CHAPTER - 2.

DIFFERENT ASPECTS RELATED TO CORONARY ARTERY DISEASE.
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2.1 IMPORTANCE OF CORONARY ARTERY DISEASE.

The coronary artery disease is a major cause of death throughout the world. The diagnosis is normally done from the Electrocardiogram (ECG), as well as from some other parameters. These details starting from heart are discussed.

2.2. DETAILS OF THE HEART. [1],[2],[3],[4],[5],[37].

The position of the heart within the body determines the "view" of the cardiac electrical activity that can be observed from any site on the body surface. There are four chambers within the heart, the upper one is called as the atrium and the lower one the ventricle. The atria are located in the top or base of the heart, and the ventricles taper toward the bottom or apex. However the right and left sides of the heart are not directly aligned with the right and left sides of the body. The long axis of the heart, which extends from base to apex, is tilted to the left and anteriorly at its epical end. Also, the heart is rotated so that the right atrium and ventricle are more anterior than the left atrium and ventricle.

2.2.1. The Cardiac Cycle.

The mechanical pumping action of the heart is produced by myocardial cells, which contain contractile proteins. The timing and synchronization of contraction of these cells are controlled by cells of the pace making and conduction system that is described below. Impulses generated within these cells create a rhythmic repetition of events called cardiac cycles. Each cycle consists of electrical and mechanical activation (systole) and recovery (diastole). The mechanical activation can also be described by terms 'shortening', 'contraction', 'emptying' for systole. For diastole, mechanical activation is described by terms like 'lengthening', 'relaxation', 'filling'. The electrical activity is described by terms like 'activation', 'excitation', 'depolarization', for systole and by 'recovery', 'repolarization', for diastole. Since the electrical events initiate the mechanical events, there is a brief delay between the onset of electrical and mechanical systole and of electrical and mechanical diastole.

During electrical diastole, the cell has a base line negative electrical potential and is also in mechanical diastole with separation of contractile proteins. An electrical
impulse arriving at the cell allows positively charged ions to cross the cell membrane causing depolarization of the cell. This movement of ions initiates electrical systole, which is characterized by an action potential. This electrical event then initiates mechanical systole in which the contractile proteins slide over each other, thereby shortening the cell. Electrical systole continues for a period of time until the positively charged ions are pumped out causing the repolarization of the cell. The electrical potential returns to its negative resting level. This return of electrical diastole causes the contractile proteins to separate again. The cell is then capable of being reactivated if another electrical impulse arrives at its membrane.

Figure 2.1. A series of four myocardial cells in their resting state in (A) and in progression through a cardiac cycle (B-E).
The electrical and mechanical changes in a series of myocardial cells as they progress through a cardiac cycle are illustrated in Fig. 2.1. In (A) the four representative cells are in their resting or repolarized state. Electrically, the cells have negative charges, while mechanically their contractile proteins are separated. An electrical current arrives at the second myocardial cell in (B) causing electrical and then mechanical systole. The wave of depolarization in (C) has spread throughout all the myocardial cells. In (D), the recovery or repolarization process begins in the second cell, which had been the first to depolarize. Finally the wave of repolarization in (E) has spread throughout all of the myocardial cells and they await the coming of another electrical current.

![Diagram of myocardial cell changes](image)

Figure 2.2. The ECG waveforms representing the activation and recovery of myocardial cells.
Fig. 2.2, shows the relationship between the intracellular electrical recording from a single myocardial cell combined with an electrocardiogram (ECG) recording from the body surface. The ECG recording is formed by the summation of electrical signals from all of the myocardial cells. When the cells are in their resting state, the ECG recording produces a flat baseline. The onset of depolarization of the cells produces a relatively high frequency waveform. Then, while depolarization persists, the ECG returns to the baseline. Repolarization of the myocardial cells is represented on the ECG by a lower frequency waveform in the opposite direction from that representing depolarization.

2.2.2. Cardiac Impulse Formation and Conduction.
The electrical activation of a single cardiac cell or even a small group of cells does not produce enough current on the body surface. Clinical electrocardiography is made possible by the activation of atrial and ventricular myocardial masses that are of sufficient magnitude for their electrical activity to be recorded on the body surface. Myocardial cells normally lack the ability for either spontaneous formation or rapid conduction of an electrical impulse. They are dependent for these functions on special cells of the cardiac pace making and conduction system placed strategically throughout the heart. This is shown in Fig. 2.3. These cells are arranged in nodes, bundles, bundle branches, and branching network of fascicles. They lack contractile capability, but are able to achieve spontaneous electrical impulse formation (act as pacemakers) and to alter the speed of electrical conduction. The intrinsic pace making rate is most rapid in the specialized cells in the atria and slowest in the cells in the ventricles. The balance between sympathetic and parasympathetic components of the autonomic nervous system alters this intrinsic rate.

Fig. 2.3 illustrates the anatomic relationships between the cardiac pumping chambers and the specialized pacemaking and conduction system. The sinoatrial (SA) node is located high in the right atrium near its junction with the superior vena cava (SVC). The SA node is the predominant cardiac pacemaker, and its highly developed autonomic regulation allows the heart to alter its pumping rate to meet the changing needs of the body. The atrioventricular (AV) node is located low in the right atrium adjacent to the interatrial septum. Its primary function is to slow electrical conduction
Figure 2.3. Three views of anatomic relationship between the cardiac pumping chambers and the structures of pace making and conduction system displayed in A, B, C.
sufficiently to synchronize atrial and ventricular pumping. Normally the AV node is the only structure capable of conducting impulses from the atria to the ventricles. In the atria, the electrical impulse spreads through the myocardium without the need for specialized conduction bundles. However, rapidly conducting bundles with branches and fascicles are present in the ventricles so that the activation of the myocardium at the base can be delayed until the apical region has been activated. Since the pulmonary and aortic outflow valves are located at the base of the ventricles, this sequence of electrical activation is necessary to achieve the most efficient level of cardiac pumping.

The intraventricular conduction pathways include a common bundle (Bundle of His), which leads from the AV node to the summit of the interventricular septum, and its right and left bundle branches, which proceed along the septal surfaces to their respective ventricles. The left bundle branch fans into fascicles that proceed along the left septal surface and toward the two papillary muscles of the mitral valve. The right bundle branch remains compact until it reaches the right distal septal surface, where it branches into the distal interventricular septum and toward the lateral valve of the right ventricle. These intraventricular conduction pathways are composed of fibers that contain the Purkije cells with specialized capabilities to both pacemaking and rapid conduction of electrical impulses. Fascicles composed of Purkinje fibers form networks that extends just beneath the surface of right and left ventricular endocardium. The impulses then proceed slowly from endocardium to epicardium throughout the right and left ventricles.

The initial wave of a cardiac cycle represents activation of the atria and is called the P wave (Fig. 2.4). The first part of the P wave represents the activation of the right atrium. The middle section of the P wave represents completion of right atrial activation and initiation of left atrial activation. The final section of the P wave represents completion of left atrial activation. The AV node is activated by the middle of the P wave. The waves that represents electrical recovery of the atria is usually obscured by the waves representing ventricular depolarization.
Figure 2.4. ECG segment with timing of activation of pacemaking and conduction system.

Figure 2.5. Monophasic, biphasic and triphasic QRS complexes.

The next group of waves recorded is the QRS complex, which represents the activation of the ventricles. By convention, a negative wave at the onset of the QRS complex is called a Q wave. The predominant portion of the QRS complex recorded is normally positive and is called R wave, regardless of whether or not it is preceded...
by a Q wave. The QRS complex normally appears as monophasic, biphasic or triphasic individual waveforms (Fig.2.5). A negative deflection following an R wave is called an S wave. When a second positive deflection occurs it is termed R'.

Figure 2.6. Recordings from ventricular myocardial cells on the
Endocardial (1) and epicardial (2) surfaces shown in A.
A schematic of ECG waveform in B

The wave in the cardiac cycle that represents recovery of the ventricles is called the T wave. Recovery of the ventricular cells causes a counter current to that of depolarization, the T wave may thought to be inverted in relation to the QRS complex. However, epicardial cells repolarize earlier than endocardial cells, thereby causing the wave of repolarization to spread in the direction opposite depolarization. This results in a T wave deflected in a similar direction as the QRS complex (Fig 2.6).
The T wave is sometimes followed by another small upright wave (the source of which is uncertain) called the U wave. The time from the onset of the P wave to the onset of the QRS complex is called the PR interval, whether the first wave in this complex is a Q wave or a R wave (Fig. 2.7). The designation PR segment refers the time from the end of P wave to the onset of QRS complex. The QRS interval measures the time from beginning to end of ventricular activation. Since activation of the thicker left ventricle requires more time than the right ventricle, the terminal portion of the QRS complex represents only left ventricular activation.

The ST segment is the interval between the end of ventricular activation and the beginning of ventricular recovery. The term ST segment is used regardless of whether the final wave of the QRS complex is a R or a S wave. The junction of the QRS complex and the ST segment is called the J point. The interval from the onset of ventricular activation to the end of ventricular recovery is called the QT interval. At low heart rates in a healthy person, the PR, ST, TP segments are at the same level and from the isoelectric line. This line is considered base line for measuring amplitudes of the various waveforms. The TP segment disappears at higher heart rates when the T wave merges with the following P wave.

Figure 2.7. Different intervals of ECG segment.
2.3. EVOLUTION OF FRONTAL PLANE LEADS.

The standard ECG used for clinical diagnosis is obtained as 12 lead ECG. By recording the electrical potential difference between a positive and a negative body surface electrode, referred to as lead. Six of these leads provide views in the frontal plane and six in the transverse (horizontal) plane. In the early 1900s Einthoven and colleagues placed recording electrode on the right and left arms and the left leg and an additional electrode on the right leg to ground the electrocardiogramme (EKG). Three leads (I, II and III) are produced using a pair of limb electrodes, one serving as the positive and one as the negative pole (Fig. 2.8). The positive poles of these leads are located to the left of inferiorly so that the cardiac waveforms appear primarily upright on the recording. For lead I, the left arm electrode is the positive pole on the right arm electrode is the negative pole. Lead II, with the positive pole on the left leg and its negative pole on the right arm, provides a view of the cardiac electrical activity. Finally lead III has its positive pole on the left leg and its negative pole on the left arm.

![Figure 2.8](image-url)  The method of ECG recording of Einthoven’s three original limb leads.
The 60° angles between leads I, II and III create wide gaps among the three views of cardiac electrical activity. Wilson and co-workers developed methods for filling these gaps by creating a central terminal, connecting all three limb electrodes through a 5000 ohm resistor. A lead using this central terminal as its negative poles and exploring electrodes at any site on the body surface as its positive poles is termed as a V lead. When the central terminal is connected to an exploring electrode on an extremity, the electrical signals are small. The amplitude of these signals in the frontal plane may be increased or augmented by disconnecting the attachment of the central terminal to the explored limb. Such an augmented V lead is termed aV. Thus aVF measures the potential difference between the left leg and the average of the potentials at the right and the left arms. The gap between leads I and II is filled by lead aVR, between leads II and III by lead aVF, and between leads III and I by lead aVL. (Fig. 2.9).

Figure 2.9. Augmented V leads, aVR, aVL, aVF.
Addition of these three aV leads to the triaxial systems produces a hexaxial system (Fig. 2.10) for viewing the cardiac electrical activity in the frontal plane with the six leads separated by angles of 30°. Using lead I (located at 0°) as the reference, positive designation increase at 30° increments in a clock wise direction to +180°, and negative designation increase at the same increments in a counter clockwise direction upto -180°. Lead II appears at +60°, aVF at +90° and III at 120° respectively. Leads aVL and aVR have designation of -30° and -150° respectively.

Figure 2.10. The hexaxial reference system.
2.4 TRANSVERSE PLANE LEADS.

The standard 12-lead ECG includes six frontal plane leads and also six leads relating to the transverse plane of the body. These leads, introduced by Wilson, are produced by connecting the central terminal to an exploring electrode placed at various positions across the chest wall. Since the sites of these electrodes are very close to the heart itself, they are termed precordial, and the electrical signals have sufficient amplitude so that augmentation is not necessary. The six leads are labeled V1 through V6 because the central terminal connected to all three of the limb electrodes provides their negative poles (Fig. 2.11). Lead V1 means positive pole on the right anterior precordium and negative pole in the center of the chest. The sites of the exploring electrode are determined by bony landmarks on the anterior and left lateral aspects of the precordium, and the angles between the six transverse plane leads are smaller and more variable than those between the six frontal plane leads.

![Figure 2.11. ECG recording with a precordial leads along with an example of lead v2](image-url)
2.5. DISPLAY OF THE 12 STANDARD LEADS.

The 12 lead ECG typically presented via a three-channel recording with the two groups of frontal plane leads preceding the two groups of transverse plane leads. The six precordial leads are presented in their sequence V1-V6. The six frontal plane leads are typically presented in the groups in which they were historically developed (I, II, III; then aVR, aVL, and aVF). The lead aVR is inverted to –aVR to provide the same leftward orientation as leads I and II. A typical ECG is shown in Fig. 2.12.

![Diagram of 12 standard leads](image)

**Figure 2.12.** The display of 12 standard leads presented in their orderly sequences in both the frontal and transverse planes.
2.6 ECG FEATURES USED FOR ANALYSIS.

For every ECG there are nine features those should be examined systematically. They are i) Rate and regularity, ii) P wave morphology, iii) PR interval, iv) QRS complex morphology, v) ST segment morphology, vi) T wave morphology, vii) U wave morphology, viii) QTc interval, ix) Rhythm.

2.6.1 Rate and Regularity.

The cardiac rhythm is rarely precisely regular. Even when the cardiac electrical activity is initiated normally in the sinus node, the rate is affected by the autonomic nervous system. When the individual is at rest, minor variations in the autonomic balance are produced by the phases of the respiratory cycle. Normally, there are the same number of P waves and QRS complexes and either may be used to determine the cardiac rate and regularity. When, in the presence of certain abnormal cardiac rhythms, the numbers of P waves and QRS complexes are not the same, the atrial and ventricular rates and regularities must be determined separately.

Figure 2.13. Different cardiac conditions according to the heart rate.
When the rate is greater than hundred beats /min it is called tachycardia and if the rate is less than 60 beats/min it is called bradycardia. The normal heart rate is between 60 to 100 beats/min, as shown in Fig. 2.13.

2.6.2 P wave morphology.

At either slow or normal heart rates, the small, rounded P wave is clearly visible just before the taller, more peaked QRS complex. At more rapid rates the P wave may merge with the preceding T wave and become difficult to identify.

i) The P wave contour is normally smooth, and it is either entirely positive or negative (monophasic) in all leads except V1. The divergence of right and left atrial activation may produce a diphasic P wave. The contributions of right and left atrial activation to the beginning, middle, and end of the P wave are indicated in Fig. 2.14.

ii) The P wave duration is normally less than 0.12 sec.

iii) The P wave amplitude is normally less than 0.25 mV in all leads.

iv) The P wave normally appears entirely upright in leads such as aVL, I, II, III, aVF, and V4-V6. It is negative in aVR.

Figure 2.14. A) The typical normal P wave in lead such as II.

B) The typical normal P wave in lead such as V1.

2.6.3 PR interval

The PR interval measures the time required for the impulse to travel from the atrial myocardium adjacent to the SA node to the ventricular myocardium adjacent to
the fibers of the Purkinje network. This duration is normally 0.10 sec. to 0.22 sec.\[2\]
A major portion of the PR interval reflects the slow conduction through the AV node, which is controlled by sympathetic-parasympathetic balance within the autonomic nervous system. Therefore, the PR interval varies with the heart rate, being shorter at faster rates when the sympathetic component predominates, and vice versa. The PR interval tends to increase with age.

<table>
<thead>
<tr>
<th>Normal PR interval duration</th>
<th>0.10-0.22 sec.</th>
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<tbody>
<tr>
<td>In childhood</td>
<td>0.10-0.12 sec.</td>
</tr>
<tr>
<td>In adolescence</td>
<td>0.12-0.16 sec.</td>
</tr>
<tr>
<td>In adulthood</td>
<td>0.14-0.22 sec.</td>
</tr>
</tbody>
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However as per American Heart Association documentation normal PR interval should be less than about 0.2 sec.\[83\].

2.6.4 QRS complex morphology.

The QRS complex is composed of higher frequency signals than are the P and T waves, thereby causing its contour to be peaked rather than rounded. The deflections in the QRS complex are specifically labeled as Q wave, R wave, and S wave.

i) Q waves: In some leads, V1, V2, and V3, the presence of a Q wave should be considered abnormal; in all other leads (except III and aVR), a normal Q wave would be very small. The “upper limit of normal” for such Q waves in leads I, II, aVL, aVF, V5, V6, is less than 0.03 sec. For V4 it is less than 0.02 sec.

![Figure 2.15 Typical display of precordial leads illustrating progression and regression of R and S wave amplitudes.](image)

ii) R waves: Since the precordial leads provide a panoramic view of the cardiac electric activity progressing from the thinner right ventricle across the thicker left
ventricle, the positive R wave normally increases in amplitude and duration from V1 to V4 or V5 as shown in Fig. 2.15. Reversal of this sequence with larger R waves in V1 and V2 can be produced by right ventricular enlargement, and accentuation of this sequence with large R waves in V5 and V6 can be produced by left ventricular enlargement. Loss of normal R wave progression from V1 to V5 may indicate loss of myocardium in the left ventricular wall, for instance myocardial infarction.

iii) S waves: The S wave also has a normal sequence of progression in the precordial waves. It should be large in V1, larger in V2, and than progressively smaller from V3 through V6 (Fig. 2.15). As with the R wave, alteration of this sequence could be produced by enlargement of one of the ventricles.

The duration of QRS complex is termed as the QRS interval, and it normally ranges from 0.07 to 0.10 sec. It tends to be slightly longer in males than in females. The QRS interval is measured from the beginning of the first appearing Q or R wave to the end of last appearing R, S, R', S'. As shown in Fig. 2.16, the use of three simultaneously recorded leads to identify the boundaries of ventricular activation. There is a possibility that the beginning or end of the QRS complex may be isoelectric as shown in leads II or III. The QRS interval has no lower limit that indicates the abnormality. However QRS prolongation may be caused by left ventricular enlargement, an abnormality in the impulse conduction, or a ventricular site of origin of the QRS complex. The amplitude of the overall QRS complex has wide normal limits. It varies with age increasing until about age 30 and then gradually decreasing. The amplitude is generally larger in males than in females. Factors contributing to higher amplitudes include youth, physical fitness, slender body build, intraventricular conduction abnormalities and ventricular enlargement.

Figure 2.16. Magnified schematic of QRS complexes recorded via leads I, II, III.
Estimation of the direction of QRS complex requires consideration of both the frontal and transverse planes. In the frontal plane the full 360° circumference is provided by the positive and negative poles of the six limb leads (Fig. 2.13). Therefore, it is possible to determine the QRS direction or axis, which represents the average direction of the spread of electrical activation throughout the right and left ventricles.

2.6.5. ST segment morphology.

The ST segment represents the period of time when the ventricular myocardium remains in an activated or depolarized state (Fig. 2.7). At its junction with the QRS (J point), it typically forms nearly 90° angle and then proceeds horizontally until it curves gently into the T wave. The length of the ST segment is influenced by factors that alter the duration of the ventricular activation. Points along the ST segment are designated with reference to the number of milliseconds beyond the J point such as “J+20”, “J+40”, “J+60”, etc. Slight elevation or depression may occur in normal ECG. The appearance of ST segment may alter during exercise, for normal individuals.

2.6.6. T wave morphology.

The initial deflection of T wave is typically longer than the terminal deflection, producing a slightly asymmetrical shape. Slight peaking of T wave may appear as normal variant, and notching of the T waves is common in children. The duration of T wave itself is not measured but is included in the QT or QTc interval. The amplitude of T wave has wide normal limits similar to QRS complex. T wave amplitude tends to vary with QRS complex amplitude and should always be greater than that of U wave, if present. The direction of T wave should be evaluated in relation with the QRS direction.

2.6.7. U wave morphology.

The U wave is normally either absent or present as a small, rounded wave following T wave. It is normally in the same direction as the T wave, but approximately 10% of its amplitude. It is usually most prominent in leads V2 or V3. The U wave is larger at slower heart rates and both diminish in size and merge with the following P wave at faster heart rates.
2.6.8. QTc Interval.

The QT interval measures the duration of activation and recovery of the ventricular myocardium. It varies inversely with heart rate. To assure that there is complete recovery from one cardiac cycle before the following cycle begins, the duration of recovery must decrease as the rate of activation increases. Therefore the "normality" of the Qt interval can be determined only by correcting the heart rate. A formula is developed [2] as,

\[ QTc = QT + 1.75 (\text{ventricular rate} - 60). \]

The maximum value of normal QTc is 0.42 sec. Fig. 2.17 indicates measurement of QT interval.

The QTc interval can also be defined by [56];

\[ QTc = \frac{\text{QT interval}}{\sqrt{\text{Preceding RR interval}}}. \]

![Figure 2.17. Measurement of correct QT interval.](image)

2.6.9. Rhythm.

The cardiac rhythm requires the consideration all of the eight features described in 2.6.1 to 2.6.8. The first three features indicate rhythm abnormalities. The features 3 to 8 may indicate the potential for development of the abnormalities.
i) The normal rhythm is sinus rhythm and is between 60 to 100 beats/min (bpm). A rate of 40 bpm may be normal during sleep and 200 bpm may be normal during vigorous exercise. Hence a rate 90 bpm would be abnormal during either sleep or vigorous exercise. ii) Alteration of normal frontal plane axis to either less than +30° or more than +75° may indicate that the cardiac rhythm is being initiated from a site in or near AV node in the right atrium or left atrium. iii) A short PR interval in the presence of a normal P wave axis suggests either an abnormally rapid conduction pathway within the AV node or the presence of an abnormal bundle of cardiac muscle connecting the atria and the ventricles and bypassing the AV node. This activates ventricles early and this pre-excitation produces tachyarrhythmia. iv) Abnormally slow impulse conduction within the intraventricular conduction pathways produce abnormalities in the QRS morphology as (a) Short PR interval and abnormal initial QRS morphology indicate rapid conduction bypassing the AV node into the ventricular myocardium. (b) Normal PR interval but abnormal QRS indicates delayed conduction through one of the bundle branches. (c) No P wave and abnormal QRS indicate that the impulse is formed beyond the His bundle. v) Marked elevation of the ST segment, tall and peaked T waves, long QTc interval, flat T wave and tall U waves indicate serious cardiac rhythm abnormalities.

2.7. CAUSES OF ABNORMALITIES IN ECG [56].

i) For short PR segment consider Wolff–Parkinson-White syndrome or Lown-Ganong-Levine syndrome. ii) For long PR interval consider first degree heart block. iii) For abnormally wide QRS consider right or left bundle branch, ventricular rhythm, hyperkalemia. iv) Long QT interval may be because of myocardial infarction, myocarditis, hypocalcaemia, hypothyroidism, subarachnoid haemorrhage, intracerebral haemorrhage, drugs, hereditary. v) Causes of ST elevation include acute myocardial infarction, left bundle branch block, normal variants like athletic heart, acute pericarditis. vii) Causes of ST depression include myocardial ischemia, digoxin effect, ventricular hypertrophy, acute posterior myocardial infarction, left bundle branch block. viii) Causes of tall T wave include hyperkalaemia, hyper acute myocardial infarction, left bundle branch block. ix) Causes of small, flattened or inverted T waves are numerous and include ischemia, age, race, hyperventilation, anxiety, drinking iced water, drugs, pericarditis, right bundle branch block and electrolyte disturbances. The following sections describe the details of most of these causes of abnormalities.
2.8 THE DETAILS OF ISCHEMIA . [2].

2.8.1. Ischemia due to increased myocardial demand.

ST segment changes are first discussed. Normally, the ST segment is part of the baseline of the ECG because it is isoelectric with the PR and TP segment. Observation of the stability of the position of the ST segment on the ECG of a patient receiving a graded exercise stress test provides clinical information regarding the presence or absence of myocardial ischemia. If coronary blood flow is capable of increasing to satisfy metabolic demands of even those cells in the left ventricular subendocardium, there is minimum alteration in ST segment appearance. There can be minor depression of the J point with the ST segment upsloping toward the upright T wave. When a partial obstruction within the coronary arteries prevents the blood flow from increasing sufficiently during a graded exercise stress test, the resulting subendocardial ischemia (SEI) is manifested by specific ST segment changes. However the ST segment changes typically disappear when the myocardial demands are returned to baseline by stopping the exercise. This suggests that the myocardial cells have been reversibly ischemic and have not actually sustained the injury.

A combination of two diagnostic criteria, on either a resting or exercise recording have been typically required in at least one ECG lead for the diagnosis of left ventricular SEI:

1) At least 0.10 mV (1.0 mm) depression at the J point
2) Either a horizontal or downward slope toward the end of the ST segment at its junction with the T wave.

Lesser deviations of the ST segments could be caused by SEI or could be variations of normal. Even the “diagnostic” ST segment changes could be due to an extreme variation of normal. When these ECG changes appear, on either resting or exercise recording, they should be considered in the context of other manifestations of ischemia such as typical or atypical precordial pain, decreased blood pressure, or cardiac arrhythmias.

The abnormality of electrical recovery, manifested on the ECG by ST segment deviation, occurs for each of the individual subendocardial cells at the time they complete their own activation process. Therefore, the subendocardial ischemia (SEI), which appears as depression of ST segment, actually begins during the QRS complex. This may result into secondary deviation of the QRS waveform in the same direction.
as that of ST segment. This distortion affects the amplitude but not the duration of the QRS waveform and affects the later more than the earlier waveform.

T Wave changes are now discussed. Normally, the directions of the QRS complexes and T waves are similar rather than opposite because of prolonged maintenance of the activated condition in the endocardial layer of the myocardium. The ischemic subendocardial cells are unable to maintain prolonged activation, thereby causing the T wave on the ECG to assume the opposite direction. These ischemic T waves are inverted in relation to QRS complexes. There is normally an angle of $<45$ between the direction of the QRS complex and the T waves in the frontal plane and $<60$ in the transverse plane. When the angle exceeds these limits in the absence of other abnormal conditions such as ventricular hypertrophy or bundle branch block, the presence of ischemic T waves should be considered.

The location of the ECG leads, demonstrating ischemic T waves, is sometimes indicative of the specific location of the ischemic area within the left ventricular myocardium. Ischemic ST segments generally deviate away from the left ventricle. However, the ischemic T waves may deviate away from the involved area of myocardium within the left ventricle.

T wave changes are not as reliable as ST segment changes for establishing the diagnosis of myocardial ischemia due to increased demand. T wave inversion is not a specific sign of left ventricular SEI. Many non-cardiac conditions have observed to cause T wave inversion. T wave inversion is also not a sensitive sign of left ventricular SEI.

Like ST segment depression, T wave inversion usually resolves when the increased left ventricular workload is removed. Unlike ST depression, however, T wave inversion is typically present for a prolonged period following the acute phase of myocardial infarction. This chronic T wave inversion should not be considered evidence for persistent ischemia. It represents an alteration in electrical recovery secondary to the infarction-induced changes in electrical activation in the same manner that T wave inversion is an expected secondary occurrence with left bundle branch block.

Pardee has described T wave inversion accompanied by ST segment elevation. This particular variety of repolarization abnormality has been associated with a high risk of acute transmural ischemia.
2.8.2 Ischemia due to insufficient blood supply.

ST segment changes are first discussed. Just as ST segment changes are reliable indicators of ischemia due to increased myocardial demand, they are also reliable indicators of ischemia due to insufficient coronary blood supply. Observation of the position of the ST segments (relative to the PR and TP segments) on the ECG of a patient experiencing acute precordial pain provides clinical evidence regarding the presence or absence of myocardial ischemia or infarction. There are cases reported in one of which, the stable appearances of the resting ECGs of two healthy young men had ST segment elevations in the precordial leads, which represent variations of normal in these men, are identical to the changes that would be considered abnormal in a patient with acute symptoms.

When a sudden, complete obstruction of a coronary artery prevents any blood flow from reaching an area of myocardium, the resulting transmural ischemia (TMI) is manifested by ST segment deviation toward the ischemic area. Another term applied to these changes is epicardial injury because experimental studies have described a current of injury produced by epicardial layer of the myocardium. When the coronary blood flow is returned to base line (say because of percutaneous transmural coronary angioplasty) then ST segment changes typically disappear abruptly. This suggests that myocardial cells are reversibly ischemic and have not sustained injury. All the layers of the ventricular wall are involved and the ECG changes occur only during the period of complete obstruction, the term transmural ischemia is more appropriate.

The deviated ST segments typically are either horizontal or slope toward the direction of the T waves. Sloping produces greater deviation of the ST segment as it moves further from the J point toward the T wave. Various positions along the ST segment are sometimes selected for measurement of ST segment deviation either for establishing the diagnosis of the TMI or for estimating its extent. "J +0.02 sec." and "J +0.06 sec." have been used in some critical situations. The ECG criteria for TMI may be accompanied by other manifestations of ischemia such as typical or atypical precordial pain, decreased blood pressure, or cardiac arrhythmias. The ST segment changes of TMI deviate toward the involved area of the ventricular myocardium and, therefore, appear positive or elevated in some combination of leftward, inferiorly, or anteriorly oriented leads. So ST segment depression appears in the ECG leads with
their positive poles oriented away from the involved area of the myocardium. The direction of maximum deviation is considered to be positive and the direction of lesser deviation is considered to be secondary or reciprocal.

TMI most commonly occurs in the distal aspect of the area of the left ventricular myocardium supplied by one of the three major coronary arteries as indicated in Fig. 2.18. The 12 sectors of the left ventricular myocardium are defined by the four quadrants and the three levels. The distributions of the coronary arteries shown in the top part of Fig. 2.18 are related to the distributions of the infarctions that result from their occlusions which is shown in the bottom part of the same figure. The infarction size is shown as small, medium, large and very large respectively by four grades of shading from light to dark is also shown in Fig 2.18.

The basal and middle sectors of the posterior-lateral quadrant of the left ventricle are located distant from positive poles of all 12 of the standard ECG leads. Therefore depression rather than elevation of the ST segment indicate posterior-lateral TMI. TMI may also involve thinner walled right ventricular myocardium when its blood supply via the right coronary artery becomes insufficient. Right ventricular TMI is represented on the standard ECG as ST segment elevation in leads V1 and V2, with greater elevation in lead V1 than in V2 and even greater elevation in the more rightward additional leads V3R and V4R. The entire ST segment elevation may
disappear when the cause (blockage) is removed say by angioplasty or intravenous thrombolytic therapy etc. In the absence of successful thrombolytic therapy, there is eventual gradual resolution of the ST segment elevation as the area with TMI becomes infarcted.

T wave changes:— Just as T wave changes are unreliable indicators of ischemia due to increased myocardial demand, they are also unreliable indicators of ischemia due to insufficient coronary blood supply. In some, the amount of T wave deviation is similar to that of ST segment deviation and, therefore, should be considered secondary. In others there is a markedly greater deviation of the T waves. These primary T wave elevations have been termed hyperacute T waves and are present for only a brief period of time in patients with acute coronary thrombosis. Hyperacute T waves may, therefore, be useful in timing the duration of the TMI when a patient presents with acute precordial pain.

QRS complex changes:— The epicardial injury current, which appears as elevation of the ST segments, actually begins during the QRS complex. This may result in secondary deviation of the QRS waveforms in the same direction as that of the ST segments. This distortion affects the amplitude but not the duration of the QRS waveform. In addition, it affects the later more than the earlier waveforms. If the increase in QRS complex amplitude is greater than that of the ST segment and also if its duration is also prolonged, then the deviation of the QRS waveforms toward the area of TMI is considered primary. The most likely cause of the primary QRS deviation is ischemic induced delay in transmyocardial electrical activation. The epicardial layer of the area with TMI is activated late, thereby producing an unopposed positive QRS waveform.

2.9 MYOCARDIAL INFARCTION.

When insufficient coronary blood supply persists after the myocardial glycogen reserves have been depleted, the cells become irreversibly ischemic and the process of necrosis or myocardial infarction begins. The QRS complex is the most useful aspect of the ECG for the evaluation of the presence, location, and extent of myocardial infarction. As mentioned in 2.8.2, the QRS waveforms deviate toward the area of potentially reversible transmural ischemia, secondarily due to the current of injury and primarily due to myocardial activation delay. The process of infarction begins in the most severely ischemic subendocardial layer.
Figure 2.19. Schematic cross section of the right and left ventricular myocardia.

QRS deviation toward the ischemic area is replaced by QRS deviation away from the infarcted area. Since there is no electrical activation of the infarcted myocardium, the summation of activation spread is away from involved area as shown in Fig. 2.19-(A). In this figure the normal sequence of activation is contrasted with the abnormal sequence resulting from an anterior infarction as shown by hatched area in Fig. 2.19-(B). In same figure the 0-10 ms isochrones are in black, the 20-30 ms are in light stippling, and the 50-60 ms in dark stippling. The arrows indicate the summated directions of the 20-30 and 50-60 ms isochrones pre and post anterior infarction.

The initial portion of QRS complex deviates most prominently away from the area of infarction, which is represented on ECG by prolonged Q wave duration. In the absence of Q waves it may be represented by diminished R waves.

The ST segment changes:--
The ST segment changes that are prominent during TMI typically disappear when the ischemic myocardium either infarcts or regains sufficient blood supply. Their time course of resolution is accelerated by refusion via the infarct related artery. When re-elevation of the ST segments is observed further TMI or a disturbance in the pericardium is suggested. When the ST elevation occurs in the leads representing multiple left ventricular areas, acute bleeding in the pericardium is considered. If this is undetected the cardiac arrest may occur. In some patients, the ST segment elevation
does not completely resolve during the acute phase of the myocardial infarction. This more commonly occurs with anterior infarcts than with those in other locations. This lack of ST segment resolution has been associated with the thinning of the left ventricular wall caused by infarct expansion.

T wave changes:--
The movement of the T waves toward the area of the TMI, like that of the ST segments, resolves as the ischemic myocardium either recovers or infarcts. Unlike the ST segments, however, the T waves do not typically return to their normal positions as the process of infarction evolves. The T waves move past the isoelectric position until they are directed away from the area of infarction. They assume an appearance identical to "ischemic T waves", even though there is no ongoing myocardial ischemia.

2.10 OTHER CAUSES OF CHANGES IN ECG.

1) Pericardial abnormalities:----- There is a small fluid-filled space called the pericardial sac that separates the heart from the other structures of the thorax. Two layers of connective tissue referred to as pericardium line the sac. These tissues can become inflamed for many reasons thereby resulting in pericarditis.

i) Acute Pericarditis:----- Typically acute pericarditis persists for 3 or 4 weeks, and ECG changes evolve through two stages. The characteristic of ECG abnormality during earliest stage of acute pericarditis is the elevation of the ST segments in many leads, accompanied by upright T waves. In pericarditis, the entire epicardium is usually involved, resulting in more widespread ST segment elevation. But if epicardial inflammation is localized it is difficult to differentiate between acute pericarditis and transmural ischemia. Additional clinical investigations are needed in this case.

ii) Pericardial Effusion:----- A generalized decrease in all of the ECG waveform amplitudes, termed low voltage, occurs if significant pericardial effusion or thickening develops. This probably occurs since cardiac impulses are short-circuited by the thickened pericardium. Thus low voltage, ST segment elevation, total electrical alternans (i.e. alteration of all ECG waveforms, P waves as well as QRS complexes) indicate pericardial effusion.

iii) Chronic Constrictive Pericarditis:----- In this the second stage ECG changes of acute pericarditis persist and accompanied by a decrease in voltage. The depth
of inversion of T waves has been reported to correlate with the degree of pericardial adherence to the myocardium.

2) Endocrine and metabolic abnormalities

I) Thyroid abnormalities. Both hypo and hyperthyroid conditions are often accompanied with typical changes in ECG. Since the thyroid hormone, thyroxin, mediates sympathetic nervous activity, hypothyroid results into sinus bradycardia and hyperthyroid state results into sinus tachycardia.

a) Myxedema: It is hypothyroid condition. The following combination of ECG changes is present.
   i) Low voltage of all waveforms.
   ii) Inverted T waves without ST segment deviation in many or all leads.
   iii) Sinus bradycardia.

b) Thyrotoxicosis: It is hyperthyroid condition. The following ECG changes are present.
   i) Increase in amplitudes of all of the ECG waveforms.
   ii) QT interval decreases as the sinus rate increases.
   iii) The corrected QT interval (QTc) may be prolonged.

II) Obesity. Obesity has potential of affecting the ECG in several ways.

a) Displacement of the heart by elevating the diaphragm.

b) Increasing the cardiac workload.

c) Increasing the distance between the heart and the recording instruments.

In a study of over 1000 obese individuals the heart rate, PR interval, QRS interval, QRS voltage, and QTc interval all showed an increase with increasing obesity. The QRS axis also tended to shift leftward.

III) Hypothermia: It is defined as rectal temperature below 36.6 C. At these low temperatures all intervals including RR, PR, QRS, and QT, may lengthen.

IV) Amyloidosis: An abnormal protein called amyloid is deposited in the heart during various disease states which eventually produces heart failure. The following combination of ECG changes may appear.

a) Low voltage of all waveforms in the limb leads.

b) Marked left axis deviation.

c) QS or minimal R waves in leads V1-V3 or in lead V4.

d) Prolonged AV conduction time.
3) Electrolyte Abnormality:— Either abnormally low (hypo-) or high (hyper-) serum levels of electrolytes potassium or calcium may produce marked abnormalities of the ECG waveforms.

I; Potassium:— The terms hypo or hyperkalemia (and not potassemia ) are commonly used for alterations in the serum levels of this electrolyte.

a) Hypokalemia:— A significant potassium deficit may be encountered in many metabolic disorders. The typical ECG signs of hypokalemia may appear when the serum potassium is within normal limits or, conversely, the ECG may be normal when serum levels are elevated. The ECG changes are,
   i) Flattening or inversion of the T wave.
   ii) Increased prominence of the U wave.
   iii) Slight depression of the ST segment.
   iv) Increased amplitude and width of the P wave.
   v) PR interval prolongation.
   vi) Premature beats and sustained tachyarrhythmia.

b) Hyperkalemia:— As in hypokalemia, there may be a poor correlation between serum potassium levels and the typical ECG changes. The variety of changes are
   i) Increased amplitude and peaking of the T waves.
   ii) PR interval prolongation.
   iii) QRS interval prolongation.
   iv) Flattening of the P wave.

The AV conduction may become so delayed that advanced AV block appears. Prolongation of the QRS complex and flattening of P waves occur because the high potassium levels delay the spread of impulse through the myocardium. This abnormally slow conduction can lead to cardiac arrest. The P waves may totally disappear.

II; Calcium:— The ventricular recovery time, as represented on the ECG by the QTc intervals altered by the extremes of serum calcium levels.

Deficiency Hypocalcemia Prolonged QTc interval.
Excess Hypercalcemia Shortened QTc interval.

The change in QTc interval is produced by an increase or decrease in the ST segment while the T wave remains relatively normal. In hypocalcemia terminal T wave inversion may occur in some leads. In hypercalcemia the proximal limb of the T wave abruptly slopes to its peak, and the ST segment
may disappear. In extreme hypercalcemia, an increase in QRS amplitude, diphasic T waves may appear.

4) Drug Effects.--Either therapeutic or toxic cardiac effects of various medications can sometimes be detected on the ECG. The term drug effect refers to therapeutic cardiac manifestations on the ECG, while the term drug toxicity refers to the cardiac arrhythmias caused by the medications.

i) Digitalis :-- It is a drug which is used both to increase the contraction of the cardiac muscle and decrease conduction through AV node. Digitalis effect occurs because the recovery or repolarization of the myocardial cells occurs early. This is manifested on ECG by,

a) ST depression;
b) Flattened T waves;
c) Decreased QTc interval.
d) Occasionally, the J point is depressed, mimicking myocardial ischemia. This extreme example of digitalis effect usually occurs only in those leads with tall R waves.

ii) Quinidine and Drugs with similar cardiac effects:---In contrast to digitalis, quinidine effect is produced by a delay in the recovery or repolarization of myocardial cells. This results in prolongation of the QTc interval. The effects of this drug on ECG are

a) Depressed, widened, notched, and then inverted T waves;
b) Prominent U waves;
c) Prolonged QTC interval;
d) Prolonged QRS complex. This occurs only with an extreme quinidine effect, and the increased duration by 25 % to 50 % is evidence of toxicity.

Quinidine effect is exaggerated by the presence of digitalis. The T wave amplitude is decreased and the U wave amplitude is increased as in hypokalemia.

5) Pulmonary abnormalities:-- When a pulmonary abnormality creates an increased resistance to blood flow from the right side of the heart, a condition of systolic or pressure overload develops. This condition is termed as "cor pulmonale" and can occur acutely or chronically.

a) Acute cor pulmonale :-- In this the ECG changes occur in frontal plane leads which mimic acute inferior myocardial infarction. Lead III is mostly involved with
i) An increase in the size of normal Q waves;

ii) Slight ST segment elevation.

iii) Shallow inversion of the T waves.

Unlike inferior infarction, there are minimal, if any, changes in lead II and aVF. The size of S wave is increased in lead I, indicating a rightward shift of the QRS axis. The typical changes of RBBB may be apparent in lead V1.

In chronic cor pulmonale there is right ventricular hypertrophy.

b) Pulmonary emphysema: It is a disease in which the alveoli are destroyed and the lungs become over-inflated. Hence chronic obstructive pulmonary disease is often characterized by emphysema. This produces anatomic changes that affect the ECG in unique ways.

i) Compression of the heart into more vertical position, results into vertical P waves.

ii) Lowering of the diaphragm gives rise to rightward shift of the QRS axis in the frontal plane.

iii) Increased volume of the thorax results into decreased amplitudes of the ECG waveforms.

iv) Exaggerated atrial repolarization waves produce >0.10 mV ST segment depression in leads II, III, and aVF.

2.11. OTHER ASPECTS OF CAD.

2.11.1. Cholesterol. [85].

One of the major contributing factors to cardiovascular disease is a fatty substance called cholesterol. Yet cholesterol is an essential chemical in the body, without which no human can survive. It is used in the synthesis of hormones like estrogen and testosterone, and it is necessary for the formation of the cell membrane. Cholesterol circulates in the blood stream in complexes called “lipoproteins” containing triglycerides (another type of fat), phospholipids (mostly lecithin), and proteins. There are four classes of these “lipoprotein” complexes.

Lipoproteins: (1) Chylomicrons: It appears in the blood stream after a meal and transport dietary triglycerides from the gut to sites where the triglycerides are used and stored. (2) Very low density Lipoproteins. (VLDL): It transports triglycerides and cholesterol that are synthesized by the liver to similar sites for utilization or storage. Many people with high triglycerides and cholesterol make too much VLDL in the liver because of an inherited tendency. (3) Low density
lipoproteins. (LDL) - The VLDL remnants are converted primarily to LDL, which is removed from the circulation mostly by being absorbed in the liver cells. For liver cell absorption of LDL to occur, the LDL must bind to the LDL receptor on the cell surface. People with familial hypercholesterolemia lack these receptors, and the result is they have LDL - cholesterol levels that are often two or three times normal. The LDL cholesterol complex is small and dense compared to chylomicrons and VLDL, and when it is present in high concentrations it tends to deposit inside the blood vessel wall. This contributes to atherosclerosis (the build-up of fatty plaque in the arteries; “Hardening of the arteries.”) (4) High density lipoproteins. (HDL) - HDL has a different function in the body. It removes excess cholesterol from the cells and helps transport it back to the liver. Higher HDL levels are associated with a reduced risk of heart disease. For this reason HDL cholesterol is known as the “good” cholesterol. However no direct evidence is available that increasing HDL can prevent or treat heart disease.

Cholesterol and lipoproteins are implicated in the development of blood vessel plaque that causes heart attacks. In parts of the world where blood cholesterol and LDL levels are low heart attacks are almost unknown. Many studies that have been completed and announced recently, it is widely agreed that lowering cholesterol does decrease the risk of second heart attack for people who are already having first heart attack. Thus treatment to lower cholesterol has become a standard part of the management of the people who have heart disease, or at a high risk of developing heart disease. The following tables, Table 2.1, and Table 2.2, show the standard reference levels. These are not necessarily one’s personal ideal levels. These are for total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides levels for men and women of various ages and all ages. These levels are measured in milligrams per deciliter of blood (mg/dL), and are indicated as mean values, of the surveyed information [78].
### TABLE 2.1.
Cholesterol details for men of all races.

**MEN - ALL RACES.**

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Cholesterol</th>
<th>LDL Cholesterol</th>
<th>HDL Cholesterol</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>189</td>
<td>123</td>
<td>47</td>
<td>119</td>
</tr>
<tr>
<td>40-59</td>
<td>216</td>
<td>140</td>
<td>46</td>
<td>176</td>
</tr>
<tr>
<td>60 or older</td>
<td>215</td>
<td>137</td>
<td>46</td>
<td>176</td>
</tr>
</tbody>
</table>

### TABLE 2.2.
Cholesterol details for women of all races.

**WOMEN - ALL RACES.**

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Cholesterol</th>
<th>LDL Cholesterol</th>
<th>HDL Cholesterol</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>186</td>
<td>111</td>
<td>55</td>
<td>106</td>
</tr>
<tr>
<td>40-59</td>
<td>214</td>
<td>131</td>
<td>56</td>
<td>129</td>
</tr>
<tr>
<td>60 or older</td>
<td>234</td>
<td>147</td>
<td>56</td>
<td>163</td>
</tr>
</tbody>
</table>

The about tables indicate fasting lipid levels. It is important to note that one’s cholesterol levels must be interpreted based on other risk factors. Normally the risk factors include, smoking habit, presence of coronary heart disease, obesity, presence of diabetic condition etc. The exact levels can be decided by consulting the physician only.

#### 2.11.2. Association of insulin resistance to ECG changes in non-obese Asian Indian subjects with hypertension.

A survey was carried out at Sir Hurkisondas Nurrotumdas Medical research Society Mumbai, by Marita et al, and is reported in 1998 [79]. To investigate the relationship between insulin resistance and electrocardiographic changes in hypertension in the absence of confounding influences, plasma glucose and insulin responses to oral glucose were studied in 26 normotensive and 38 hypertensive
subjects. Resting ECG was taken and was classified into normal or abnormal ECG. Among 38 subjects, 16 had ECG abnormalities. Multiple logistic regression analysis using mean blood pressure, serum total cholesterol, LDL cholesterol / HDL cholesterol, sex, insulin level at 60 min in oral glucose tolerance test (OGTT), treatment, serum triglyceride, presence of family history of diabetes, Coronary heart disease(CHD), hypertension and tobacco as independent variables causing ECG changes, revealed correct classification in 84 % of cases. Among the variables insulin level in OGTT contributed the most to ECG abnormalities. The data suggest that in the non-obese, non-diabetic Asian Indian hypertensive subjects, the presence of electrocardiographic abnormalities might be partly related to hyperinsulinemia or insulin resistance in them.

2.11.3. Evidence mounts in favor of Triglycerides as a risk factor.
A study shows that the more triglycerides one has in the blood, the greater is the risk of the heart attack [80]. It reports that people with high scores of triglycerides are more likely to develop heart disease. Dr. Jorgen Jeppesen of Copenhagen University Hospital in Denmark and his colleagues report about this. The study was carried out on males. The researchers studied 2,906 white men ages 53 to 74 who were free of heart disease at the outset of the trial. Within 8 years, 229 of the participants had a heart attack. The men with the highest fasting triglycerides concentrations were more than twice as likely to have heart attack than men with lowest levels, even after the team controlled for such risk factors as smoking, being sedentary, and being diabetic. People with triglycerides levels as low as 142 mg / dL were still at risk of having a heart attack, which was surprising because levels below 200 mg /dL were considered normal. Borderline high triglycerides levels are between 200 to 400 mg / dL; high triglycerides levels are between 400 to 1000 mg / dL; and very high levels are over 1,000 mg / dL. The reasons why triglycerides increase a person’s risk of heart disease remains unclear. High triglycerides are associated with low levels of HDL cholesterol and with increased amounts of small dense LDL, the worst form of LDL, along with other risk factors like obesity, diabetes etc.

2.11.4 Stable Angina [81].
Coronary artery disease is by far the most common cause of angina. Blockages in the coronary arteries, called plaques, prevent enough blood from reaching the heart muscles. Activities or situations that require increased blood flow to the heart may cause angina. These include exercise, heavy meals, and stress. Less common causes
of angina include coronary artery spasm, diseases of heart valves, heart failure, and abnormal heart rhythms. The risk factors for angina include male sex, cigarette smoking, high LDL cholesterol and low HDL cholesterol, high blood pressure, diabetes, a family history of coronary heart disease before age 55, a sedentary lifestyle, and being more than 30% over ideal body weight.

2.11.5 Borderline blood pressure levels present risk for heart disease [82].

Systolic blood pressure measures the blood pressure as the heart contracts; diastolic pressure measures the pressure of the heart at rest between beats. Borderline isolated systolic hypertension is the official term for those patients with a systolic measure of between 140 and 159 mm Hg, and a diastolic measure of below 90 mm Hg. The conventional treatment for high blood pressure had focussed on those patients with systolic levels above 160, as well as those patients with elevated diastolic pressure, which is traditionally the primary focus of treatment regimens. The study sponsored by several Massachusetts hospitals and coordinated by the Physician's Health Study team, indicates that even borderline systolic levels should be considered harmful and should be treated. In an 11 year panel study of over 18,000 "apparently healthy" male doctors, it was expected that heart disease risk would be greater among those diagnosed with traditional hypertension (160/90 or higher). The results supported this assumption: those with hypertension were more than two times more likely to have fatal or non-fatal stroke; twice as likely to die of any cardiovascular disease, and 78% more likely to have a fatal or non-fatal heart attack, as reported during the 11 years of study. What was surprising to the researchers was the variation in the risk factors between the borderline systolic and the "normal" group. Among those in the borderline group, there was a 42% increased risk of fatal and non-fatal stroke; 56% higher risk of death from cardiovascular causes and a 26% higher risk of fatal and non-fatal heart attack. Researchers also noted that the risk of stroke and heart disease increased progressively as the systolic pressure rose. These findings indicate that further research on both men and women should be undertaken, and a new approach could be considered for "border-line" patients, estimated to be more than 10% of the adult population.

2.11.6 Heart Disease in women. [84].

More accurate diagnosis of heart disease in women can be made when physicians add another measure to their ECG reading during exercise stress test: the
QT dispersion. Certain types of changes in the ECG with exercise can suggest a possible blockage in the coronary artery. However, accurate diagnosis of women using stress testing can be difficult due to the large number of false positive results that occur (i.e., changes on the ECG occur but the women do not actually turn out to have significant coronary blockages). In women ST-depression occurs many times during the ECG test; this waveform can falsely indicate that women have heart disease. The reason for the appearance of the ST-depression in women is unknown. Dr. L. N. Stoletni and other scientists as the Loma Linda University school of Medicine in California examined 64 women who had undergone exercise stress ECG test and subsequently underwent coronary angiography, an x-ray of the artery. When changes in the ST segment occurred during the stress ECG test, only 41% of the women were found to actually have significant blockages (a typical finding in women). However, Dr. Stolrtni also used another reading from the ECG called “QT dispersion”. QT dispersion measurements were taken both at rest and when the women were undergoing exercise stress test. The researchers found that using the QT dispersion measurement together with the ST segment reading improved the accuracy of the reading to 100%. Thus, stress testing in women is notoriously difficult to interpret, often resulting in so-called “false positives” due to changes in the ECG ST segment. These ST depressions actually represent ischemia (i.e., decreased blood flow of the heart). Better ways for making more specific diagnosis are thus needed for stress testing.

2.11.7 Blood Tests. [2], [3], [85], [86], [87], [88], [89].

The myocardial ischemia is indicated on ECG by ST segment depression. Inverted T waves in the leads tapping the affected area may appear. Very rarely unusual tall and pointed T waves may also be from ischemia at some distant heart area. Angina is a clinical equivalent of ischemia. The resting ECG is abnormal in only 60% of patients with angina. Sometimes the Q waves are not recorded and there are changes only in ST segment and T waves. ST segments are more often depressed. The T waves are inverted. Such ECG infarcts in the absence of Q wave are known as subendocardial or non-Q wave infarctions. Such infarcts may be anterior or inferior. These are called non-transmural infarcts. By looking only at ECG, one can’t differentiate between subendocardial ischemia and subendocardial infarction. It is only the clinical history and the study of cardiac injury enzymes, which would help to settle the diagnosis [3]. Carrying out some Blood Tests will thus do the exact
diagnosis. Blood tests confirm (or refute) suspicions raised in the early stages of evaluation that may occur in an ICU. The most commonly used blood test to confirm existence of heart muscle damage is the creatine kinase, or CK. A small fraction of the CK enzymes, CK-MB, is often measured as well [85], [86]. CK is an enzyme found in high concentration in skeletal muscle (2500U/g), cardiac muscle (500 U/g), brain tissue (200 U/g), and in smooth muscle of the colon, small intestine, uterus, prostate, lungs, kidneys (less than 100 U/g). In muscle energy is stored as creatine phosphate. Creatine kinase is the enzyme that catalyzes the transfer of phosphate group from creatine phosphate to adenosine diphosphate (ADP), forming adenosine triphosphate (ATP), the main source of usable energy. The test is used to diagnose myocardial infarction, infarct extension and size, and muscle disease. Creatine kinase is a two chain molecule with three isoenzymes, CK-MM, CK-MB, and CK-BB. The M chain derives its name from skeletal muscles and the B chain from brain tissue. CK-MB is predominantly found in cardiac muscle, which is composed of 20-40% CK-MB; the rest is composed of CK-MM. CK-MB shows an increase above normal in a person's blood test about six hours after the start of heart attack. It reaches its peak level in blood in about 18 hours and returns to normal in 24 to 36 hours. The peak level and the return to normal can be delayed in a person who’s had a large heart attack, especially in the absence of early and aggressive treatment.

In recent years tests have been developed to measure the level of other cardiac muscle proteins called troponins, especially troponin T (cTNT) and troponin I (cTNI). These proteins control the interactions between actin and myosin, which contracts the heart muscle. In one study [87], Dr. Elliott Antman at Brigham and Women’s hospital in Boston stated that the measurement of cardiac Troponin I is a good indicator of heart attacks since it is not found in healthy persons. In his study that measured cardiac Troponin I levels, researchers measured the levels of protein in 1,404 patients most of whom were diagnosed with unstable angina. Several significant results emerged: 573 patients whose blood contained this protein were found to have suffered damage to the heart muscle, which results from a heart attack. After 42 days, these 573 patients who did have at least a specific level of the protein in their blood (0.4 ng per milliliter) had death rates that were higher than the other patients in the study: 3.7% compared to 1%. Furthermore, the risk of death increased as the level of protein increased. The other study [87], led by Dr. E. Magnus Ohman from Duke University also found that higher levels of protein Troponin T were associated with higher death
rates. The New York Times reported that 12% of those patients with high levels of protein died within a month. Dr. Ohman advised that people arriving in emergency rooms with chest pain that may be linked to heart disease be tested.

2.12. CONCLUDING REMARKS.

In this Chapter 2, effort is made to cover different details, which will be needed in the design of a diagnostic system of Coronary Artery Disease. Here most of the physiological parameters are considered. The details of Artificial Neural Network are discussed in subsequent Chapters.