Myocardial infarction

The normal views
What is Ischemic Heart Disease?

- **Ischemic heart disease** is caused by an imbalance between the myocardial blood flow and the metabolic demand of the myocardium.
- Reduction in coronary blood flow is related to progressive atherosclerosis with increasing occlusion of coronary arteries. Blood flow can be further decreased by superimposed events such as vasospasm, thrombosis, or circulatory changes leading to hypoperfusion.
- Coronary artery perfusion depends upon the pressure differential between the ostia (aortic diastolic pressure) and coronary sinus (right atrial pressure). Coronary blood flow is reduced during systole because of Venturi effects at the coronary orifices and compression of intramuscular arteries during ventricular contraction.

Factors reducing coronary blood flow include:

1. Decreased aortic diastolic pressure
2. Increased intraventricular pressure and myocardial contraction
3. Coronary artery stenosis, which can be further subdivided into the following etiologies:
   - Fixed coronary stenosis
   - Acute plaque change (rupture, hemorrhage)
   - Coronary artery thrombosis
   - Vasoconstriction
4. Aortic valve stenosis and regurgitation
5. Increased right atrial pressure
40 micron collateral vessels are present in all hearts with pressure gradients permitting flow, despite occlusion of major vessels. In general, the cross-sectional area of the coronary artery lumen must be reduced by more than 75% to significantly affect perfusion. Coronary atherosclerosis is diffuse (involving more than one major arterial branch) but is often segmental, and typically involves the proximal 2 cm of arteries (epicardial).

"Thrombolytic therapy" with agents such as streptokinase or tissue plasminogen activator (TPA) is often used to try and lyse a recently formed thrombus. Such therapy with lysis of the thrombus can re-establish blood flow in a majority of cases. This helps to prevent significant myocardial injury, if early (less than an hour or so) in the course of events, and can at least help to reduce further damage.
There is a severe degree of narrowing in this coronary artery. It is "complex" in that there is a large area of calcification on the lower right, which appears bluish on this H&E stain. Complex atheroma have calcification, thrombosis, or hemorrhage. Such calcification would make coronary angioplasty difficult.

This distal portion of coronary artery shows significant narrowing. Such distal involvement is typical of severe coronary atherosclerosis, such as can appear with diabetes mellitus or familial hypercholesterolemia. This would make a coronary bypass operation difficult.

There is a pink to red recent thrombosis in this narrowed coronary artery. The open, needle-like spaces in the atheromatous plaque are cholesterol clefts.

This is the normal appearance of myocardial fibers in longitudinal section. Note the central nuclei and the syncytial arrangement of the fibers, some of which have pale pink intercalated disks.

This high magnification of the atheroma shows numerous foam cells and an occasional cholesterol cleft. A few dark blue inflammatory cells are scattered within the atheroma.
Patterns of Ischemic Heart Disease (IHD)

Angina pectoris - a symptom complex of IHD characterized by paroxysmal attacks of chest pain, usually substernal or precordial, caused by myocardial ischemia that falls short of inducing infarction. There are several patterns:

1. **Stable angina (typical)** - paroxysms of pain related to exertion and relieved by rest or vasodilators. Subendocardial ischemia with ST-segment depression

2. **Variant or Prinzmetal's angina** - angina that classically occurs at rest and is caused by reversible spasm in normal to severely atherosclerotic coronary arteries. ST-segment elevation or depression maybe seen during attacks.

3. **Unstable angina** - prolonged pain, pain at rest in a person with stable angina, or worsening of pain in stable angina. ST-segment depression (usually) and ST-segment elevation.

4. **Sudden cardiac death** - Unexpected death from cardiac causes usually within one hour after a cardiac event or without the onset of symptoms. Usually high-grade stenosis with acute coronary changes.

Myocardial infarction

- A myocardial infarct represents **permanent cellular injury and necrosis** after a prolonged ischaemic episode.

- In the vast majority (ca. 90%) of cases it follows from a thrombotic occlusion superimposed on atherosclerotic obstructive coronary artery disease.

- Rarely infarction follows coronary emboli, spasm, dissection or vasculitis.
### Myocardial infarction

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Most Patients</strong></td>
<td>Retrosternal chest pain &quot;heaviness&quot;,&quot;tightness&quot;, &quot;weight&quot;. Poor response or failure to respond to nitrates.</td>
</tr>
<tr>
<td><strong>Diabetics</strong></td>
<td>There may be none. Heart failure unexplained.</td>
</tr>
<tr>
<td><strong>Heart Transplant</strong></td>
<td>No pain. Failure or shock (sudden death)</td>
</tr>
<tr>
<td><strong>Elderly</strong></td>
<td>May be none. Typical pain and/or breathlessness. Unexplained heart failure.</td>
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### INFARCT LOCALIZATION

Infarcts are categorized into:

- **ANTERIOR**, which usually involve occlusion of the left coronary artery, in particular the left anterior descending (LAD)
  (The subdivisions: anteroseptal, lateral, anterolateral)
- **INFERIOR**, which usually reflect right coronary occlusion but occasionally circumflex occlusion
  (The subdivisions: interior, inferolateral, infero-septal)
- **POSTERIOR**, which may involve right or circumflex system.
The gross morphologic appearance of a myocardial infarction can vary. Patterns include:

- **Transmural infarct** - involving the entire thickness of the left ventricular wall from endocardium to epicardium, usually the anterior free wall and posterior free wall and septum with extension into the RV wall in 15-30%. Isolated infarcts of RV and right atrium are extremely rare.

- **Subendocardial infarct** - multifocal areas of necrosis confined to the inner 1/3-1/2 of the left ventricular wall. These do not show the same evolution of changes seen in a transmural MI.

### MYOCARDIAL INFARCTION

**Gross morphologic changes evolve over time as follows:**

<table>
<thead>
<tr>
<th>Time from Onset</th>
<th>Gross Morphologic Finding</th>
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<tbody>
<tr>
<td>18 - 24 Hours</td>
<td>Pallor of myocardium</td>
</tr>
<tr>
<td>24 - 72 Hours</td>
<td>Pallor with some hyperemia</td>
</tr>
<tr>
<td>3 - 7 Days</td>
<td>Hyperemic border with central yellowing</td>
</tr>
<tr>
<td>10 - 21 Days</td>
<td>Maximally yellow and soft with vascular margins</td>
</tr>
<tr>
<td>7 weeks</td>
<td>White fibrosis</td>
</tr>
</tbody>
</table>
The anterior surface of the heart demonstrates an opened left anterior descending coronary artery. Within the lumen of the coronary can be seen a dark red recent coronary thrombosis. The dull red color to the myocardium as seen below the glistening epicardium to the lower right of the thrombus is consistent with underlying myocardial infarction.

This is the left ventricular wall which has been sectioned lengthwise to reveal a large recent myocardial infarction. The center of the infarct contains necrotic muscle that appears yellow-tan. Surrounding this is a zone of red hyperemia. Remaining viable myocardium is reddish-brown.
This cross section through the heart demonstrates the left ventricle on the left. Extending from the anterior portion and into the septum is a large recent myocardial infarction. The center is tan with surrounding hyperemia. The infarction is "transmural" in that it extends through the full thickness of the wall.

### MYOCARDIAL INFARCTION
Microscopic morphologic changes evolve over time as follows:

<table>
<thead>
<tr>
<th>Time from Onset</th>
<th>Microscopic Morphologic Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 3 Hours</td>
<td>Wavy myocardial fibers</td>
</tr>
<tr>
<td>2 - 3 Hours</td>
<td>Staining defect with tetrazolium or basic fuchsin dye</td>
</tr>
<tr>
<td>4 - 12 Hours</td>
<td>Coagulation necrosis with loss of cross striations, contraction bands, edema, hemorrhage, and early neutrophilic infiltrate</td>
</tr>
<tr>
<td>18 - 24 Hours</td>
<td>Continuing coagulation necrosis, pyknosis of nuclei, and marginal contraction bands</td>
</tr>
<tr>
<td>24 - 72 Hours</td>
<td>Total loss of nuclei and striations along with heavy neutrophilic infiltrate</td>
</tr>
<tr>
<td>3 - 7 Days</td>
<td>Macrophage and mononuclear infiltration begin, fibrovascular response begins</td>
</tr>
<tr>
<td>10 - 21 Days</td>
<td>Fibrovascular response with prominent granulation tissue</td>
</tr>
<tr>
<td>7 Weeks</td>
<td>Fibrosis</td>
</tr>
</tbody>
</table>
The earliest change histologically seen with acute myocardial infarction in the first day is contraction band necrosis. The myocardial fibers are beginning to lose cross striations and the nuclei are not clearly visible in most of the cells seen here. Note the many irregular darker pink wavy contraction bands extending across the fibers.

This high power microscopic view of the myocardium demonstrates an infarction of about 1 to 2 days in duration. The myocardial fibers have dark red contraction bands extending across them. The myocardial cell nuclei have almost all disappeared. There is beginning acute inflammation. Clinically, such an acute myocardial infarction is marked by changes in the electrocardiogram and by a rise in the MB fraction of creatine kinase.

In this microscopic view of a recent myocardial infarction, there is extensive hemorrhage along with myocardial fiber necrosis with contraction bands and loss of nuclei.

This myocardial infarction is about 3 to 4 days old. There is an extensive acute inflammatory cell infiltrate and the myocardial fibers are so necrotic that the outlines of them are only barely visible.
This is an intermediate myocardial infarction of 1 to 2 weeks in age. Note that there are remaining normal myocardial fibers at the top. Below these fibers are many macrophages along with numerous capillaries and little collagenization.

There is pale white collagen within the interstitium between myocardial fibers. This represents an area of remote infarction.

The mentioned gross and microscopic changes over time can vary. In general, a larger infarct will evolve through these changes more slowly than a small infarct. Clinical complications of myocardial infarction will depend upon the size and location of the infarction, as well as pre-existing myocardial damage.
COMPLICATIONS CAN INCLUDE:
- Arrhythmias and conduction defects, with possible "sudden death"
- Extension of infarction, or re-infarction
- Congestive heart failure (pulmonary edema)
- Cardiogenic shock
- Pericarditis
- Mural thrombosis, with possible embolization
- Myocardial wall rupture, with possible tamponade
- Papillary muscle rupture, with possible valvular insufficiency
- Ventricular aneurysm formation

Sudden death is defined as death occurring within an hour of onset of symptoms. Such an occurrence often complicates ischemic heart disease. Such patients tend to have severe coronary atherosclerosis (>75% lumenal narrowing). Often, a complication such as coronary thrombosis or plaque hemorrhage or rupture has occurred. The mechanism of death is usually an arrhythmia.

Echocardiogram after acute inferior myocardial infarction. The posterobasal and diaphragmatic segments are akinetic.
One complication of a transmural myocardial infarction is rupture of the myocardium. This is most likely to occur in the first week between 3 to 5 days following the initial event, when the myocardium is the softest. The white arrow marks the point of rupture in this anterior-inferior myocardial infarction of the left ventricular free wall and septum. Note the dark red blood clot forming the hemopericardium. The hemopericardium can lead to tamponade.

An example of hemopericardium: such a massive amount of hemorrhage can lead to cardiac tamponade.
In cross section, the point of rupture of the myocardium is shown with the arrow. In this case, there was a previous myocardial infarction 3 weeks before, and another myocardial infarction occurred, rupturing through the already thin ventricular wall 3 days later.

A complication of infarction is aneurysm formation, which is the bulge seen here in the left ventricular wall. Note the very thin white wall of the aneurysm toward the apex.
Ischemic Cardiomyopathy

In this condition, there may be previous myocardial infarction, but the disease results from severe coronary atherosclerosis involving all major branches. The result is an inadequate vascular supply which leads to myocyte loss. The myocyte loss coupled with fibrosis in the form of interstitial collagen deposition results in decreased compliance, which along with the accompanying cardiac dilation, results in overload of remaining myocytes. This keeps the process going, with compensation by continuing myocyte hypertrophy. There may even be compensation through myocyte hyperplasia as well as hypertrophy, which can explain the enormous size (2 to 3 times normal size) of the resulting heart. Eventually, the heart can no longer compensate, and cardiac failure ensues with arrhythmias and/or ischemic events.

Thus, clinically, there is slow, progressive heart failure with or without a history of a previous MI or anginal pain. Ischemic cardiomyopathy is responsible for as much as 40% of the mortality in IHD.

The myocytes here are hypertrophied, marked by the large, dark nuclei, and there is interstitial fibrosis. This is an example of cardiomyopathy. In this case, long-standing, severe occlusive atherosclerosis led to "ischemic" cardiomyopathy.
Electrocardiogram (ECG)

The ECG represents an excellent means of evaluating and recognizing acute myocardial infarction. However, if recorded early enough it may be normal in about one-third of patients. Thus a normal initial ECG does not rule out infarction or CAD; however, it does seem to indicate a low likelihood of complications. Typically, twelve-lead ECGs is used for diagnosis and localization of acute infarction.
Electrocardiogram (ECG) of a normal single heartbeat. The profile consists of 5 major waves: P, Q, R, S, and T. The P and QRS peaks represent atrial and ventricular contractions, respectively. The T wave reflects electrical recovery of the ventricles.

Electrocardiogram (ECG) hours to days after an acute myocardial infarction (AMI). Typical characteristics are elevation of the ST segment, inversion of the T wave and an enlarged Q wave.

Evolving ECG Changes of Myocardial Infarction
**EVOLVING ECG CHANGES OF MYOCARDIAL INFARCTION**

ST segment elevation with tall peaked T waves in the leads orientated to the damaged areas – the hyperacute phase of epicardial injury.

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**EVOLVING ECG CHANGES OF MYOCARDIAL INFARCTION**

Q waves appear within hours and ST elevation persists. Pathological Q waves are usually 0.04 seconds or greater in duration and/or to a depth equivalent to 25% of the height of the R wave.
In the subsequent days the ST segments gradually return to baseline and T wave inversion occurs.

Over weeks the ST segment usually reverts to normal; persistent elevation after six weeks suggests aneurysm formation. Although Q waves usually remain at follow-up, 10% may have normal ECGs.
Laboratory Diagnosis of Myocardial Infarction

A number of laboratory tests are available. None is completely sensitive and specific for myocardial infarction, particularly in the hours following onset of symptoms. Timing is important, as are correlation with patient symptoms, electrocardiograms, and angiographic studies.

The following tests are available as markers for acute myocardial infarction:

- Creatine Kinase - Total
- Creatine Kinase - MB Fraction
- CK-MB Isoforms
  - Troponins (I and T)
- Myoglobin
- Lactate dehydrogenase

Creatine Kinase - Total:

The total CK is a simple and inexpensive test that is readily available using many laboratory instruments. However, an elevation in total CK is not specific for myocardial injury, because most CK is located in skeletal muscle, and elevations are possible from a variety of non-cardiac conditions.
Creatine Kinase - MB Fraction:

Creatine kinase can be further subdivided into three isoenzymes: MM, MB, and BB. The MM fraction is present in both cardiac and skeletal muscle, but the MB fraction is much more specific for cardiac muscle: about 15 to 40% of CK in cardiac muscle is MB, while less than 2% in skeletal muscle is MB. The BB fraction (found in brain, bowel, and bladder) is not routinely measured.

Thus, CK-MB is a very good marker for acute myocardial injury, because of its excellent specificity, and it rises in serum within 2 to 8 hours of onset of acute myocardial infarction. Serial measurements every 2 to 4 hours for a period of 9 to 12 hours after the patient is first seen will provide a pattern to determine whether the CK-MB is rising, indicative of myocardial injury. The CK-MB is also useful for diagnosis of reinfarction or extensive of an MI because it begins to fall after a day, dissipating in 1 to 3 days, so subsequent elevations are indicative of another event.

A "cardiac index" can provide a useful indicator for early MI. This is calculated as a ratio of total CK to CK-MB, and is a sensitive indicator of myocardial injury when the CK-MB is elevated.

CK-MB Isoforms:

The CK-MB fraction exists in two isoforms called 1 and 2 identified by electrophoretic methodology. The ratio of isoform 2 to 1 can provide information about myocardial injury.

An isoform ratio of 1.5 or greater is an excellent indicator for early acute myocardial infarction. CK-MB isoform 2 demonstrates elevation even before CK-MB by laboratory testing.

However, the disadvantage of this method is that it is skilled labor intensive because electrophoresis is required, and large numbers of samples cannot be run simultaneously nor continuously. False positive results with congestive heart failure and other conditions can occur.
Troponins:
Troponin I and T are structural components of cardiac muscle. They are released into the bloodstream with myocardial injury. They are highly specific for myocardial injury--more so than CK-MB--and help to exclude elevations of CK with skeletal muscle trauma. Troponins will begin to increase following MI within 3 to 12 hours, about the same time frame as CK-MB. However, the rate of rise for early infarction may not be as dramatic as for CK-MB. Troponins will remain elevated longer than CK--up to 5 to 9 days for troponin I and up to 2 weeks for troponin T. This makes troponins a superior marker for diagnosing myocardial infarction in the recent past--better than lactate dehydrogenase (LDH). However, this continued elevation has the disadvantage of making it more difficult to diagnose reinfarction or extension of infarction in a patient who has already suffered an initial MI. Troponin T lacks some specificity because elevations can appear with skeletal myopathies and with renal failure.

Myoglobin:
Myoglobin is a protein found in skeletal and cardiac muscle which binds oxygen. It is a very sensitive indicator of muscle injury. The rise in myoglobin can help to determine the size of an infarction. A negative myoglobin can help to rule out myocardial infarction. It is elevated even before CK-MB. However, it is not specific for cardiac muscle, and can be elevated with any form of injury to skeletal muscle.
Lactate dehydrogenase:

The LDH has been supplanted by other tests. It begins to rise in 12 to 24 hours following MI, and peaks in 2 to 3 days, gradually dissipating in 5 to 14 days. Measurement of LDH isoenzymes is necessary for greater specificity for cardiac injury. There are 5 isoenzymes (1 through 5). Ordinarily, isoenzyme 2 is greater than 1, but with myocardial injury, this pattern is "flipped" and 1 is higher than 2. LDH-5 from liver may be increased with centrilobular necrosis from passive congestion with congestive heart failure following ischemic myocardial injury.

Serum enzyme elevation in acute myocardial infarction

(AST=Aspartate transaminase, CK=creatine kinase, CK-MB=isoenzyme for cardiac muscle, LDH=lactate dehydrogenase)
General scheme of management

Infarction < 6 hours
Cardiogenic shock
Streptokinase

Stable
Infarct 2–3 hours
Check for contraindications
Streptokinase iv 1 million units
Reperfusion
Angiography
Infarction
Conventional therapy

Infarct > 3 hours
Conventional therapy

PRACTICAL POINTS
- Relief of pain is essential. Ask patients frequently; they often suffer in silence.
- Oxygen is not routine but may help in heart failure.
- Anxiety responds to explanation and pain relief.
- Subcutaneous heparin is used to prevent deep venous thrombosis.
- Average hospital stay is 8–10 days with rapid mobilization.
- Cardiac care units optimize trained staff and deal with complications.
- Cardiogenic shock is invariably fatal but thrombolysis and angioplasty offer new hope.
- Pericarditis occurs in nearly one-third of patients and responds to indomethacin.
- Prompt attention to arrhythmias may save life as the period of electrical instability is usually short.
- Thrombolysis and angioplasty are likely to increase as forms of immediate therapy, though the ventricle is irreversibly lost if deprived of blood for over 3–4 hours.