area', often defined as between 100 and 500 pg/mL, for which the test is considered

inconclusive, but, in general, levels above 500 pg/ml are considered to be an indicator of heart failure. This so-called gray zone has been addressed in several studies, and using clinical history or other available simple tools can help make the diagnosis. BNP may be a reliable predictor of cardiovascular mortality in diabetics. BNP was found to have an important role in prognostication of heart surgery patients and in the emergency department. Bhalla et al. showed that combining BNP with other tools like ICG can improve early diagnosis of heart failure and advance prevention strategies. Utility of BNP has also been explored in various settings like preeclampsia, ICU and shock and ESRD. The effect or race and gender on value of BNP and its utility in that context has been studied extensively.

NT-proBNP levels (in pg/mL) by NYHA functional class

	NYHA I	NYHA II	NYHA III	NYHA IV
5th Percentile	33	103	126	148
Mean	1015	1666	3029	3465
95th Percentile	3410	6567	10,449	12,188

The BNP test is used as an aid in the diagnosis and assessment of severity of heart failure. A recent meta-analysis concerning effects of BNP testing on clinical outcomes of patients presenting to the emergency department with acute dyspnea revealed that BNP testing led to a decrease in admission rates and decrease in mean length of stay, although neither was statistically significant. Effects on all cause hospital mortality was inconclusive. The BNP test is also used for the risk stratification of patients with acute coronary syndromes. When interpreting an elevated BNP level, values may be elevated due to factors other than heart failure. Lower levels are often seen in obese patients. Higher levels are seen in those with renal disease, in the absence of heart failure.

Therapeutic application

Recombinant BNP, nesiritide, has been suggested as a treatment for decompensated heart failure. However, a clinical trial failed to show a benefit of nesiritide in patients with acute decompensated heart failure. Blockade of neprilysin, a protease known to degrade members of the natriuretic peptide family, has also been suggested as a possible treatment for heart failure. Dual administration of neprilysin inhibitors and angiotensin receptor blockers has been shown to be advantageous to ACE inhibitors, the current first-line therapy, in multiple settings.

TROUBLESHOOTING

Cardiac marker
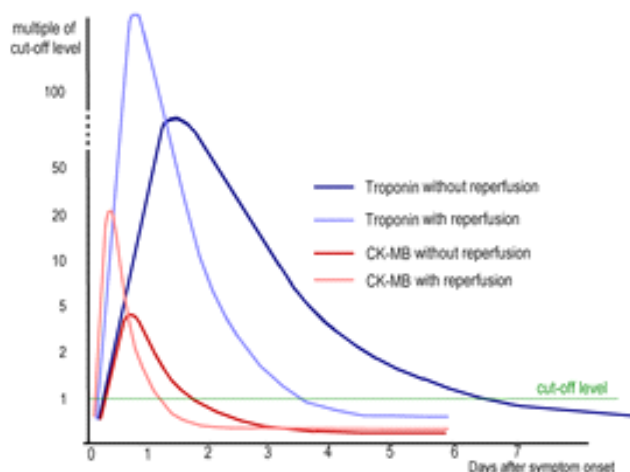
Kinetics of cardiac markers Troponin and CK-MB in myocardial infarction with or without reperfusion treatment.

Cardiac markers are biomarkers measured to evaluate heart function. They can be useful in the early prediction or diagnosis of disease. Although they are often discussed in the context of myocardial infarction, other conditions can lead to an elevation in cardiac marker level. Most of the early markers identified were enzymes, and as a result, the term "cardiac enzymes" is sometimes used. However, not all of the markers currently used are enzymes. For example, in formal usage, troponin would not be listed as a cardiac enzyme.

Applications of measurement

Measuring cardiac biomarkers can be a step toward making a diagnosis for a condition. Whereas cardiac imaging often confirms a diagnosis, simpler and less expensive cardiac biomarker measurements can advise a physician whether more complicated or invasive procedures are warranted. In many cases medical societies advise doctors to make biomarker measurements an initial testing strategy especially for patients at low risk of cardiac death. Many acute cardiac marker IVD products are targeted at nontraditional markets, e.g., the hospital ER instead of traditional hospital or clinical laboratory environments. Competition in the development of cardiac marker diagnostic products and their expansion into new markets is intense. Recently, the intentional destruction of myocardium by alcohol septal ablation has led to the identification of additional potential markers.

Types

Types of cardiac markers include the following:

Test	Sensitivity and specificity	Approximate peak	Description
Troponin test	The most sensitive and specific test for myocardial damage. Because it has increased specificity compared with CK-MB, troponin is composed of 3 proteins- Troponin C, Cardic troponin I, and Cardiac troponin T. Troponin I especially has a high affinity for myocardial injury.	12 hours	Troponin is released during MI from the cytosolic pool of the myocytes. Its subsequent release is prolonged with degradation of actin and myosin filaments. Isoforms of the protein, T and I, are specific to myocardium. Differential diagnosis of troponin elevation includes acute infarction, severe pulmonary embolism causing acute right heart overload, heart failure, myocarditis. Troponins can also calculate infarct size but the peak must be measured in the 3rd day. After myocyte injury, troponin is released in 2–4 hours and persists for up to 7 days. Normal value are - Troponin I <0.3 ng/ml and Troponin T <0.2 ng/ml
Creatine Kinase (CK-MB) test	It is relatively specific when skeletal muscle damage is not present.	10–24 hours	The CK-MB isoform of creatine kinase is expressed in heart muscle. It resides in the cytosol and facilitates movement of high energy phosphates into and out of mitochondria. Since it has a short duration, it cannot be used for late diagnosis of acute MI but can be used to suggest infarct extension if levels rise again. This is usually back to normal within 2–3 days. Normal range - 2-6 ng/ml

Test	Sensitivity and specificity	Approximate peak	Description
Lactate dehydrogenase (LDH)	LDH is not as specific as troponin.	72 hours	Lactate dehydrogenase catalyses the conversion of pyruvate to lactate. LDH-1 isozyme is normally found in the heart muscle and LDH-2 is found predominantly in blood serum. A high LDH-1 level to LDH-2 suggest MI. LDH levels are also high in tissue breakdown or hemolysis. It can mean cancer, meningitis, encephalitis, or HIV. This is usually back to normal 10–14 days.
Aspartate transaminase (AST)			This was the first used. It is not specific for heart damage, and it is also one of the liver transaminases.
Myoglobin (Mb)	Low specificity for myocardial infarction	2 hours	Myoglobin is used less than the other markers. Myoglobin is the primary oxygen-carrying pigment of muscle tissue. It is high when muscle tissue is damaged but it lacks specificity. It has the advantage of responding very rapidly, rising and falling earlier than CK-MB or troponin. It also has been used in assessing reperfusion after thrombolysis.
Ischemia-modified albumin (IMA)	Low specificity		IMA can be detected via the albumin cobalt binding (ACB) test, a limited available FDA approved assay. Myocardial ischemia alters the N-terminus of albumin reducing the ability of cobalt to bind to albumin. IMA measures ischemia in the blood vessels and thus returns results in minutes rather than traditional markers of necrosis that take hours. ACB test has low specificity therefore generating high number of false positives and must be used in conjunction with typical acute approaches such as ECG and physical exam. Additional studies are required.
Pro-brain natriuretic peptide			This is increased in patients with heart failure. It has been approved as a marker for acute congestive heart failure. Pt with < 80 have a much higher rate of symptom-free survival within a year. Generally, pt with CHF will have > 100.
Glycogen phosphorylase isoenzyme BB	0.854 and 0.767	7 hours	Glycogen phosphorylase isoenzyme BB (abbreviation: GPBB) is one of the three isoforms of glycogen phosphorylase. This isoform of the enzyme exists in cardiac (heart) and brain tissue. Because of the blood–brain barrier, GP-BB can be seen as being specific to heart muscle. GP-BB is one of the "new cardiac markers" which are considered to improve early diagnosis in acute coronary syndrome. During the process of ischemia, GP-BB is converted into a soluble form and is released into the blood. A rapid rise in blood levels can be seen in myocardial infarction and unstable angina. GP-BB is elevated 1–3 hours after process of ischemia.

Limitations

Depending on the marker, it can take between 2 and 24 hours for the level to increase in the blood. Additionally, determining the levels of cardiac markers in the laboratory - like many other lab measurements - takes substantial time. Cardiac markers are therefore not useful in diagnosing a myocardial infarction in the acute phase. The clinical presentation and results from an ECG are more appropriate in the acute situation. However, in 2010, research at the Baylor College of Medicine revealed that, using diagnostic nanochips and a swab of the cheek, cardiac biomarker readings from saliva can, with the ECG readings, determine within minutes whether someone is likely to have had a heart attack.

BOUQUET

In Lighter Vein

Exams are good.
They make
me realize that I can
sit idle for
3 hours without my phone

1 Kid asked me
What is Stress??

I Locked him in a Room
with High Speed Internet
and 1% Battery.

Me: I have many hidden talents

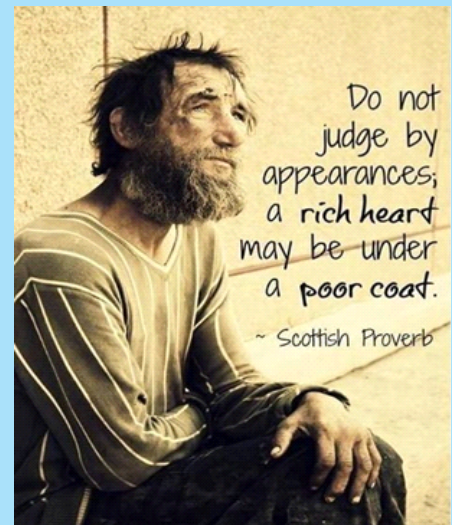Someone: Like what?

Me: I don't know, they're all hidden

Interviewer: Please Be Comfortable

Me:

Ohyaaro.com

Wisdom Whispers

BE MOTIVATED BY THE FEAR OF BEING AVERAGE

Do not judge by appearances; a rich heart may be under a poor coat.
~ Scottish Proverb

"There comes a time when you have to stop crossing oceans for people who wouldn't even jump puddles for you."

Brain Teasers

1. **Where is Brain Natriuretic Peptide produced?**
   A. Spleen   B. Liver   C. Heart   D. Kidneys

2. **Which is the first biomarker to rise after an episode of Myocradial Infarction?**
   A. CK –MB   B. Myoglobin   C. Troponin I   D. LDH

3. **How many types of TRoponins are there?**
   A. Troponin I   B. Troponin C   C. Troponin T   D. All of the above

4. **What is the normal range of CK MB in ng/mL?**
   A. 2-6   B. 6-12   C. 12-25   D. 25-50

ANSWER: 1: C, 2: C, 3: D, 4: A

TULIP NEWS

CHEST PAIN

...Every Second is Crucial

AMICHECK-TROP I
WB

Rapid test for Detection of cardiac Troponin I in human whole blood

For accurate diagnosis of cardiac event

- **Highly specific and sensitive result** - The test incorporates monoclonal antibodies to cTnI.

- **Detects even minor Myocardial Injury** - Detects cardiac troponin I ≥ 0.3 ng/ml.

- **Ideal for point of care testing** - Whole blood as specimen.

- **Rapid Turnaround Time** - 20 minutes assay.

- **Convenient Pack Size & Storage** - 10 tests pack, 4-30^0 C storage.

FOR SAFE DECISION MAKING AT INTENSIVE CARE FACILITIES!

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