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EC CARDIOLOGY
Research Article

Major Cardiovascular Diseases and its Clinical Diagnosis

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Received: December 24, 2019; **Published:** February 17, 2020

Abstract

The main aim of cardiovascular research is to evaluate CVD chance of occurrence by clinical record, general practices and evaluate changes of CVD chance in population. Cardiovascular disease is major subscriber to the occurrence of atherosclerosis and many other diseases the most common which are discussed in this study are Heart failure, Coronary artery disease, Cardiomyopathies, Valvular heart disease, Congenital heart disease, Endocarditis inflammation, Coronary heart disease, hypertensive heart disease, Pulmonary artery disease, Cardiac dysrhythm, Myocarditis inflammation, Inflammatory heart disease, Cardiomegaly inflammation and rheumatic high fever. CVD remains the major cause of death in United States and worldwide 20% worldwide deaths per year. In low and middle income countries about 80%CVD deaths take place. For use in health care facilities, no guidelines are available. Annually more people die from CVDs than from any other cause. Most cardiovascular diseases can be prohibited by give a lecture about behavioral risk factors such as tobacco use, unhealthy diet and obesity, physical inactivity and harmful use of alcohol using population wide strategies. Cardiovascular disease person or who are at high cardiovascular risk (due to the presence of one or more risk factors such as hypertension, diabetes, hyperlipidemia etc.) need early detection and management using counseling and medicines. CVD found in both Youngers and adult. In cardiovascular system the abnormal function of arteries, heart, veins and capillaries directly leads to different cardiovascular disorder the most common are discussed in this review. It is estimated that, cardiovascular is the main reason of large number of death all over the world and also in established countries. The total amount of deaths caused by CVD in 2005 (especially rheumatic heart disease, coronary heart disease, stroke, and heart failure) has increasing 17.5 million all over the world from the 14.4 million by 1990. Cardiovascular risk factors are: (1) sex, age (2) systolic and diastolic blood pressure (3) history of dyslipidemia (4) diabetes and (5) smoking status. The risk of CVD increased with age of the patient. Regeneration of damaged myocardium and treatment of CVDs is exhibit by great stems cells-based therapy. For the treatment of cardiovascular disease, Ultrasound (US) has been considered as a valuable diagnostic tool and stem cell based therapy is also used for the transformation of drug at the site of infection or injury. Traditional cell-based therapy is evolved in the totipotent cells, which is able to distinguish into various mature cells forming functional tissue required for embryonic formation. Other relevant new therapy utilization of pluripotent or multipotent (adult cells), are conceivable for making specialized mature cell lines. The treatment of cardiovascular disease has richness in life saving and better improvement in the condition of patient, also associated with an aging population, which directly leads to outbreak of heart failure which is a type of disorder with increased rate of mortality and morbidity.

Keywords: *CVD; Clinical Diagnosis; Nanotechnology*

Introduction

Cardiovascular disease is a multifactorial disorder showing large diversity of phenotypes. Globally CVDs are the number 1 cause of death. An estimated 17.5 million people died from CVDs in 2012, 31% of all global deaths. Heart diseases and blood vessel disease is included in CVD. Most cardiovascular diseases can be prohibited by make a speech about behavioral risk factors. Cardiovascular disease people or who are at high cardiovascular need early detection and management using counseling and medicines, as appropriate January 2015, reported by World Health Organization). In cardiovascular system the failure of normal function of heart, arteries, capillaries and veins leads to different cardiovascular diseases mostly reported are atherosclerosis, hypertension and aging [1,2]. Cardiovascular diseases consisted of more than one disease. They include; 1-Atherosclerotic CVD, 2 -Congenital heart disease, 3-Rheumatic heart disease, 4-Atherosclerotic CVD" includes coronary artery disease 5-Cerebral artery disease, 6-Ischaemia, 7-Peripheral artery disease, 8-Atherosclerotic CVD [3].

Cardiovascular infection is crucial subscriber to atherosclerosis belonging to pathology of cardiovascular disease. Severe stage stimulant acting as fibrinogen, high sensitivity C-sreactive protein (hsCRP) and identification of vascular wall infection like emulsifiable intracellular cohesion fragment-1(sICAM-1) are consist of biological markers of cardiovascular disease, each indicate the chance of future cardiovascular occurrence, allowing for event for myocardial infarction and stroke. Especially between women Jenny. Procedure of inflammation show potent communication between cardiovascular pathology, chance to high blood pressure, cholesterol levels and metabolic condition such as diabetes, obesity, resilience to insulin and behavioral characteristics like exercise and smoking [4]. In hemodialysis patients the highest cause of death is cardiovascular disease. In order to evaluate the popularity and risk factor of cardiovascular disorder, 49 patients on severe hemodialysis were isolate in coronary arteries and cardiac valves by 64 multi-slice ultra-fast CT and transthoracic echocardiography. In this population the cardiovascular disease occurs at earlier age and quickly developed then in general population. Therapy of cardiovascular aspect has appear in sudden decline in the happening of cardiovascular pathology in the last 30 years [5,6]. Even though development, cardiovascular disease goes on the main reason of death throughout the whole population, and also in developed countries.

Moreover, alike in superior therapy process and oversee huge-probability of cardiovascular victims, a predominant remaining cardiovascular possibility are follow up. Nearby the task of conventional aspects, fact finding and epidemiology documentation that contagion is include from the beginning of atherosclerotic disorder. The capacity of gram negative bacteria on the function and structure of artery well, display a relationship between endotoxemia and carotid atherosclerosis in a probably community-based education. The major and important endotoxin receptor is a link in between dissolvable blood level CD14 and arotic rigidity. The aortic rigidness is result of the unplanned experiment that showed vaccination against gram negative bacteria. In the intestinal or oral origin, the presence of bacteria was analyzed in atherosclerotic panel and more dominantly, contrast with oral samples and gut, Atherosclerotic plaques contain appreciable great level of some Firmicutes and (Pbac) proteobactero. In this way we currently define a human blood microbiome idea of tissue microbiota balanced as a powerful aspect in health of human is introduced as a result of gut microbiota. Certainly a point of information illustrate that gut microbiota dysbiosis play a vital role in many disorders e.g. diabetes of type 1 celiac disease [7] e.g. fecal sample from patients with celiac disorder had minimized the amount of Bifidobacterium and higher proportions of Prevotella or Bacteroidees and bowel disease e.g. in infection bowel disease microbial diversity was reduced. In the flashing of this data, as a substitute analyze the action of some microbes, we needed to research the effects of microbiota equanimity on the starting site of CVD disorder with an emphasize on proteobacteria phylum in a habitual population [8].

Cardiovascular disease stands a foremost killer of health of mankind and corresponds for the mortality and disorder in developing countries like china and developed countries. Regeneration of damaged myocardium and treatment of CVDs is exhibit by great stems cells-based therapy. The ideal sources of stem cells-based therapy are adipose tissue-derived stem cells, induced pluripotent stem cells (iPSCs), embryonic stem cells (ESCs) mesenchymal stem cells (MSCs), and endothelial progenitor cells (EPCs) have indication of therapeutic potential on CVDs [9]. Especially because of MSCs contain multipotent differentiation ability and paracrine activity and also have ability to differentiate into osteoblasts, adipocytes, chondrocytes, CMCs, endothelial cells (ECs), and vascular smooth muscle cells [10] the MSCs transplantation have been demonstrate as advanced favorable therapeutic application for CVDs. MSCs basically originate from ectoderm and mesoderm throughout early embryonic development, and also found in many types of tissues and organs likes fat, muscle,

lungs, pancrease, bone marrow, liver, and synovial membrane besides the introduction of secure microenvironments and cellular aspects *in vivo* or *in vitro*. It has been generally identified that inoculate MSCs differentiated into CMCs and partially for therapeutic effects of MSCs transplantation MSCs also differentiate into VSMCs and ECs, which participate in revascularization [11].

MSCs also have ability of loss of vascular cells and CMCs in the myocardial infarction (MI) and also upgraded the cardiac function of damaged heart. Only a minimum MSCs survived and engrafted after transplantation, MSCs also can secrete functional paracrine factors e.g. basic fibroblast growth factor, insulin-like growth factor-1, vascular endothelial growth factor (VEGF) and to produce different immune effects such as promoting vascular regeneration repairing damaged kidney, making myocardial repair possible and improved cardiac remodeling. Interestingly, new application exposed that transplanted. MSCs may secret abundant particles written as exosomes, which can minimize tissue damage and also improve tissue repair. Exosomes are cholesterol-rich, phospholipid vesicles enriched with microRNAs (miRNAs) which can well regulate gene expression in a post-transcriptional process and play a vital role in different pathological processes. Exosomes influence on cardiovascular system, it is suggested that exosomes secreted by MSCs will be presented as a classical therapeutic mark for CVDs in near future.

Epidemiology of (CDV) cardiovascular disease

Currently the predominance of long term disorder crucial benefactor to whole world mortality has combined and has been earlier defined elaborately anywhere [12] WHO, (2008). The total amount of deaths caused by CVD in 2005 (especially rheumatic heart disease, coronary heart disease, stroke, and heart failure) has increasing 17.5 million all over the world from the 14.4 million by 1990. From the 7.6 million contribute to coronary heart disease (CHD) and stroke contributed to 5.7 million. It is observed that > 80% of the deaths appear in median power and income countries. The (WHO) World Health Organization predicts that ~ 20 million CVD (cardiovascular disease) rate found in 2015, considering for 30 percent of all deaths globally. Researcher data that non-transmissible diseases will consider for higher than third part of worldwide deaths in 2050.

Cardiovascular disease singly will be answerable for extra extinction or death in power earning nations than contagious disorder (involving HIV/AIDS, malaria and tuberculosis), perinatal and maternal and nourishment disease merged. Hence, cardiovascular disease is becoming, the popular major alone attribute to world mortality and will stay predominate mortality movement in the upcoming or future. Wide efficient factors that attribute to the planet load of CVD, such as citizen and internalization. They resemble with shift in CVD burden and to the average describe single chance of each aspect [13]. Since 1970 many developed countries have found with low rate of cardiovascular mortality while the developing countries with high rates. The United States society is aging. According to recent prediction people of united state with 25-year age and the past will be 20% of the total population by 2060 which are 14% higher from the recent prediction. It is predicted that those with 85-year age and aged will become three times higher at that time.

Age associated changes	Organ	Cardiovascular Disease
Increased intimal thickness	Vasculature	Systolic hypertension
Arterial Stiffening		Coronary artery stenosis
Increased pulse pressure		Peripheral artery stenosis
Increased pulse wave velocity		Carotide artery stenosis
Early central wave reflection		
Decreased endothelial-mediated vasodilation		
Increased left arterial size	Atria	Atrial fibrillation
Arterial premature complexes		
Decreased maximal heart rate	Sinus node	Sinus node dysfunction ,sick sinus syndrome
Decreased heart rate variability		
Increased conduction time	Atrioventricular node	Second, third –degree block
Sclerosis, calcification	Valves	Stenosis, regurgitation
Increased left ventricle wall tension	Ventricles	Left ventricular hypertrophy
Prolonged myocardial infection		
Prolonged early diastolic filling rate		Heart failure (with or without systolic dysfunction)
Decreased maximal cardiac output		
Right bundle branch block		
Ventricle premature complexes		Ventricular tachycardia, fibrillation

Table 1: *Age-associated changes and cardiovascular disease in the cardiovascular system.*

Life expectancy has also been rising continually and it is estimated to reach approximately 80 years by 2015. Age is a powerful chance for essentially all kind of cardiovascular diseases (CVD) basically, heart failure, hypertension, coronary artery disease and stroke, fundamental widespread that arise systematically with age. The widespread diseases arise from 12.8% in case of men and 10.1% in case of women in range of 20 to 39 year old people to 83% in case of men and 8.1% in case of women those with 80 year age or old or aged.

Age related physiological change to cardiovascular disease

There is several age associated disorder found with cardiovascular process. These do not certainly affect to pathological state decrease the hold of aged people. In table 1 many diseases changes and their state of disease and organ are listed: Particularly age associated changes all over the body and in essentially all organ process.

Genomics of CVD

Cardiovascular disease genomics fields have two well defined objectives that are the true understanding of physiological mechanism and then applying the knowledge to individualized medicine. Information of molecular processes can cause to enhance medicinal therapy on wide basis despite of genotype of individuals or specifically targeted to the genotype. Many of cardiovascular loci are discover throughout the past few years. In the coming years we will be analysis the tens of thousands of cardiovascular disease patients combine testes of missense, common and rare variants (genome wide associations) by sequences. Discovery of each new cardiovascular disease has probably to consequences many individuals. Yet a comprehensive research by medical management experts and mature understanding of genetics techniques and process crucial for combine genetics ingredients into ascetics applications. Leading CVD are begin by modifications in the DNA (deoxyribonucleic acid) sequence and Mendelian (mutation in a single gene), and their specific template of inheritance. The risk of transmission to baby is may be high as 50 percent with the changes in cardiovascular conduction, aberrant function and structure, and vascular biology.

Mutation in single cardiac gene affects many individuals in all ethnic groups and concludes in in mature cardiovascular death and morbidity. Inheritant deformity of ventricular and atrial division into by septum resulted by the genetic mutation of cardiac specific genes TGFBR2 and NKX2.5.

Major diseases	No. of disease	Percentage (%)
Major cardiovascular disease CVD	14,836	100.0%
a. Coronary heart disease	6,824	46.0%
b. Hypertensive heart disease	470	3.2%
c. Diseases of heart	11,167	75.3%
d. Congestive heart failure	1,419	9.6%
e. Other diseases of heart	2,454	16.5%
Primary hypertensive/hypertensive renel disease	401	2.7%
Cerebrovascular disease(stroke)	2,632	17.7%
Atherosclerosis	104	0.7%
Other diseases of circulatory system	532	3.6%

Table 2: *According to Death category of Major cardiovascular disease.*

Types of CVD

Cardiovascular risk factors are following (1) sex, age (2) systolic and diasystolic blood pressure (3) history of dyslipidaemia (4)diabetes and (5)smoking status etc.

Coronary artery disease (also called ishematic heart disease and coronary heart disease), Coronary artery disease is a disease in which a waxy substance called plaque builds up inside the carotid arteries (major arteries carry oxygenated blood from heart to the head). Ishemaic heart disease is range of disorder that rest the dominant cause of death globally in both genders male and female leads to $1/5^{th}$ of the death. Coronary artery ectasia is the anomalous expansion of a segment of coronary artery to 1.5 times or more the size of opposite natural segment of the artery. The occurrence of coronary artery dilation has been reported to be 0.3 to 5.3% of patients encounter coronary angiography. 20 to 30% of victims of coronary dilation are observed chronic and the others are received. Of the received cases, 50% are allocated to atherosclerosis while 10% to 20% are corresponding with inflammatory and connective tissue diseases (like Ehlers-Danlos syndrome, Kawasaki disease, and scleroderma), syphilis, and bacterial infections [14]. The most frequent clinical demonstration is angina. Other exhibition includes arrhythmias, spontaneous dissection of a dilation coronary artery, ST-elevation myocardial infarction, non-ST-elevation myocardial infarction and unexpected death. The ratio of the diameter of ectasia segment to that of the adjacent normal coronary segment is characterized as the ectasia ratio.

Thrombolysis in Myocardial Infarction frame count is a symptom of coronary flow as a constant measuring variable. Its measurements are associated with flow velocity measured with a flow wire throughout baseline and hyperemia. Experiments have exhibited that there is retarded coronary flow with raising TIMI framework accounts in coronary dilation victim. Because CAE provide patients to higher chance of myocardial ischemia regardless of the degree of stenosis.

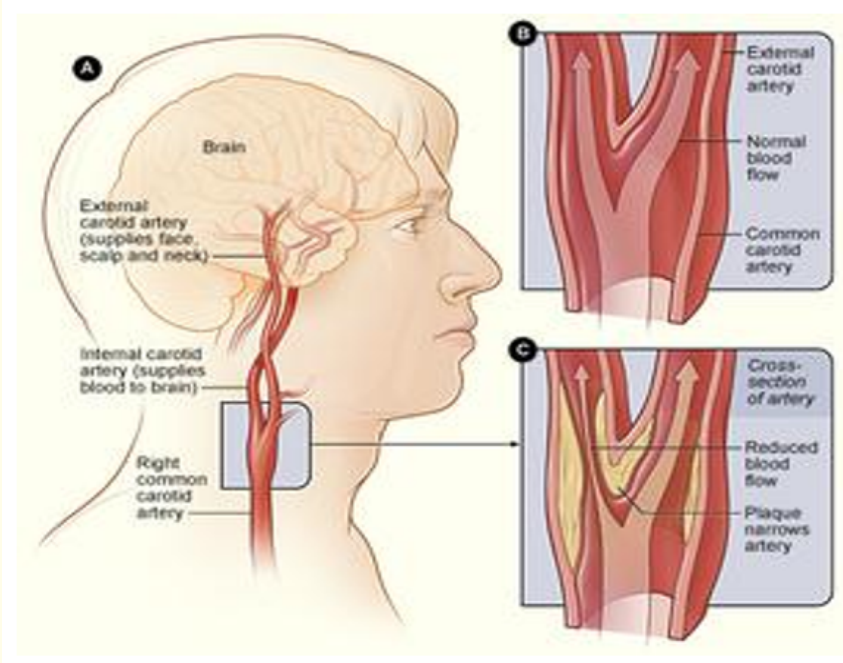

Figure 1: *This diagram shows plaque formation in carotid artery (National Heart, Lung, and Blood Institute: NCBI glossary).*

In case of specific cardiomyopathies involve heart muscle disease, correlated with myocarditis, general systematic disease and specific cardiac disease. While in case of primary cardiomyopathies are disorders or abnormalities to myocardium itself and are distributed as patho-physiologically. In this category hypertrophic cardiomyopathies (HCP), restrictive myocardiopathies (RMP), unclassified myocardiopathies, arrythymogenic right ventricular cardiomyopathies (ARVC) and dilated cardiomyopathies (DCM) are involved. DCM is most familiar reason of congenital heart failure in youngers and its widespread is calculated at a rate 36.5/100 000 person or creature in USA. DCM is specifying by rising in myocardial mass and depletion in cardiac wall diameter.

Cardiomyopathy - Diseases of cardiac muscle

Cardiomyopathy is described as disorder of the myocardium which induces cardiac abnormalities along with arrhythmia, heart failure and eventually death. Cardiomyopathies characterized as extensive source of mortality and morbidity in Youngers and children's and persistence indicator for cardiac transfer. Cardiomyopathies distributed into two main category in 1995 by World Health Organization (WHO)/ International society and federation of cardiology (ISFC). The first category is specific cardiomyopathies while second on is primary cardiomyopathies. The heart muscle becomes enlarged, thick, or rigid. In rare cases, the muscle tissue in the heart is replaced with scar tissue and heart becomes weaker. It is less able to pump blood through the body and cannot maintain a normal electrical rhythm. This can lead to heart failure or irregular heartbeats called arrhythmias and then heart failure can cause fluid to build up in the lungs, ankles, feet, legs, or abdomen. Cardiomyopathy can be acquired or inherited. This disease can affect people of all ages. There are main types of cardiomyopathy these are; (1) Dilated cardiomyopathy (2) Hypertrophic cardiomyopathy (3) Restrictive cardiomyopathy (4) Arrhythmogenic right ventricular. Treatments for this disease include changes in lifestyle, medicines, surgery, implanted devices to correct arrhythmias, and a nonsurgical procedure. These treatments can control symptoms, reduce complications, and stop the disease from getting severe.

Dilated cardiomyopathy appropriate by left ventricular dilation and systolic disjunction is a backward disease of cardiac muscle that gives rise to premature death and heart failure. Myocarditis and coronary heart disease are more popular recognizable cause in children's and youngers severally so far DCM is an idiopathic state of 66% in children's and 50% in youngers and the vital indicator of cardiac transplantation in both ages of children's and youngers [15,16].

Arrhythomogenic right ventricular cardiomyopathy (ARVC) is well known disorder that is appropriated by right ventricle fibro fatty degeneration which induced arrhythomogenesis and ventricular dysfunction. RCM (Restrictive cardiomyopathy) is most familiar type of cardiomyopathy and is identified by decreased diasystolic volume and restrictive filling of individual or both ventricular with wall thickness and normal or closely normal systolic function [17]. RCM is frequently outcome of endo-myocardial disorder of board analysis or myocardial which ''thicken'' the heart by fibrosis or infiltration. Furthermore, RCM also distributed as primary and secondary restrictive cardiomyopathy. In primary RCM endo-myocardial fibrosis (EMF), idiopathic RCM and Loeffer endocarditis are involve. Hypertrophic cardiomyopathy (HCM) is well known autosomal genetic disease influencing 1:500 of the public. HCM is analyzed macroscopically by left ventricular hypertrophy, which may be uniformly and not uniformly. The uniform HCM report one over third of the chance is identified by stiffing of the left ventricle along with small ventricular cavity.

Hypercholesterolemia, atrial fibrillation

It is a monogenic genetic disorder that causes severe hypercholesterolemia. Cholesterol is a rigid, hydrophobic molecule that consults structural integrity to plasma membranes of vertebrate cells, Excess cellular cholesterol is reacted with fatty acids to form cholesterol esters, which are either stored as lipid droplets in cells or packaged with other Apo lipoproteins to form VLDL (very low density lipoprotein) or in the liver chylomicrons in the intestine has provided molecular appetizers into the biosynthetic and regulatory pathways that

produce and remove cholesterol and has led to the development of effective pharmacological agents that dramatically reduce circulating levels of cholesterol. Missense mutation in Arg3500Gln can cause familial defective apoB-100 (FDB).

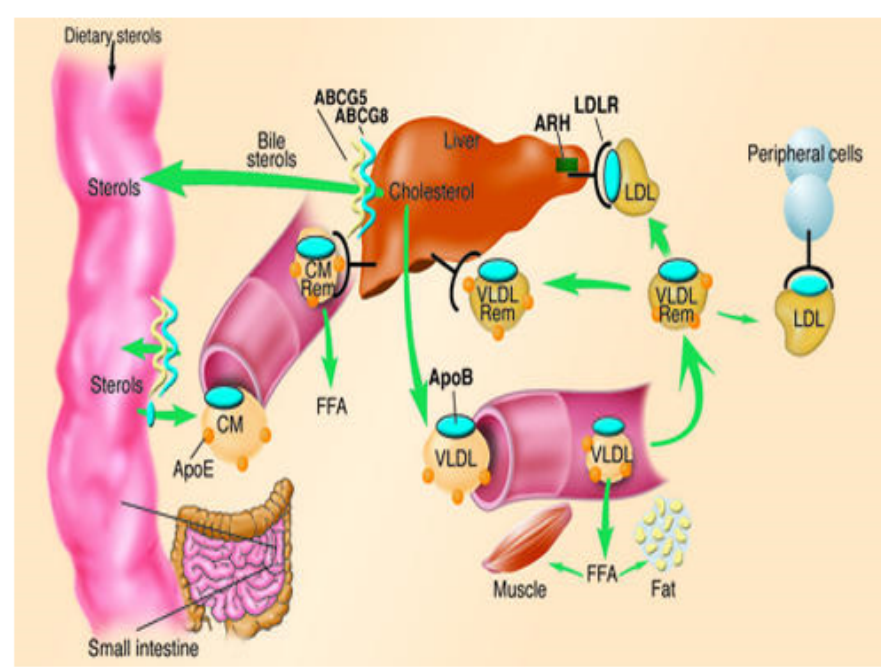

Figure 2: *Shows LDL metabolism in humans. Cholesterol and triglycerides which is dietary are packed with Apo lipoproteins in the enterocytes of the small intestine, secreted into the lymphatic system as chylomicrons. Chylomicrons circulate as the core triglycerides.*

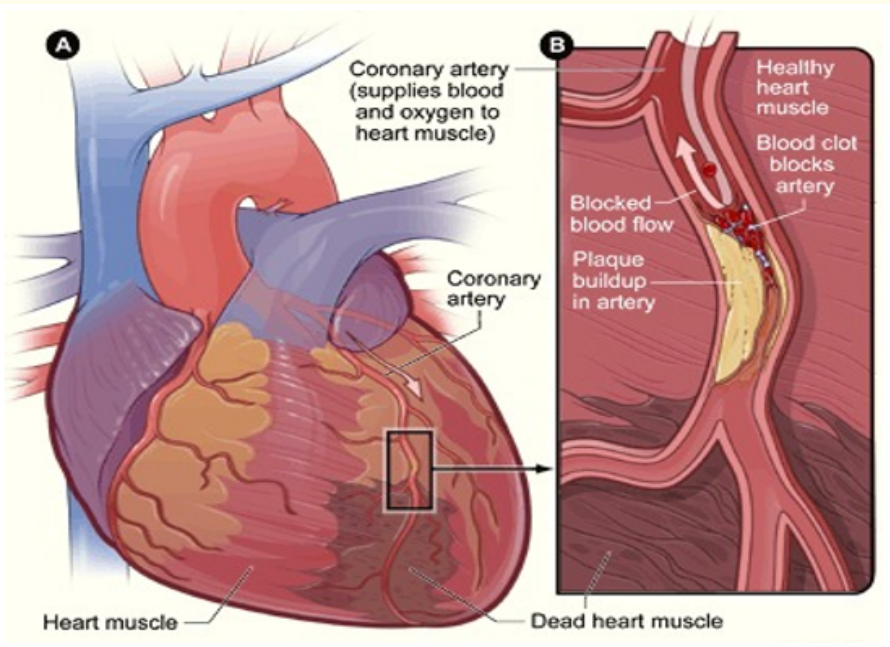

Figure 3: *Shows the blockage of blood flow into the coronary artery.*

It is autosomal dominant hypercholesteremic disease in which causative gene is *PCSK9* encodes neural apoptosis-regulated enzyme convertase 1 (NARC-1). The hypercholesterolemia failed to segregate with either the LDLR (low density lipoprotein) Or the APOB gene; this disorder was named autosomal recessive hypercholesterolemia (ARH). Concern with the treatment lipid-lowering medications will be provided to the patient.

Myocardial infarction

Also called as heart attack in which the flow of oxygenated blood to a segment of heart muscle abruptly blocked and the heart can't get oxygen. If blood flow is not restored quickly, the segment of heart muscle begins to die. It is leading killer in both genders. Treatment work best when given right after symptoms occur and the symptoms are;

- Chest pain or discomfort. Mostly heart attacks involve uneasiness in the center or left side of the chest. The uneasiness usually lasts more than a few minutes or goes away and comes back. It can feel like heaviness, pressing, pain. It also can feel like stomachache or heartburn. Upper body discomfort. Patient will feel pain or discomfort in one or both arms, back, shoulders, neck, jaw, or upper part of the stomach.

- Littleness of breath. It may occur before or along with chest pain or discomfort. It can occur when someone resting or doing a little bit of physical activity. Some Other possible symptoms include: cold sweating, unusually feeling tiredness for no reason, sometime

- For days, Nausea and vomiting.

Coronary heart disease

CHD also called as Atherosclerosis a disease in which a waxy substance called plaque builds up inside the coronary arteries. These arteries supply oxygenated blood to heart muscle. Psychosocial factors involved in this disease, behaviors such as smoking, diet, alcohol consumption, or physical activity. Access of medical care may probably be influenced, i.e. social supports (but there is little influence), socioeconomic status is inversely associated with coronary heart disease for the prevention of this disease specific fatty acid is used in diet.

Peripheral artery disease

It is complex and multitude diseases in which Patients may experience, claudication, ischemic rest pain, ischemic ulcerations, repeated hospitalizations, revascularizations, and limb loss. Symptoms are; in the thigh calf hip and buttock pain, discomfort, heaviness, tiredness, tightness or burning occurs. Which is reproducible with similar level of walking, disappear after several minute of standing, once walking has resumed occurs at the same distance. This may cause of poor quality of life and a high rate of depression. Different therapies and screening test are conducted for the treatment of this disease for example Ankle brachial index is an excellent screening test for the presence of PAD. If medical therapy is ineffective establishing a supervised exercise program or performing a revascularization procedure [18].

Hypertensive heart disease – disease of secondary heart to hypertension or high blood pressure

Hypertension is a vital possible characteristic for cardiovascular mortality and morbidity. The existence of hypertension resulting in double chance of occurrence of coronary heart disease inclusive, Acute myocardial infraction (AMI) and unexpected death and more than triple chance of congenital heart disease (CHD) including strokes. Victim along with high blood pressure usually have deformities in cardiovascular function, as well as left ventricular hypertrophy (LV) and in exceptional cases overt heart failure. Left ventricular hyper-

trophy has known from many years as a crucial clinical diagnosis item. Epidemiological investigation has identified that left ventricular hypertrophy as such related with raised mortality for heart failure, myocardial infraction and stroke. There is prolonged classify correlation in-between left ventricular mass and the enlargement of cardiovascular disease. Hypertensive is most popular experienced unique type of chronic disease develop by the HES (Health examination survey) found in American youngers. Hypertensive remainder is a vital public health complication linked with appreciable mortality and morbidity. Hypertensive heart disease is an intention of deformities that involve left ventricle hypertrophy, systolic and dia-systolic dysfunction and their analytic demonstration involve in arrhythmias and heart failure.

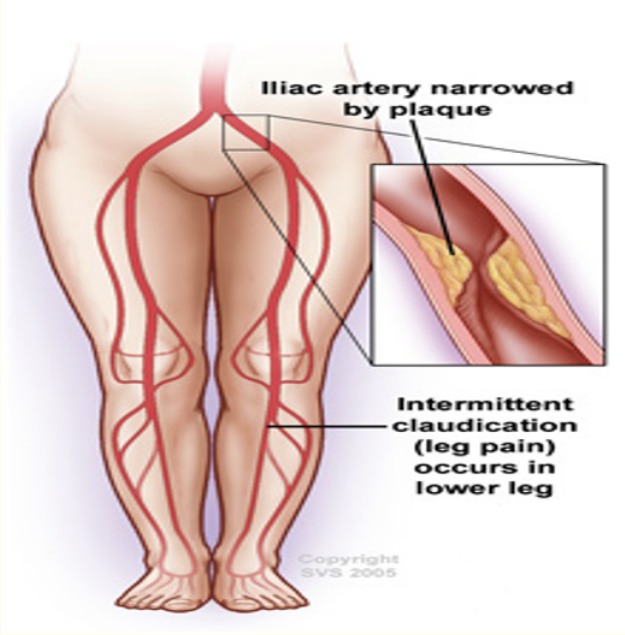

Figure 4: *Shows the plaque formation in the artery of lower leg.*

The academic standard of hypertensive heart disease is that left ventricle (LV) surface consistency in return to elevated blood pressure as advantageous process to reduce the load of surface or wall [19]. The advancement from the blood pressure finding of the investigation to treat hypertension heart disease included a mean of the three blood pressure and restricted standards to be used for the distribution of these standard pressure as consider hypertension. Several steps were included from findings to diagnosis of this disorder. The first analyzing X-ray film and electrocardiographic tracing and the second step was manufacturing a set of treatment standard. The third was establishment of procedure for evaluation of X-ray film and electrocardiography. Hypertensive heart disease is a type of vascular disease which is identified by raising pressure in pulmonary artery which may cause right heart failure and eventually death. Pulmonary infection originates by hypoxia while bronchopulmonery dysplasia induced by hyperopia may report for the establishment of (PH) pulmonary heart disease. Management of MSCs has been support to consult more superior prediction or projection of PH then cure that utilize in hospitals now and has been broadly examine in PH rates to discover its fundamental strategy. PH (pulmonary heart disease) below pulmonary vascular remaking is greatly coordinate with pulmonary infection caused by hypoxia [20,21].

Heart failure

Heart failure is a condition in which heart is enabling to pump enough blood to fulfill the needs of body. Heart failure means the heart is unable to perform function in the body, means the obstruction or hurdle in blood pumping it may be of the left side or on the right side of the heart or may be on both sided. Any hurdle in the pumping of heart may leads to; blood and fluid move back into lungs instead of heart, the gall of fluid in the leg, ankle and in the feet called edema and problem in breathing. Most familiar reason of heart failure in adults is due to high blood pressure, diabetes and coronary artery disease. The age of onset of this disease is higher in 65-year-old people or over 65 years old. The chance of heart failure is higher in men as compared to women. Heart failure is a complicated exhausting disorder that leads to cardiac dysfunction that impedes the capability of the ventricle to fulfill or emit blood. Patients with heart failure disease accomplished more number of deaths and also leads to cardiac disorders, but this may leads to those victim which are under monitoring may be possible to cure under the specific care center and may minimize the effect of cardiovascular disorder [22-25]. There are two primary cause of heart failure one is over circulation and second is pump failure. Approximately 1% of new born babies have structural defects in heart, there may be hole at right side of left cavity of the heart or inside the heart due to this blue and red blood merged to gather. These deformities led to over circulation of blood. Pump failure may be due to any viral infection or may be deformity from birth. If heart failure is due to over circulation with congenital heart defect, then surgery is essential to repair this deformity. If heart failure is due to pump improper working, then lower blood pressure is used to help the heart pump work properly and may be surgery also needed for replacement of defective heart valve.

Pulmonary heart disease – with the involvement of respiratory system a failure at the right side of the heart

Pulmonary heart disease results in right side heart failure and eventually leads to death. PHD is a golden childhood disorder with increased mortality. Even with the enlargement of pharmacological factor e.g. endothelia receptor antagonists, prostaglandin E1 and nitric oxide the mortality rate is quite increased especially with those patients who have serious right sided heart failure correlate with New York Heart Association. Without any diagnosis the life span of children is only one year or may be less than one year. Mortality correlated with some recently known agents which are pulmonary arterial pressure, right atrial pressure and cardic. It is estimated that patient of pulmonary heart disease with Eisenmenger physiology have more life span instead of those patients with primary pulmonary hypertension which have complete atrial sputum. Left heart failure is the most widespread result of pulmonary hypertension (PH) and this is due to the raised in left ventricular and pulmonary venous pressures seen in this condition. Still, a portion of patients with left heart failure will have a pulmonary arterial disease that not appropriate to the initial increase of left-sided pressures. Any mechanism involved, the appearance of PH is a powerful marker, because it figures out the minimized exercise resilience and continuity. All tribunals using therapies accepted for pulmonary arterial hypertension (PAH) failed to reveal welfare in the circumstances of heart failure without or with PH. Furthermore, the contrast between studies is reduced by relevant differences in definitions, methodology, and timing of assessment. A novel rigid hemodynamic (study of forces that play role in blood circulation) classification based on the diastolic pulmonary differenced slop has been now advanced to better characterize this form of PH. This will develop uniformity in patient populations and end-points for future clinical cases. The DPD has several advantages: it is virtually absent in healthy individuals, is less dependent than the Trans pulmonary gradient. An abnormal increase of pressures in the pulmonary vascular bed, or PH, can be a relatively common consequence of several cardiac, pulmonary, and systemic disorders but also of the aging process. Left heart diseases (LHDs), mainly HF with preserved or reduced ejection fraction (HFpEF or HFrEF) and Valvular heart disease, exhibit the most occurring reasons of PH (PH-LHD) through the increase of left ventricular filling pressures and pulmonary venous pressures. Presence of PH-LHD is correlated with a decrease in exercise resilience, increasing of dyspnea (breathlessness), and decreased survival. Various drug rehabilitation approved for PAH (a rare disease) have been tested in clinical cases to cure heart failure, with or without PH-LHD.

Cardiac dysrhythmias – abnormalities of heart rhythm

Cardiac dysrhythmia is an aberrant heart beat: the heart rate may be varying or rhythm might be asymmetrical in its tread. Some dysrhythmias are possible life alarming while on the other side dysrhythmias (like sinus arrhythmia). Moreover, most of the arrhymias are refreshing and non-lethal; some may induce severe effect of cardiac function. Any rhythm can cause cardiac arrest, so always ensure patient has adequate result (i.e. pulse) before worrying about fine points of diagnosis. Arrthymia also known as dysrhythmia is an abnormal heart beat. Heart rate can be irregular while in case normal heart beat 50 to 100 beats per one minute. Abnormal heart beat rate and arrhythmias must not be present both at the same time. Arrthymia can found along with very slow and as well as fast flow rate. Slow heart rate also known as bradyarrhythmias < 50 beats/mints while fast heart rate also referred to as tachyarrhythmias > 100 beats/mints. According to an investigation in United states it is estimated that > than 850,000 people are suffering from this disease in annually. Major symptoms of cardiac dysrhythmias are palpitations, dizziness, a fluttering in your chest, chest pain, slow heartbeat, fainting or near to fainting etc., this disorder may be occurring without any symptoms or signs. Some major factor involves which leads to cardiac arrthymia: hypertension, hear attack, blocked arteries, air pollution, electric shock, stress, Diabetes, smoking, drug abuse etc. In some cases, this disorder is treated with surgery or other medications of fast and slow heart beat rate respectively.

Inflammatory heart disease

The inflammation of heart disease including muscles deformities e.g. myocarditis, which is a layer of thin membrane wrapped around the heart known as pericarditis, and the myocardium or the inner lining of heart, heart muscles such as endocarditis are referred to as inflammatory heart disease or disorder. The main source of the occurrence of this disorder is viruses, bacteria, infectious agent, parasite, fungi or may be due to hazardous material from the surrounding, air, food, water, gases, pollution, or smoke or may be due unidentified source. Myocarditis occurs due to infection on heart muscle, this infection is caused by viruses e.g. sarcoidosis and immune disorder. The sings of these disorders are angina, pain or infection in heart muscle, edema, chest pain, fatigue and swelling of feet or ankles. The strategies or techniques which are now used for the treatment of this disorder are ECG, MRI and X-ray while testing of blood sample and increased level of enzyme may induce deformities in the proper working of heart the diagnosis involve use of antibiotics for the medication and inflammation of heart muscle. Furthermore, there are many biomarkers are described for the inflammatory heart disorder. The three main types of inflammatory heart disease are: (1) Myocarditis (2) Pericarditis (3) Endocarditis.

Myocarditis – infection of the myocardium, the muscle part of the heart

Myocarditis defined as inflammatory disorder that occur within the heart muscle due to infection which may be because off viruses such as, sarcoidosis, and distinct immune disorder. The major sing of this disorder is chest pain. For the treatment major strategies are ECG, MRI or Electrocardiogram etc. ECG is used for the detection of heart beat. Myocarditis is a clinically and pathologically cardiac disorder related with infection and aberration of the myocardium. Various viruses may lead myocarditis in humans. Although, coxsackievirus is quiet recognized predominant analysis vehicle [26]. Cardiovascular magnetic resonance (CMR) is an inestimable explanatory mechanism for non-invasive (precancerous tissues) detection of acute myocarditis. Although, since CMR researches requires more time and expensive its diagnostic validity still not perfect and identify those individuals in which CMR research is the addition of important information leading to exact and timely diagnosis of acute myocarditis. The diagnostic worth of CMR was induced in a population of young patients with clinically suspected acute myocarditis in relation to ECG and serum cardiac enzyme findings. Myocarditis in children can lead to significant morbidity and mortality; however, limited prognostic data is present, tachyarrhythmias are related with significant increases in mortality and resource utilization in children that suffering myocarditis. The long-term prognosis of biopsy-proven myocarditis is under investigation. We hypothesized that a detailed pathological examination of an endomyocardial biopsy would un- cover guessing statistical data in patients with acute myocarditis infection. Detailed pathological provide an assessment on an EMB that guessing statistical data in patients with acute myocarditis. EMB evaluation should be account for the patients with doubted myocarditis.

Endocarditis – inflammation

Endocarditis caused by an infection on the inner lining of heart or endocardium. This infection directly leads to inflammation. It may occur when pathogen from other part of the body contaminate the bloodstream and fixed to infected site of the heart. If it is not diagnosed properly, it will lead to half or full destructive to the heart valve or may be generate a condition which is injurious to health. The risk of the disease is higher in those patients who have degeneration of heart valve or artificial heart valve. It does not normally infect on healthy people. The symptoms of these disorders are: sudden weight loss, joint and muscular pain, chills and fever, constant coughing, blood in the urine, Edema, night's sweats and many more. Treatments are use of antibiotics in less severity while surgery is recommended at the site of infection. Inflammation of the inner lying of heart and valves splenomegaly and embolic issues may happen from vegetation particles moving through circulation. Sign and symptoms of endocarditis are fever anorexia, abdominal discomfort, cardiac murmurs, weight loss, fatigue and clubbing of finger in sub-acute forms of endocarditis inflammation. Diagnostic test: CBC, immune testing, blood culture and sensitivity, urine analysis and ECG.

Inflammatory cardiomegaly

According to Melissa Conrad Stapler, MD cardiomegaly is a medical term normally referred to as enlargement of heart. Cardiomegaly caused by many reasons such as, disease of heart muscle or heart valve, arrhythmias, high blood pressure and pulmonary hypertensions. In penetrate disorder of the heart e.g. amyloidosis in which abnormal proteins are formed or hemochromatosis is excess iron assemble within the heart tissue can also be a reason of heart enlargement. While in pregnancy temporary heart enlargement is demanded. Enlargement of heart is not a disorder but it is an indication of various disorders and conditions. The diagnosis of this disorder is relying on the cause only. The symptoms of this disease is analyzed when a hurdle or problem found in blood pumping while in normal case body need to work properly. There are some signs of inflammatory cardiomegaly; thyroid problem, weight gain, swollen legs, edema shortness of breath, palpitations, cough, chest pain and abnormal heart rhythms. The chance of causing heart enlargement involving many components which are Valvular heart disease, high blood pressure, family history of cardiomyopathy, coronary artery disease, obesity, congenital heart disease, cardiac ischemia and history of heart attack. The treatment of cardiomegaly is decided by the patient medical history and the outcome of various experiments involving an echocardiogram (Ultrasound of heart). After checking out symptoms and test report of patient test or procedure of treatment is decided.

An echocardiogram is a treatment strategy which provides us accurate measure of pumping and heart size. While other strategy is electrocardiogram, blood test, chest X-ray, stress test, cardiac computerized tomography (CT scan), MRI (magnetic resonance imagining) which are used to help physician to sort out the problem regarding cardiac enlargement.

Valvular heart disease

Heart valve disease is most familiar disorder with 2.5% widespread in the western world. And this number is increasing directly with aging of population. Heart Valvular diseases are possibly killing, and have great impact on the quality of life and daily living. The treatments of choice for the diagnoses are surgical diagnose or valve repair or replacement. Therefore, after surgery treatment, the conversion to daily living may be act as mental, physical and social problem.it is hypothesized that, an inclusive cardiac project can enhance physical ability and self-used mental health, decreasing number of hospitalization and expenditure of health care after heart valve surgery. The unarranged clinical experiment, Copen Heart VR, purposes is to identify whether cardiac improvement or recovery in insertion to general care is better than the treatment after heart valve surgery. The test will randomly assign 210 patients. The involvement of 12 week of physical exercise and idea of this test was to add patients in percutaneous heart valve or open heart surgery technique [27].

Congenital heart disease (CHD)

Congenital Heart Disease (CHD) is most familiar type of birth fault, the chance of occurrence of this disease is 1% per annual birth [28]. Congenital heart obstruction is anatomical abrasion or wound that manifest abnormal in size, communication or linkage of the heart

chamber or veins and arteries joined to the heart. The physiological outcome of CHD obstruction that deviates broadly, find out accidently in adult hood, and need immediate surgical involvement in the neonatal interval. With raise improvement of modern surgical and medical organization of this state, many children are now able to survive in adulthood with this disease and the risk or prevalence of CHD (congenital heart disease) has risen. MRI (Magnetic Resonance Imaging) plays a vital role in the treatment and examines these states. MRI cardiac analysis consist of two major constitute or components.

The first constitute lie on understanding of obstructional disorder that is accomplished by successive fragmental approximate to CHD that was about 25 year earlier and in current naturally used in the access of congenital heart disease. While the cardiac constitution used as first assay in 3 different parts – first is atrium second is ventricles and the last one are great vessels (pulmonary artery and aorta artery).

The physical and structural features determine each part which is evaluated individually. The relationship between these segments is at the atrioventrical and ventriculararterial level. Finally, the abrasions which are linked to the abnormalities are analyzed. The second constitute for evaluation of cardiac MRI test is the evaluation of physiological outcome of anatomical disorder. These outcomes consist of abnormal function of ventricles, abnormal blood flow and dysfunction of valves of the heart.

Role of MRI in congenital heart disease

Magnetic Resource Imaging (MRI) play multifunctional task in the maintence or patients diagnosis with CHD.MRI is compulsory in the beginning treatment, analysis of diagnosis and surgical development and also long term flow up for the evaluation of abnormalities or obstacle.

MRI additionally gives us data amount in blood flow and the work of ventricular which yield authentic way for longitudinal flow up. This consistently entail additional time of one hour and need management by knowledgeable cardiac image to fortify that image are gained in the accurate direction and position with genuine choice of imagining while is patients quite under monitoring. MIR at the same time label each single primitive constitute of imaging identification of CHD which can be greatly distributed as: (1) Quantification of ventricular volume and function, (2) quantity of blood flow, (3) By seeing intracardiac and extracardiac blood flow and structures [29].

Rheumatic heart disease

ARF (Acute rheumatic fever) is reminder of a group of streptococcal injury which was prominent source of rheumatic heart disease in childhood internationally. The chance of occurrence of this disease is 0.55-11 case per 1000 children. ARF more commonly found in advanced countries for instance, China, India, Egypt, Brazil, Sri Lanka and Zimbabwe, where approach to medical care is restricted and children survive in scarcity situation. Cardistis is more significant declaration of ARF outcome will be chronic Valvular lesions or wound along with macrophages infiltration, macrophages and autoantibody ejection.

Our observation evaluates that greater epitope of human in Rheumatic Carditis is cardiac myosin yield combined case of the disease which originate by the inflammation along with several dissimilar group A streptococcal M kind throughout globe. Rheumatic fever is an autoimmune disorder the reason behind it is that, inflammation caused by immune system to the bacteria. This disease can found at any stage of age but have higher chance on children which have age range between 5 to 14 years without any medication this disease become more and more severe type of disorder [30].

Atherosclerosis

Atherosclerosis is a disease in which plaque (a fatty substance) builds up inside arteries. In the body it can affect any artery, as well as arteries in the heart, brain, arms, legs, and pelvis, and as a result different diseases may develop (According to national institute of health) due to this disease about 50% of all deaths occur in westernized societies.

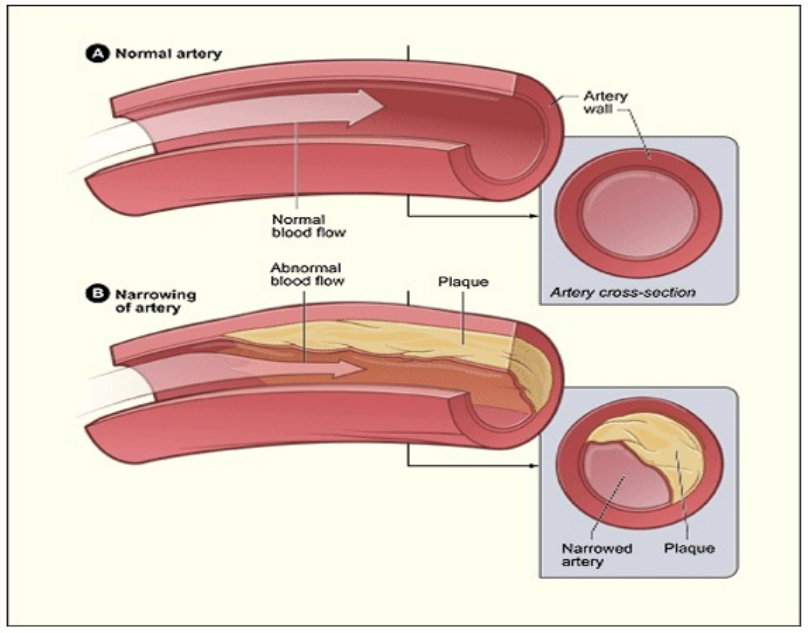

Figure 5: *This diagram shows the plaque formation in artery.*

It can affect people at any age. Until people reach forties and fifties usually doesn't pose a threat. Other name of obesity and its phenotype are still unknown. In this disorder numbers of genes are involved whose expression can be influenced by environmental factors. Several years ago causative gene was isolated in animals. This causative gene encodes Leptin protein which consists of 165 amino acids. Leptin produced by adipocytes hormone. Leptin is key substance of controlling homeostasis of body weight and energy balance. The individuals mostly display hyperleptinemia which is normally caused by a post receptor disorder. Leptinemia reached up to 70ng/ml in some obese individuals.

Environmental factors

Multiple evidences show that environmental factors associated to incidence and severity of cardiovascular diseases. Changes in environment (Migrant studies) show that significantly change CVD risk in a genetically stable population.

Nutritional and lifestyle choices can affect CVD risk. Environmental toxins also influence CVD which is suggested by recent studies in the field of environmental cardiology. Revelation to tobacco smoke associated with increased cardiovascular morbidity and mortality is core example of such environmental risk. In animal representations of experiment of tobacco smoke induces endothelial dysfunction and prothrombotic responses and exacerbates atherogenesis and myocardial ischemic injury. Several large population-based studies indicate

that air pollution increases CVD morbidity and mortality. Polyaromatic hydrocarbons, aldehydes, and metals have also been reported to upraise CVD risk by affecting atherogenesis, thrombosis, or blood pressure regulation. When several drugs, toxins, and infection have been introduced in maternal body these causes cardiac birth defects and premature CVD in later life. As a result, it shows that chronic environmental stress is an important contributing factor of CVD risk. Socioeconomic status, maternal infections, nutritional factors, maternal infections, iatrogenic and nutritional factors and environmental pollution are also associated with CVD.

Genetic factors

Cardiovascular diseases are affected by multiple factors like genetic as well as environmental. From the family combination Genetic factors are susceptible for developing cardiovascular diseases. Using Genomic, Epigenetic and exosmic techniques to improve the quality of life of patients and to the contribution of modified medicines of cardiovascular disease analysis requires general approach. Analogous phenotypic evidences are crucial for detailed understanding of the affiliation between disease and genes, as well as understanding the role of various extrinsic factors on different component of various genotypes for the accurate consequences. This complexity also contributes to difficulties in diagnosis and prognosis of the disease.

Clinical research

The main aim of cardiovascular research is to evaluate CVD chance of occurrence by clinical record, general practices and evaluate changes of CVD chance in population. At the end of 2012 clinical practice data of 2010 to 2012 were taken from general practice (GP) in northwest Adelaide in South Australia. The clinical data were associated with SA1 (Statistical Area Level 1).

Basic research

The SA1 including 148 while other GP (general practices) are 14 performed at the same place. The number of patients from large area they were condensed on Lefevre peninsula and constitute about 18% of the whole population estimated of this area. According to collected data 14,969 numbers of patients were collected from the practice from which 8,630 of these patients were 30 to 75-year-old without any previous history of cardiovascular disease i.e. coronary heart disease, stroke, peripheral heart disease or heart failure etc. Patient were eliminated in case when data were not provided for 7 cardiovascular risk agent, which are available to analyzed the FRE (Framingham Risk Equation) which is used to find out risk perception of CVD. The main segment of CVD estimation dependent on geography and the number of patients were distributed to SA1 in which the lived. The clinical patients generally came from LeFever peninsula or the closet area while some of them came from lager distance. To keep balance positively, less than five patients from SA1 analysis is eliminated from total 701 patients abandon a sample of 4,740 patients. Australian health care center act as a primitive health care system and round about 85% of the population has linked with GP. The main objective of this research is to estimate risk of CVD at area-level and the part of population at giant risk by using Clinical records. Basic research publication on cardiovascular disease has continuously arisen in Brazil and Latin America in the past years. An alternative research by Colantonia., *et al*. published as a unique article in Brazilian of cardiology, the mean percentage is estimated 12.9% per year from 1999 to 2008, while in the last five years the number of publication on cardiovascular disease is promoted at high rate in the same country 1,500 publication is analyzed in 2013. The analysis on cardiovascular research in Latin America reveal that there is close link between the Human development index (HDI) and Gross domestic product (GDP) per capita of the examine country. Throughout the whole research the estimation, the significant increase in the publications on myocardial infraction, high blood pressure, congestive heart failure and coronary artery disease disorder widespread, as well as prohibition and diagnosis have become persistence, with largest impact on the population survival rate is also increased. In spite of continual increase in number of publication, the different feature related to scientific production in cardiology and cardiovascular science rise from Latin America countries distinctly indicate that we still have to invent related level of impact at international level. This condition is become more and more complicated by the presence of cultural and economic differences in country. At the same time many clinical centers, multicenter and multinational registries on the cardiovascular disease must be encourage to increase and identified data, as well as understanding of national.

Translation from "bench to beside"

The Bench-to-Beside program (B2B) is a fund research team to explain scientific evaluations into therapeutic development for patients and to raise understanding of major disorder processes. The B2B award program was firstly intervened by the director of clinical center, with the Director, NIH in 1999. The B2B programmer fulfill this goal by labeling barriers, e.g. the conventionally safe in between general and standard clinical research in biomedical field which can impede advancement towards analyzing new therapeutic strategies for patients.B2B team contain basic clinical research from various different center and NIH institute.

In 2006 the B2B program cost was enlarged to combine the struggle of internal and external NIH research. Internal research is a type of research that takes place in NIH institute under the guideness of federal employees, while external research is paid by NIH and demonstrated by investigator and institutions outside of NIH. The B2B program illustrates the advantage linked with internal and external association. The external community attain to the clinical centers of ideal resources and internal community used for novel or unconventional research with an external investigator. A B2B award gives up to $135,000for two year. Projects, which are paid by various offices and institutes, have constituted various research categories: AIDS, behavioral and social sciences, rare diseases, women's health, minority health, rare drug establishment, pharmacy genomics and general. At the end of 2013 program cycle round about 700 basic principle and investigator have cooperate on 219 funded projects with $50M contributed in total bench-to-beside funding. The external cooperation in 2006 has leads to partnership of 79 institute 30 of which are clinical a transitional sciences award site [31].

Stem cell therapy

Stem cell therapy use in transformation of drug medicine there are two basic concepts of stem- based cell therapy. Traditional cell-based therapy is evolved in the totipotent cells, which is able to distinguish into various mature cells forming functional tissue required for embryonic formation. Other relevant therapy utilization of pluripotent or multipotent (adult cells), are conceivable for making specialized mature cell lines. There are basically 2 categories of stem cells: embryonic stem cells, from halted embryos produced through in lab implementation, and mature stem cells, from minor tissues, e.g. brain, muscle, bone marrow, placental cord and baby teeth. Stem cells remain in microenvironments called "niches", and exposed to soluble agents that give aid and signals performing self-regeneration and differentiation. The capability to reform tissue of cell type in which they inhabit are depend upon the kind of environment in which they are nourish in recent study increased the chance of cells from one type of tissue bring about to another cell type, called plasticity.

Stem Cell-based strategy can be applying to reform, alter, repair, cure disturbed malignant of organs by treating patients with PVD and RHF to motivate the tissues at the molecular and cellular level to regenerate by itself. Bone marrow derived from endothelial progenitor cells (EPCs), which use to repair or reform blood vessels, endothelial nitric oxide synthatase (eNOS) organized EPCs apply to stop the infection and repair microvasculature function and structure in monocrotaline-induced PAH. The murine hind-limb ischemia preparation is a model of peripheral arterial disease PAD, and is useful for testing new therapies or remedy.

MSCs repair different type of tissues after damaging and are recently being applied in clinical experiments to cure person with CVD. The specific mechanism and the capacity of myocyte regeneration contrast to angiogenesis, are still opposite. [32-35]. Anterior infarction and chronic ischemia, of canian model that was Ventricular activation was studied in 20 patients with ischemic heart disease at the time of surgery for myocardial revascularization large amount of MSCs were introduced without causing damage. Actual fact was that MSCs differentiated into endothelial cells and smooth muscle cells developing remarkable left ventricular and tendency headed for decreased fibrosis and increase vascular density. Perceiving viable mechanisms by which stem cells re-establish or replace function pressurize into returning to the crucial role for mitochondrial function which not only play significant role in the maintence of energy and metabolism yield and also command many process such as, stress reactions, apoptosis, necrosis, and organ leisure.

Concepts of exosomes and its characteristics

Exosomes are nano-sized membrane vesicles with 30-100nm diameter and origins from multi vesicular endosome and excreted with the help of cells into exterior environment of the cell. There are multiple contents in exosomes containing protein, lipid, cytokines, mRNA, miRNA and ribosomal RNAs. Exosomes can be secreted by different cells such as B cells, T cells, mast cell, Platelets, reticulocyte, and tumor cells. They are totally different from other micro vesicles (extracellular vesicles) that diameter is ranging from 100-1000mm, their origin is plasma membrane.

Exosomes secreted by MSC, s

MSCs can also produce and excrete effective exosomes that are cholesterol abundant phospholipid vesicles e.g. Adipose MSCs excretes exosomes and micro vesicles, and then also has potential to control angiogenesis. Additionally, vaccination of exosomes from MSCs into stroke rats could diminish the symptoms by supporting angiogenesis. MSCs exosomes through the miR-16-mediated down regulation of VEGF (vascular endothelial growth factor) generate a compelling inhibition of angiogenesis. MiRNAs-bearing endosomes are easily incorporated into CMCs (cardiomyocytes), and ECs (endothelial cells) giving rise to cardiomyocytes protection and angiogenesis advancement. There are many researches that reveal significant roles of miRNAs enclosed in exosomes in the progress of CVDs.

Effects of exosomes on cardiovascular system

- **Anti-apoptosis:** Myocardial infarction is distinguished by continuous loss of cardiomyocytes (CMCs) therefore resulting in congestive heart failure, then become a tough task because of the collapse of CMCs to exchange apoptotic cells. Exposure and prominence of MSCs offer an innovation for MI therapies because of their potential to instantly discriminate into CMCs and their anti-apoptotic effect from paracrine action [36]. MSCs have capability to promote ischemic CMCs damaging by shifting miR-22 in exosomes targeting methyl CpG binding protein 2 (Mecp2) to minimize apoptosis.

- **Anti-cardiac remodeling:** Cardiac remodeling or Cardiac alteration, improved outcomes of CVDs like myocardial hypertrophy and fibrosis, commonly results into heart failure due to lack of regular therapy and proper treatment. MSCs transplantation minimized clog size, develop left ventricular ejection fraction (LVEF) and also change remodeling after persistent myocardial infraction. Recently research reveal that exosomes derived from MSCs was able to enhance myocardial activity and inhibit disadvantageous remodeling after restore blood flow through a blocked arteries typically after a heart attack (MI) in thrombolytic therapy via activating pro-survival signaling, not only rehabilitating bioenergetics but also minimizing oxidative stress. After all anti-cardiac remodeling consequences of MSCs-derived exosomes were accepted but appliance of exosomes mediated insurance have not been authentic or proved.

Cardiac regeneration

Necrosis and apoptosis of CMCs (cardiomyocytes) because of therapeutic microenvironment or injured factors is ready to heart failure. Cardiac regeneration by MSCs and cardiac stem cells (CSCs) differentiation is heightened as a policy for healing CVDs. MSCs are capability to promote endogenous cardiac regeneration. Micro vesicles and exosomes secreted by cardiomyocytes progenitor cells (CPCs) can lead to cardiac regeneration and give improvement to cardiac function by promoting migration of ECs and secretion of VEGF resulting in angiogenesis.

The mixture of human MSCs and human cardiac stem cells have a good effect on the decreasing of infarct size and improve cardiac consequences than MSCs [37]. Although, even if exosomes participate in cardiac regeneration of MSCs still remains ambiguous, and the activity of exosomes in cardiac regeneration wants more analysis.

Bioengineering approaches

From the last few decades, dying speed of cardiovascular diseases (CVD) have reduced appreciably because of recent development in medical diagnosis and promote healthcare. The American people are surviving for a long time, having good health with CVD. For instance, the total economic expenditure of cardiovascular disease in the USA arises to about $298billion in 2008. CVD is became a major chronic and costly strengthen which is spreading in population by aging. For the diagnosis of this severe type of disease bioengineering plays a vital role in inventing replacement and ideal strategies especially for the diagnosis of peripheral arterial disease, atherosclerosis and congestive heart failure. Currently, increased appreciation of tissue characteristics and specific biomaterial is allowing engineers and group of scientists to produce tissue reserve for heart valve replacement, reduction in discolor after myocardial infraction, improvement of heart functions and repairing of blood vessel. Establishment of tissue engineering tools for the diagnosis of heart failure and vascular disorder is a research greatest improvement for the institute of National Heart, Lung, and Blood (NHLBI). MATES (Multi- Agency for Tissue Engineering Science) is used to explain tissue engineering and the use of biological, chemical and physical engineering techniques to handle and exact sum of the behavior of cells. The center of tissue engineering is the building of three dimensional tissues by utilizing biomaterials which deliver mechanical support, cell growth and tissue maintenance. Tissue engineering some time used as an alternative tool with regenerative medicine, biomaterials to enhance repairing mechanisms to heal ruptured tissue or organ and engineering. Bell and Weinberg firstly, in 1986 shown that, the aim of germinating a living blood vessel, the area of tissue engineering has raising continuously. For instance, healthcare center is now being improved by tissue engineering approaches. Clinical research is going to be linked in the cardiovascular, kidney, liver and endocrine areas [38].

Future directions

Tissue engineering approaches for the diagnosis of cardiovascular disease keep meaningful promise for new therapeutic techniques. Further investigation of stem cell technique and generally use of cells differs from induced pluripotent stem cell and formation of microenvironments for tissue formation, repaired and growth. This betterment led to the better approved option for heart valve, revascularization, repair arrhythmias and congenital malformations in population.

Bio artificial organs to assist regeneration in mammal tissues and organs

Tissue Engineering illustrate that a prospective area of research in which a lot of cells, scaffold or bioreactors are employ to manufacture to produce copy, exchange or reformation of faulty tissue or organ. Bio artificial organ (heart) is now possible to regenerate or repair by artificial heart muscle (AHM) which is composed of neonatal rat cardiac myocytes, fibrin gel, decellurized scaffold, construct by manipulate adult rat heart to a string of decellurization solution. By stitching the artificial heart muscle to outer part of the decellurized heart and culturing. As a result, bioartificial hear (BAH) display victorious decellurization of the scaffold and adjacent cell with rich artificial heart muscle outside the perimeter of heart. With this treatment of regeneration for heart failure have rescued my lives. The capability of cardiac regeneration in young mammals is spectacular while the heart of children is more capable for cardiac regeneration e.g. after surgery modification left coronary artery originate from pulmonary artery or with univentricuar heart in children's who shows various morphological changes after volume offload. Regeneration therapies involve bioengineering tissue transplantation and cell insertion; have capacity to diagnose serious heart failure. Cell sheet based tissue transplantation engineering technology is most popular treatment recently accessible for heart failure is heart transplantation [39].

Human induced pluripotent stem cells (iPS) are distinguished into cardiomyocytes to create cardiomyocytes sheets. Firstly, three layers of iPS cardiomyocytes (hiPSCM) sheets transported on tissue of naked rats. Then, invent thick tissue and three layers of sheet are transferred on one day, furthermore three-layers of sheet transferred to on given day after the initial sheet is changed. On the third day the final three layers of sheet are again transplanted or transported, making nine layers. In the final step six layers of sheets are transferred to on fat tissue which combined with arteries and veins to create transportable bud with communicable vessels. The regeneration of tissue damage or lost due to tumor or disorder is thought a model for regenerate or to repair in this case donor deformities appear in different part of the body. In recent year molecular and cellular techniques of healing, possibilities for regeneration have been established. Cell based technique in which Mesenchymal stem cell (MSC) from adipose tissue is mostly used which leads to good healing outcome with reduced donor site morbidity. For example, growth factor based approaches or platelet-rich plasma attains excellent result in the area of bone healing and wound. The skin is a complicated organ involving of the dermis, skin appendages, epidermis including hair follicles and sebaceous gland. In adult mammals wound healing leads to trauma formation without any skin attachment. It is estimated that, cellular and molecular based techniques are basic strategies of skin regeneration and wound healing in mammals.

Outcome research

The research development estimate biomarkers of infection as evaluated by plasma levels; (1) hsCRP (mg/L), (2) Fibrinogen (mg/dl) and (3) sICAM-1(ng/ml) each determined individually. The analysis which is used to evaluate the level of biological marker has been defined.

State-level socioeconomic condition

Earlier indicator inconstant was evaluates the state-level socioeconomic conditions: (1) Labour productivity, (2) wealth and prosperity, (3) average annual economic growth, (4) income and inequality and (5) Labour productivity. State-level wealth was analyzed with 2 different evaluation (a) GDP (gross domesticated product) from Bureau of economic analysis in 1990 were state level per country. (b) State level house hold income in 1990 from US Census. In the 1990 the state level of GDP was determined by Bureau of Economic Analysis utilizing the Budget Standard Industrial Classification (SIC) and Office of Management. In 1990 US Decennial Census manage Median Household income and serve as money income obtained in 1989 calendar per year and the age of members is 15 year or over from related or non-related family members means some of them have blood relation and some of them are not. Median Income at the state-level was determined by US Census from interest income, wages, income, rental salary income, self-employment, dividends, money income and royalty income from welfare income, assistance of public and social security.

The work output value determined by state level labour productivity. While on the other edge wealth is obtained b capital income. In 1990 from US Denennial Census Survey Scarcity was gained and quantified as total number of population and their annually income 1989 federal poverty including the age of house holders and size. While in 1990 Decennial Census established on 1989 household earning data were used to gain state-level Gini coefficient. The annual center for the evaluation of growth rate at the state –level used to determine economic growth per capita with GDP. The statistical analysis can be measured by the Baureu of Economic Analysis the period for biological marker data were combined in the research from 1990 and 1996.

Novel tools for the treatment of cardiovascular disease

For the treatment of cardiovascular disease, Ultrasound (US) has been considered as a valuable diagnostic tool and a potent promoter of beneficial tissue bio effects. Ultrasound (US) contrast agent or mechanical vibration of circulating micro bubbles which can be enveloped and protect a therapeutic agent in the blood stream are mediated by these effects. vibrating micro bubbles can produce stresses directly on neighboring tissues or generate fluid effect that effect on drug stubbing in vascular tissue, lyse thrombi or direct drug to ideal site for delivery.

- **Drug delivery for cardiovascular disease:** The barrier between vascular tissue and bloodstream play a vital role in the drug delivery. Macromolecules can aggregate to the luminal side of this barrier if specific ligand occur it will bound and transport in to the local tissue. Methods for drug delivery of cardiovascular disease are under development. Atherosclerosis is more studied cardiovascular disease that is identified by the accumulation of lipid, cholesterol and other material in the arterial wall and the formation of plaque. This plaque giving rise an immune response.

- And become unstable, exfoliating fatty deposits and hard matter into lumen. The plaque fragments thereafter downstream small diameter vessels, or become nuclei for thrombi, taking to myocardial infarction or stroke. The treatments of Atherosclerosis and other cardiovascular pathologies such as congenital heart disease, rheumatic heart disease and cardiomyopathy are restricting by the inability to deliver therapeutics across endothelium safely and efficiently.

Barriers to drug delivery

Many characteristics obstruct the perforation of therapeutics from vascular lumen into arterial tissue bed, along with blood flow, luminal concentration of drug, pressure induce convection, barrier permeability and intracellular transport rates. Endothelial was the superior barrier to perforation, the internal elastic lamina (IEL) was answerable for up to 25% of perforation resistance. The vascular endothelial barrier conflicts from organ type based on the function and level of control required for maximal fulfillment. Significant contrast has been found in structure, selectively, permeability and signaling control. Cardic microvascular endothelial is a distinctive barrier that also interfaces with neural cell to synchronize that control heart rate and blood flow. Interference and disturbance in these barriers may effect on normal cardiac function when influence tight coupled proteins in the heart [40-44].

Most research attempt conduct with regard to drug deliver from lumen into the tissue bed, and sustain to be emphasis on the blood-brain barrier (BBB). This favoritism is mainly because of latest understanding of cardiovascular and neurological diseases that have possible benefit of potent therapeutic delivery. The BBB (Blood brain barrier) is most exclusively and close fitting modulate endothelial barrier. A complicated lattice of intracellular protein forms a close fitting interface. Only demanding molecules are able to enter by size exclusion. Within the endothelial cell these proteins are bound to intracellular structures and signaling proteins. Protein linked tightly only with compatible molecules [41,45].

Vehicles for enhanced drug delivery

US have been developed as a powerful external enhancer for drug delivery with respect to acoustics awkward vesicles containing enveloped gas molecules. Man other drug delivery vesicles which are used to enhance drug delivery are encapsulated therapeutics e.g. nanogels, micelles and par fluorocarbon droplet. Drug and bioactive gas molecules are enveloped in a nanometer and micro sized vesicles liposomes. Food and Drug Administration (FDA) have been approved (for the diagnostic use to treat cancer and meningitis by liposomal dispersion.

Medical and ethical issues concerning cardiovascular disease and therapy

The latest therapies in cardiovascular medication goal are to stop death rate and upgrade patient status of life. Although, cardiologist emphasis on what can be done instead of what should be done and the previous medication for cardiovascular disease may be failed in the mid of therapeutic buoyancy. The treatment of cardiovascular disease has richness in life saving and better improvement in the condition of patient, also associated with an aging population, which directly leads to outbreak of heart failure which is a type of disorder with increased rate of mortality and morbidity. New therapies of heart failure are established to save life. The element of a chain is "Careers in Cardiology Research" a reader for modern therapies will speech ethical performance of research count in humans. The considerable reduction in cardiovascular mortality supply evidence to social benefits of research that give rise to modern therapies and curing system.

The performance of these modern inventions has resulting in ethical issues with highly publicized instance of, investigations of research on humans. Most physicians who are expert in ethic, control experiment of biomedical research, "self-starting" does not permantaly encounter prediction. Dr. Barry Coller sharp out that has less internal mortality. However, the estimate able objective is better improvement in patient care, understandable process of disorder, or preserving society from recognized danger do not explain neglecting basic principle of human rights that advice and regulate the research.

Epidemiology of CVD in Pakistan

- Hypertension most common disease in Pakistan is hypertension. About 12 million people in Pakistan are hypertensive. Hypertension affects one in three individuals over the age of 45 years in Pakistan. Only 3% of the hypertensive population in Pakistan is effectively controlled. According to National Health Survey Pakistan (NHSP) hypertension affect 18% of adults aged less than 15 years and about 33% of adults above 45 years this Population study was conducted in 1965.

- Ischemic heart disease in 1973 prevalence rate of ischemic heart disease is 0 to1.5% in rural and 0.7% to 3.7% in urban population of Karachi, 4% for diabetes. Higher percentage of heart attack reported in Women greater than 30-years age than men 8.2% while probability is less than 0.04 and over all prevalence was 6.2%.

- Diabetes was reported 8.6% men and 10.4% in women. (Delivering enhanced cardiovascular (Hypertension) disease care through private health facilities in Pakistan).

- Congenital heart disease, with a prevalence of 8 per 1000 births.

- Globally, Globally total number of cardiovascular disease (CVD) deaths (mainly coronary heart disease, stroke, and rheumatic heart disease) had increased 17.5 million from 14.4 million in 1990 (2005).

Coronary heart disease

Coronary heart disease 7.6 million and stroke is 5.7 million. More than 80 percent of the deaths occurred in low and middle income countries. The World Health Organization (WHO) estimates there will be about 20 million CVD deaths in 2015, accounting for 30 percent of all deaths worldwide. Cohort studies of 2030, researchers project that non-communicable diseases will account for more than three-quarters of deaths worldwide; CVD alone will be responsible for more deaths in low income countries than infectious diseases (including HIV/AIDS, tuberculosis, and malaria). Thus, CVD is today the largest single contributor to global mortality and will continue to dominate mortality trends in the future. Acquired CVDs, such as rheumatic heart disease and Chagas still remain a major health problem in low- and middle-income countries. Chagas affects approximately 12 million individuals, most of them children, and about 9million people in South America alone. These neglected diseases need attention because the majority of those affected are poor, few curative options exist and the market potential is insufficient to stimulate the private sector to develop better treatment options.

Conclusion

Cardiovascular disease are the chief incidence and transience source in the sphere and 25% of the mature population even though it fluctuates in provinces and areas. Non-invasive remedy like medicine pile and life adaptation or operating remedy like coronary artery bypass are involve in the treatment of CVD. The most common examples of drugs which are most frequently used in the treatment of CVD are angiotensin receptor blocker, beta blocker, anti-clotting drug, angiotensin converting enzyme inhibitor etc. Current drug remedy used to control heart disease is able to control blood pressure, cholesterol, avert or liquify blood clots and prevent angina signs or recover the beat or strength of the heart shrinkages. Cardiovascular disease is board extent of medical complaint influencing the heart of the blood

vessel of the body which contain coronary artery disease, atherosclerosis, disorder of peripheral vascular system, heart valve disease, hypertension, endocarditis, aorta atrial and orthostatic hypertension disorders. The significance of nanotechnology in diagnostics can be further segmented into three parts: *in vivo, in vitro* and medical diagnosis strategies. Conventionally *in vitro* diagnosis for medical significance is difficult job. While with advancement of scientific area nanotechnology is most recent field which is able for the improvement of tiny, quicker and inexpensive novel generation medical strategies. Coronary heart disease (CHD) is the reason of death of the billions of the people around the world annually. The coronary blood vessel imparts glucose and oxygen towards the heart muscle. While in case of CHD limits the supply as a result leads to the tissue death and myocardial infraction. The chief probability aspect of rising the chance of disease are lack of exercise, lifestyle, smoking and poor diet. Nanotechnology displays potential to became the basis of future medicine. It deals with more specificity in drug management and better quality image the body. Current research has revealed that there are 2 kinds of tablet: unprotected and protected. In case of protected tablet has been considered the possible reason of the death in unanticipated cardiac arrest. The blood moving through the veins by creating a force and it may cause unprotected tablet which frequently conduct to obstruction and myocardial infraction. Recently there is no suitable resolution of unprotected tablet, but a resolution is predicted from the "Program of Excellence in Nanotechnology" through the national heart, lung and blood institute of the National Institutes of Health (NIH). Nanomedicine build use of nano electronic biosensor and nano particles.in the upcoming era nano medicine will be appear as most beneficial tool for the molecular field of nanotechnology, with the support of nano medicine initial finding, control, better diagnosis, proper treatment and continuation of disease is convincible. Furthermore, with the support of nanotechnology injured tissue can be repaired and recreate. Nanoparticles retaining antioxidant characteristic have recently arisen as strong beneficial factor due to their possible application in various discipline of life for developing the excellence of life and prolonged existence. Consequently, the antioxidant property of nano materials is expanding in pharmaceutical, biomedical, cosmetic, food and nutritional area. Nano materials are very tiny particles because of their smaller size they have greater the ability to penetrate, raised movement in the body and also biocompatible to improve oxidative pressure, now they have developed as a crucial factor for monitoring elderly and its related pathologies, involving cardiovascular disorder, neurodegenerative disorder and pulmonary disorder.

Bibliography

1. Anthea M., *et al*. "Human Biology and Health". Englewood Cliffs, New Jersey (1993).
2. Dantas AP., *et al*. "Vascular aging: facts and factors". *Frontiers in Physiology* 3 (2012).
3. Eakin CM., *et al*. "Caribbean corals in crisis: record thermal stress, bleaching, and mortality in 2005". *PloS One* 5 (2010): e13969.
4. Ndumele CD., *et al*. "Publication of recruitment methods in focus group research of minority populations with chronic disease: a systematic review". *Journal of Health Care for the Poor and Underserved* 22 (2011): 5-23.
5. Carandang R., *et al*. "Trends in incidence, lifetime risk, severity, and 30-day mortality of stroke over the past 50 years". *Journal of the American Medicine Association* 296 (2006): 2939-2946.
6. Yeh RW and Go AS. "Rethinking the epidemiology of acute myocardial infarction: challenges and opportunities". *Archives of Internal Medicine* 170 (2010): 759-764.
7. Hovorka R., *et al*. "Manual closed-loop insulin delivery in children and adolescents with type 1 diabetes: a phase 2 randomised crossover trial". *The Lancet* 375 (2010): 743-751.
8. Amar J., *et al*. "Blood microbiota dysbiosis is associated with the onset of cardiovascular events in a large general population: the DESIR study". *PLoS On*e 8 (2013): e54461.

9. Christoforou N and Gearhart JD. "Stem cells and their potential in cell-based cardiac therapies". *Progress in Cardiovascular Diseases* 49 (2007): 396-413.

10. Silva GV., *et al*. "Mesenchymal stem cells differentiate into an endothelial phenotype, enhance vascular density, and improve heart function in a canine chronic ischemia model". *Circulation* 111 (2005): 150-156.

11. Dufourcq P., *et al*. "Secreted Frizzled-Related Protein-1 Enhances Mesenchymal Stem Cell Function in Angiogenesis and Contributes to Neovessel Maturation". *Stem Cells* 26 (2008): 2991-3001.

12. Kanneganti T-D., *et al*. "Intracellular NOD-like receptors in host defense and disease". *Immunity* 27 (2007): 549-559.

13. Beaglehole R and Bonita R. "Global public health: a scorecard". *The Lancet* 372 (2008): 1988-1996.

14. Barone E., *et al*. "Long-term high-dose atorvastatin decreases brain oxidative and nitrosative stress in a preclinical model of Alzheimer disease: a novel mechanism of action". *Pharmacological Research* 63 (2011): 172-180.

15. Dipchand AI., *et al*. "The Registry of the International Society for Heart and Lung Transplantation: sixteenth official pediatric heart transplantation report—2013. focus theme: age". *The Journal of Heart and Lung Transplantation* 32 (2013): 979-988.

16. Lund LH., *et al*. "The Registry of the International Society for Heart and Lung Transplantation: thirtieth official adult heart transplant report—2013. focus theme: age". *The Journal of Heart and Lung Transplantation* 32 (2013): 951-964.

17. Kushwaha SS., *et al*. "Restrictive cardiomyopathy". *New England Journal of Medicine* 336 (1997): 267-276.

18. Olin JW and Sealove BA. "Peripheral artery disease: current insight into the disease and its diagnosis and management". *In Proceedings of Mayo Clinic Proceedings* (2010): 678-692.

19. Frohlich ED., *et al*. "The heart in hypertension". *New England Journal of Medicine* 327 (1992): 998-1008.

20. Lee C., *et al*. "Exosomes mediate the cytoprotective action of mesenchymal stromal cells on hypoxia-induced pulmonary hypertension". *Circulation* 126 (2012): 2601-2611.

21. Jeffery T and Morrell N. "Molecular and cellular basis of pulmonary vascular remodeling in pulmonary hypertension". *Progress in Cardiovascular Diseases* 45 (2002): 173-202.

22. Clark RA., *et al*. "Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis". *British Medical Journal* (2007).

23. Polisena J., *et al*. "Home telemonitoring for congestive heart failure: a systematic review and meta-analysis". *Journal of Telemedicine and Telecare* 16 (2010): 68-76.

24. Clarke M., *et al*. "Systematic review of studies on telemonitoring of patients with congestive heart failure: a meta-analysis". *Journal of Telemedicine and Telecare* 17 (2011): 7-14.

25. Inglis SC., *et al*. "Which components of heart failure programmes are effective? A systematic review and meta-analysis of the outcomes of structured telephone support or telemonitoring as the primary component of chronic heart failure management in 8323 patients: abridged Cochrane Review". *European Journal of Heart Failure* 13 (2011): 1028-1040.

26. Esfandiarei M., *et al*. "Dilated cardiomyopathy and other cardiomyopathies". *Cardiovascular Genetics and Genomics for the Cardiologist* 55 (2007).

27. Nishimura RA., *et al*. "ACC/AHA 2008 Guideline update on valvular heart disease: focused update on infective endocarditis: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons". *Journal of the American College of Cardiology* 52 (2008): 676-685.

28. Hoffman JI and Kaplan S. "The incidence of congenital heart disease". *Journal of the American College of Cardiology* 39 (2002): 1890-1900.

29. Zhang T., *et al*. "Fast pediatric 3D free-breathing abdominal dynamic contrast enhanced MRI with high spatiotemporal resolution". *Journal of Magnetic Resonance Imaging* 41(2015): 460-473.

30. Feldman RD. "American health care: government, market processes, and the public interest". Transaction Publishers: 2000.

31. Butler D. "Translational research: crossing the valley of death". *Nature News* 453 (2008): 840-842.

32. Wang TJ., *et al*. "Multiple biomarkers for the prediction of first major cardiovascular events and death". *New England Journal of Medicine* 355 (2006): 2631-2639.

33. Rangappa S., *et al*. "Transformation of adult mesenchymal stem cells isolated from the fatty tissue into cardiomyocytes". *The Annals of Thoracic Surgery* 75 (2003): 775-779.

34. Bakeeva L., *et al*. "Mitochondria-targeted plastoquinone derivatives as tools to interrupt execution of the aging program. 2. Treatment of some ROS-and age-related diseases (heart arrhythmia, heart infarctions, kidney ischemia, and stroke)". *Biochemistry* (Moscow) 73 (2008): 1288-1299.

35. Aguirre A., *et al*. "Notch and EGFR pathway interaction regulates neural stem cell number and self-renewal". *Nature* 467 (2010): 323-327.

36. Khubutiya MS., *et al*. "Paracrine mechanisms of proliferative, anti-apoptotic and anti-inflammatory effects of mesenchymal stromal cells in models of acute organ injury". *Cytotherapy* 16 (2014): 579-585.

37. Moruzzi VL. *et al*. "Calculated electronic properties of metals". Elsevier (2013).

38. Zarin DA., *et al*. "The ClinicalTrials. gov results database—update and key issues". *New England Journal of Medicine* 364 (2011): 852-860.

39. Sekine H., *et al*. "Myocardial tissue engineering: toward a bioartificial pump". *Cell and Tissue Research* 347 (2012): 775-782.

40. Weis SM and Cheresh DA. "Tumor angiogenesis: molecular pathways and therapeutic targets". *Nature Medicine* 17 (2011): 1359-1370.

41. Luissint A-C., *et al*. "Tight junctions at the blood brain barrier: physiological architecture and disease-associated dysregulation". *Fluids Barriers CNS* 9 (2012): 23.

42. Król S., *et al*. "PBDEs in environmental samples: Sampling and analysis". *Talanta* 93 (2012): 1-17.

43. Kuruvilla L and Kartha CC. "Molecular mechanisms in endothelial regulation of cardiac function". *Molecular and Cellular Biochemistry* 253 (2003): 113-123.

44. Weis SM., *et al*. "Compensatory role for Pyk2 during angiogenesis in adult mice lacking endothelial cell FAK". *The Journal of Cell Biology* 181 (2008): 43-50.

45. Luissint A-C., *et al*. "JAM-related proteins in mucosal homeostasis and inflammation". *In Proceedings of Seminars in Immunopathology* (2014): 211-226.

Volume 7 Issue 3 March 2020