Lipoprotein Particle Structure Provides solubility for transport in the blood. Efficient mechanism for transporting lipid to & from cells. Deposition of lipid; especially cholesterol leads to plaque formation & atherosclerosis. Lipoprotein Particles 1) Chylomicrons 2) VLDL (very low density lipoprotein particle) 3) LDL (low density lipoprotein particle) 4) HDL (high density lipoprotein particle) Familial Hypercholesterolemia It is known as type II hyperlipidemia (hyper-lipoproteinemia). It is genetic disorder characterized by high cholesterol levels & high LDL. It is due to mutation in LDL receptor gene (LDLR gene) that encodes the LDL receptor protein, which normally removes LDL from the circulation. Patients who have one abnormal copy (heterozygous) of the LDLR gene may have cardiovascular disease at age of 30 to 40. While those who have two abnormal copies (homozygous) may cause severe cardiovascular disease in childhood. Yellow deposits of cholesterol rich fat may be seen in various places on the body known as xanthoma. Pathogenesis of atherosclerosis Pathogenesis of atherosclerosis 1- Low density lipoproteins (LDL) infiltration, retention and modification. 2- Low density lipoproteins drive leukocyte recruitment, transmigration and differentiation. 3- Vascular remodeling. 4- Vulnerable plaque. 5- Plaque rupture and plaque erosion. 1- LDL infiltration, retention and modification: A high level of plasma lipids, particularly LDL is a major cause of vascular damage. LDL entrance and retention within the subendothelial layer may be affected by several factors such as: high plasma levels of LDL cholesterol, lipoprotein size Once sequestered in this microenvironment; LDL particles susceptible to modifications aggregation, fusion and oxidation (via lipoxygenase, myeloperoxidase, free radicals), intimal become including 2- LDL drive leukocyte recruitment, transmigration and differentiation: Modified LDL particles induce endothelial secretion of chemotactic substances which favour monocyte recruitment, adhesion and transmigration into the arterial wall. Once monocytes reach the intimal space, they are transformed into macrophages. Then they uptake many of the cholesterol molecules contained in modified LDL particles becoming foam cells. Foam cells release cytokines, growth factors and ROS therefore maintaining the inflammatory response, inducing vascular remodelling Vascular remodeling. The key process in intimal thickening and vascular remodeling is the migration of vascular smooth muscle cells from the vascular media to the vascular intima. 4- Vulnerable plaque. 5- Plaque rupture and plaque erosion. Structure and function of the heart The main function of the heart is to pump blood to the organs of the body, to deliver oxygen and nutrients where they are needed and to remove waste products from the tissues. The heart is enclosed in a double-layered fibrous membrane (sac) called the pericardium. The inner layer of the pericardium and the outer layer of the pericardium are separated by a coating of fluid (pericardial fluid) that prevents friction between the two layers when the heart beats. The heart is divided into two upper and two lower chambers. The upper chambers are termed the right and left atria, and the two lower chambers are termed the right and left ventricles. The right and left sides of the heart are separated by a septum. Each atrium is attached to its ventricle by an atrioventricular valve. The atrioventicular valve on the left side of the heart is called the mitral valve, and on the right side of the heart is called the tricuspid valve. The wall of the heart is composed of three layers: the epicardium (outer layer), the myocardium (middle layer), and the endocardium (inner layer). The myocardium contains striated muscle fibers that alternate between contraction and relaxation, which allows the heart to do its work. These fibers are

composed of cardiac-specific contractile proteins called actin and myosin and regulatory proteins called troponins. In addition, these fibers also contain myoglobin protein and a number of enzymes such as creatine kinase (CK), and lactate dehydrogenase (LDH) that have been used as markers of cardiac injury. Acute Myocardial Infraction (AMI) Myocardial infarction; also known as heart attack, is defined in pathology as the death of cardiac muscle due to prolonged severe ischemia. Blockage of the coronary arteries may be caused by spasm of the artery or by atherosclerosis with acute clot formation. The blockage results in damaged tissue and a permanent loss of contraction of this portion of the heart muscle. Risk factors for AMI 1- Hyperlipidemia. 2- Diabetes mellitus. 3- Hypertension. 4- Smoking. 5- Male gender. 6- Family history of atherosclerotic arterial disease. Signs and Symptoms 1) Chest pain described as a pressure sensation, fullness, or squeezing in the midportion of the thorax. 2) Radiation of chest pain into the jaw or teeth, shoulder, arm, and/or back 3) Dyspnea or shortness of breath 4) Epigastric discomfort with or without nausea and vomiting 5) Diaphoresisorsweating 6) Syncope or near-syncope without other cause 7) Impairment of cognitive function without other cause Creatine kinase (CK) Responsible for contractile muscle. 1- Skeletal muscle: in muscle dystrophy, IM injection and physical activity 2- Heart muscle: in acute myocardial infarction, ischemia and angina. 3- Brain tissues: in CNS disorders (seizures, nerve degeneration), cerebrovascular accident and CNS shock. ATP regeneration in CK Creatine phosphate + ADP Tissue sources: Creatine + ATP 1- CK-Isoenzymes: CK is a dimer enzyme consisting of 2 subunits: B – brain , M – muscle Three isoenzymes: CK-BB (CK-1) CK-MB (CK-2) CK-MM (CK-3) Lactate dehydrogenase: Interconversion of lactic and pyruvic (anaerobic glycolysis). Lactate + NAD+ Tissue sources: 1- Heart. 2- Liver. 3- Skeletal muscles. 4- Kidney. 5- Erythrocytes. pyruvate + NADH + H+ 2- LDH- Isoenzymes: LDH is a tetramer enzyme consisting of 4 subunits: H—heart, M—Muscle Five isoenzymes: HHHH (LD-1): MI HHHM (LD-2). HHMM (LD-3). HMMM (LD-4). MMMM (LD-5): hepatic & muscle disorders Aspartate Transaminase (AST) Called glutamic oxaloacetic transaminase (GOT) need pyridoxal phosphate (PLP) as a coenzyme. Tissue sources: 1- Heart. 2- Liver. 3- Skeletal muscle. 4- Cardiac troponin (cTn) Troponins are structural and regulatory proteins of skeletal and cardiac muscle cells and are of essential importance in the regulation of muscle cell contraction. The Troponin protein complex consists of three distinct proteins encoded by separate genes which are troponin T, troponin I and troponin C. cTn-C has an identical amino acid sequence in both skeletal and cardiac tissues and thus has no potential role as a cardiac-specific marker. However cTn-T and cTn-I have different isoforms in cardiac and skeletal muscle encoded by separate genes and consequently have different amino acid sequences thus they can be used once they are released into the blood stream; as highly specific markers of myocardial damage.