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A Review on Atherosclerosis

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ABSTRACT

Atherosclerosis is the condition in which deposition of cholesterol on inner linings of arteries take place. In atherosclerosis plaque builds up in a series of stages inside arteries resulting into obstruction to blood flow. Atherosclerosis is the most leading cause of death in industrialized countries. Mostly arteries in the brain, heart, arms, legs & pelvis are affected. The disease is responsible for heart attacks, strokes, aortic aneurysms & peripheral vascular disease. This inflammatory disease is precipitated by elevated levels of low density lipoprotein cholesterol in blood. Endothelial dysfunction is the main stimuli for development of disease. Risk factors of atherosclerosis are both unmodifiable& modifiable which are important in assessment and should be monitored beginning in childhood, even in asymptomatic patients. . The plaques can be predicted by invasive & non-invasive imaging techniques. The blockages are treated by coronary artery bypass, heart catheterization. Medicines along with lifestyle improvement are also useful in management of atherosclerosis. Successful treatment minimizes chances of cardiovascular events, morbidity & mortality.

Key-words: Atherosclerosis, cholesterol, LDL, endothelial dysfunction, risk factors, treatment

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INTRODUCTION:

The term Atherosclerosis is derived from the Greek, athero (meaning gruel or porridge) referring to soft lipid rich material in the center of atheromas and sclerosis (scarring) referring to connective tissue in the plaques. [1] Atherosclerotic vascular disease is the cause of heart attacks, stroke, aortic aneurysms, and peripheral vascular disease, which together represent the most frequent causesof death in the industrialized world. Atherosclerosis is a progressive disease of medium and large sized arteries characterized by focal intimal lesions called atheromas or atherosclerotic plaques that protrude into vessel lumen and eventually leading to various complications. Economicdevelopments, habits of diet and diminished physical activity can favour atherogenesis. Such factors have now become globalize, so that we face an epidemic of atherosclerosis that reaches far beyond Western societies. Risk factors include are non-modifiable like age, male gender, genetics & Modifiable like smoking, obesity, physical inactivity, lipid disorder, hypertension, diabetes, stress. Although low-density lipoprotein (LDL) remains the most important risk factor for atherosclerosis, immune and inflammatory mechanisms of atherosclerosis have gained tremendous interest in the past 20 years. [2-6]

PATHOGENESIS OF ATHEROSCLEROSIS:

Atherosclerosis progresses in a series of stages, although some lesions at each stage may not progress further or may even regress if inciting events, such as hypercholesterolemia, smoking, or hypertension, are controlled.Atherosclerosis is a chronic, immunoinflammatory, fibro proliferative disease of medium and large sized arteries. The concepts of atherogenesis haveevolved from vague ideas of inevitable degeneration to a well defined scenario ofmolecular and cellular events. It is now known that endothelial cells, leukocytes,and intimal smooth muscle cells play the key roles in the development of thisdisease. There are three stages in the life history of an atheroma i.e. initiation, progression and complication [7-9].

INITIATION:

Recruitment of mononuclear leucocytes to the intima characterizes initiation ofthe atherosclerotic lesion. Specific adhesion molecules expressed on the surfaceof vascular endothelial cells, under the effect of atherogenic stimuli, mediate leukocyte adhesion of mainly monocytes and to a lesser extent, T-lymphocytes tothe intima. These adhesion molecules are selectins and members of theimmunoglobulin super family such as Vascular Cell Adhesion Molecule-1 (VCAM-1), Intercellular Adhesion Molecule-1(ICAM-1). Once adherent, the leucocytesenter the intima directed by chemo attractant chemokines such as macrophagechemoattractant protein-1 (MCP-1), Tumor Necrosis Factor (TNF) .Cytokines(e.g., interleukin-8) also may play a role in monocyte-macrophage trafficking.The monocytes get transformed to macrophages in the intima. With chronichyperlipidemia, lipoproteins accumulate inside the intima, subsequently oxidizedby the action of oxygen free radicals generated by intimal macrophages. OxidizedLDL further stimulates the release of cytokines and chemokines and flares up theongoing inflammation. Macrophages internalize oxidized LDL through scavengerreceptors and are then called foam cells. Accumulation of foam cells is the hallmarkof early and asymptomatic atheromatous precursor, the fatty streak.

PROGRESSION:

As the disease progresses, the inflammatory response is accompanied by afibro proliferative response mediated by intimal smooth muscle cells. Progressingatheroma involves accumulation of smooth muscle cells which elaborateextracellular matrix macromolecules. Smooth muscle cells and the collagen richmatrix they produce, confer stability to plaques, protecting them against the dreadedconsequences of plaque rupture and thrombosis. The smooth muscle cell is theprincipal connective tissue producing cell in the normal and atherosclerotic intima.Synthetic activity of smooth muscle cells is regarded beneficial whereas their lossis detrimental for the plaque stability. Lack of smooth muscle cells at sites ofrupture is

attributed to apoptotic cell death [10, 11]. Progressing atheroma often accumulates calcium. Calcification probably has a stabilizing effect on the plaque.Neovascularisation is frequent in advanced atherosclerosis. It is probablya marker of ongoing disease activity and characterizes high-risk plaques as thenew vessels aggravate risk of intraplaque haemorrhage as well as play role indrawing in more inflammatory cells into the plaque.An atheromatous plaque is composed of cellular component in form ofmacrophages, smooth muscle cells, T cells, extracellular matrix including collagen,elastic fibres and proteoglycans and lipids, intracellular as well as extracellular.Morphologically, there is an outer fibrous cap composed of collagen and smoothmuscle cells. Deep to the cap is a more cellular area containing macrophages, Tcells and smooth muscle cells. Beneath it is a necrotic core containing lipid,debris of dead cells, foam cells, fibrin and smooth muscle cells[12].

COMPLICATIONS ASSOCIATED WITHPLAQUES:

A stenoticplaque can gradually occlude a vessel, compromise bloodflow and cause ischemic injury to myocardium depending on the blood supplyby the affected vessel. In the coronary circulation this occurs when there is loss of70% of area through which blood can flow. This is known as critical stenosis.The clinical condition is known as stable angina.On the other hand, vulnerable plaques are more prone to acute plaque change likerupture/fissuring, erosion/ulceration and haemorrhage into the atheroma orintraplaque rupture. Intraplaque haematoma further increases the intraplaquepressure making it prone to physical disruption. Plaque vulnerability anddestabilization is of multifactorial etiology with inflammation, cap matrix andnecrotic lipid core remodeling being important pathobiological processes associated with vulnerability and destabilization. Reduced matrix synthesis aswell as increased matrix degradation predisposes vulnerable plaques to rupture inresponse to extrinsic mechanical or hemodynamic stresses. Other contributingfactors towards disruption of plaque are vasospasm, low flow, decreased fibrinolyticactivity, procoagulant states etc. Modification of endothelial dysfunction andreduction of vulnerability to plaque rupture and thrombosis may lead to plaquestabilization. A ruptured plaque may manifest clinically as unstable angina,myocardial infarction or sudden death. However, if the plaque disruption is minor,local flow is high, and the fibrinolytic system is active, thrombus formation maybe minimal and plaque may remain silent for years and may pose life threateningsudden complications if left undetected. A thrombus may propagate and accumulateadditional platelets. Older thrombi may become organized and recanalized. Recentthrombi may dissolve by fibrinolysis.

BIOCHEMICAL BASIS OFATHEROSCLEROSIS:

The Thickening of artery walls is associated with deposits of cholesterol whichoriginate from LDL particles that circulate in the blood. Current research suggeststhat damage to the endothelial cell inner lining of the vessel allows LDL particlesand blood platelets to enter the arterial wall. The LDL contains polyunsaturatedfatty acids, which can be attacked by free radicals, generated as a part of normalmetabolic processes. As a result LDL becomes oxidized and gives rise to productsthat that are toxic to the cells of the artery wall. Macrophages attempt to remove theoxidized LDL but are unable to degrade the cholesterol, which accumulates asdroplets thereby giving a foamy appearance. Cholesterol laden foam cells givecharacteristic appearance to the fatty streaks. The toxic products can kill the foamcells leaving cholesterol deposits, and the accumulated cholesterol, cells and debrisconstitute an atheroma. Conditions such as hypercholesterolemia, which isassociated with defective LDL receptor increases the risk of atherosclerosis. BesidesLDL there are other key players having an important role in atherogenesis as wellas its prevention. Numerous large-scale epidemiological studies persistentlydemonstrated an inverse relationship between plasma high-density lipoproteincholesterol (HDL-C) level and the risk of coronary heart disease (CHD)[13].

TYPES OF PLAQUE:

On the basis of pathological characteristics, two types of plaques are identified.

i)Vulnerable plaque:It is also known as non stenotic plaque which isprone to rupture, thrombosis and other complications of plaque. It has a large lipidcore, thin fibrous cap, clusters of inflammatory cells mainly foamymacrophages, fewer smooth muscle cells. Vulnerable plaque also shows outward remodeling of media, which preserves the vessel lumen known as compensatoryenlargement or positive remodeling often leading to underestimation of size byX-ray angiography.

ii) Stable plaque or stenotic plaque:It is characterized by athick fibrous cap, small lipid core, more of collagen synthesizing smooth musclecells, less inflammation. It shows less compensatory enlargement.It graduallyoccludes the vessel well visualized by traditional angiographic techniques. Stenoticlesions give rise to blood vessel luminal compromise. These lesions are easilyassessed with conventional radiographic methods[14].

FATE OF ATHEROMATOUS PLAQUE:

Inflammatory response also plays a role in the development of complications of atheromatous plaque, i.e., rupture followed by thomboembolic phenomenon which is mainly responsible for acute complications of atherogenesis like stroke and myocardial Infarction. The activated macrophages produce proteolytic enzymes which degrade the collagen and weaken the protective fibrous cap. This, coupled with the production of tissue factor by macrophages provides a prothrombotic mileu leading to thrombosis when plaque ruptures [17].

Thus, atherosclerosis can be considered to be a form of chronic inflammation resulting from interaction between modified lipoproteins, monocyte derived macrophages and T-cells that migrate from blood and the normal cellular elements of the arterial wall.

SITE OF DEVELOPMENT:

The lesions of atherosclerosis occur principally in large and medium sized arteries. The nature of the flow, i.e., shear stress or turbulence, appears to be important in determining where the lesions occur. Changes in flow alter the expression of molecules involved in atherogenesis. Rolling and adherence of monocytes and T-cells occur more at these sites and appear to be critical in determining the sites of lesions [18].

RISK FACTORS:

I) RISK FACTORS THAT CANNOT BE CHANGED:

1) Age:

The risk of cardiovascular events increases as we get older. Age remains one of the strongest predictors of disease. Of course, nothing can be done to reduce age. However, careful attention to diet and maintaining fitness may delay the degenerative changes associated with aging.

2) Gender:

Men are more likely than women to develop coronary heart disease, stroke, and other cardiovascular diseases that are manifestations of atherosclerosis. Whether this is because male hormones—androgens —increase risk or because female hormones— estrogens—protect against atherosclerosis is not completely understood. It is likely that both play a role, but that the protective role of estrogens is the predominant factor. This seems to be supported by the fact that heart disease risk for women rises dramatically after menopause, when their bodies stop producing estrogen.

3) Heredity:

There is no question that some people have a significantly greater likelihood of having a heart attack or stroke because they have inherited a tendency from their parents. In some instances, such as familial hypercholesterolemia (very high levels of cholesterol in the blood), the pattern of inheritance is well understood and the specific biochemical defects are well characterized. For most cardiovascular risk factors, however, the specific way in which inheritance plays a role is not at all clear. As in almost all situations in medicine, both heredity and environment play a roleand it is often difficult to know where one stops and the other begins. Prior generations did not have the level of medical care we now enjoy, nor the general awareness about health; the details of the illness that one's grandparents or even parents had may not be precise. Prior to the 1960s, many more people smoked and little attention, if any, was paid to diet and fitness. So it is possible that environmental factors, not genes, were responsible for Grandpa's heart attack or stroke.In practical terms, anyone who has a family history of heart disease that occurred at an early age (below 55) should be especially careful to reduce the impact of any risk that can be controlled. Even if one can successfully control known risk factors, there are, unfortunately, a number of inherited characteristics that we have not yet identified and so cannot favorably affect. Individuals with a history of atherosclerotic cardiovascular disease in the family simply have to be more vigilant if they wish to avoid heart attacks and strokes. We should remember, however, that almost every family has some member who died of a heart or blood vessel disease, since about half of all deaths are attributable to these diseases. If these episodes occurred in relatives who were 75 or 80, it may not be a major cause for concern.

II) RISK FACTORS THAT CAN BE CHANGED:

1) High Blood Pressure:

There are several ways to classify hypertension. It is generally agreed that high blood pressure is defined as readings that consistently exceed 140/90 mm Hg, when measured over a period of time with a blood pressure cuff (sphygmomanometer). Experts focused on diastolic blood pressure, the lower of the two numbers, which represents the resting pressure between heartbeats. Anyone with a reading equal to or greater than 90 mm Hg has diastolic hypertension, regardless of the level of the higher number, which represents the systolic, or pumping, pressure. Some individuals, particularly those over 65 or 70 years of age, have what is called isolated systolic Hypertension.

The most recent expert committee defines this as a systolic blood pressure of 160 mm Hg ormore, when the diastolic blood pressure is less than 90 mm Hg. Actually, the levels of both systolic and diastolic blood pressures determines an individual's risk. In fact, of the two readings, the systolic blood pressure may be the superior predictor of all the complications we attribute to hypertension.

There is a wealth of studies to show that successfullytreating hypertension will substantially reducethe increased risk associated with it. Fortunately, too,we now have many well-tolerated antihypertensivemedications that lower blood pressure and can betaken indefinitely. Although most of the treatmentdata are based on drugs, such measures as weightloss, salt restriction, and exercise may also lowerblood pressure other complications of hypertension.

2) High Blood Cholesterol and Related Lipid Problems:

Elevated levels of serum lipids (cholesterol and triglycerides)are extremely common and are one of themost important of the heart disease risk factors thatcan be changed. The levelof total cholesterol in the blood is a strong predictorof the likelihood that an individual will develop coronaryheart disease and, to a much lesser degree, astroke. Most experts consider levels under 200 mg/dlto be normal and those between 200 and 239 mg/dlto be borderline high. Levels above 240 mg/dl presentan increased risk for a heart attack-more thandouble the risk of levels below 200 mg/dl.

The most important and best studied are highdensitylipoproteins (HDL cholesterol, or HDL-C) andlow-density lipoproteins (LDL-C). These levels andtheir relationship to each other maybe more importantthan total cholesterol levels in predicting heartdisease risk. LDL levels over 160 mg/dl are definitelyassociated with increased risk, while values from 130to 159 mg/dl are borderline. In contrast, HDL cholesterolis the fraction of cholesterol that appears toprotect against coronary heart disease. The higherthe level of HDL, the lower the risk. Ideally, it shouldbe at least 35 mg/dl. A ratio of LDL to HDL greaterthan 3.5 or 4:1 is generally agreed to increase risk.While an individual's lipid profile is affected byage (total cholesterol rises with the years), gender(women tend to have higher levels of HDL), and heredity(elevated cholesterol and triglycerides tend torun in families, and certain families have extremelyhigh levels), the picture can be significantly changedby life-style modifications. A diet low in saturated fatand cholesterol will lower serum cholesterol an averageof 5 percent, but this diet maybe more effectivein some people. The general rule of thumb is that riskof coronary heart disease decreases by 2 percent forevery 1 percent drop in total serum cholesterol.Reducing alcohol intake in heavy drinkers and (forthose who are overweight) body weight can significantlyreduce triglyceride levels. Regular exercise willlower triglycerides and increase HDL cholesterol,and stopping smoking will also raise HDL cholesterol.For people with very high total cholesterol and LDLcholesterol levels, diet and exercise alone may notresult in a great enough reduction and these life-stylemeasures may need to be combined with cholesterolloweringdrugs.

3) Lipoprotein (a):

Lipoprotein (a) or "Lp (a)" was discovered in 1963 until recently.Lp (a) is a molecule composed of the protein portionof low-density lipoprotein (LDL), which is calledapoB100, and another protein called Ape(a). Ape(a) isvery similar chemically to plasminogen, a naturallyoccurring substance that participates in dissolvingclots that form in the bloodstream. Lp(a) has the oppositeeffect, however it interferes with the normalprocess of clot lysis (dissolving) and thus may increasethe likelihood that once a clot forms, a heartattack or stroke will occur.The impact of Lp (a)levels on the risk of coronary heart disease is asstrong as that seen with total cholesterol levels orreduced high-density lipoprotein (HDL) levels, andthe increase in risk attributable to high Lp (a) levels isindependent of other risk factors.

4) Cigarette Smoking:

Cigarette smoking is a major contributor to coronaryheart disease, stroke, and peripheral vasculardisease—even though smokers tend to be thinner andto have lower blood pressure than nonsmokers.Individuals, who smoke, regardless of their level ofother risk factors or family history, are at significantrisk of premature coronary disease and death. Smokers,for example, have less of a chance of survivinga heart attack than nonsmokers. Smoking is thenumber one risk factor for sudden cardiac death andfor peripheral vascular disease.Smoking cigarettes that are low in nicotine and tardoes not decrease the risk of heart disease, which isincreased by the effect of smoke on blood vesselwalls. In fact, some people tend to smoke more andinhale deeply when they switch to this type of cigarette,increasing their exposure to the carbon monoxidein the smoke itself.Fortunately, the risk of heart disease begins to declinerapidly as soon as smokers—even heavy, longtimesmokers—stop. Ultimately, their level of risk isalmost the same as that of people who have neversmoked.

5) Obesity:

Any level of overweight appears to increase heartdisease risk. Obesity can predispose the developmentof other risk factors, and the greater the degree ofoverweight, the greater the likelihood of developingother antecedents of atherosclerosis (such as highblood pressure and diabetes) that will increase theprobability that heart disease will develop. Those whoare obese (more than 30 percent over their ideal bodyweight) are the most likely to develop heart disease,even if they have no other risk factors.

There are two basic patterns of obesityone in which excess fat is found primarily in the abdominalarea (the "beer belly" or apple shape) andone in which excess fat deposits from around the hipsand buttocks (the pear shape). The former type iscalled male-pattern obesity or android obesity; thelatter, female-pattern or gynecoid obesity. Android obesity, which is also found in some women (especiallyafter menopause), is associated with an increasedrisk of cardiovascular disease, specifically,coronary heart disease and stroke. A general rule ofthumb is that a man's waist measurement should notexceed 90 percent of his hip measurement and thata woman's waist measurement should be no morethan 80 percent of her hip measurement.Android obesity appears to be most closely relatednot only to risk but also to other cardiovascular riskfactors—namely hypertension, elevated triglycerides,low HDL cholesterol, elevated blood sugar levels,and diabetes mellitus.

6) Diabetes Mellitus And Insulin Resistance:

Individuals with diabetes mellitus, especially thosewhose diabetes occurs in adult life, have an increasedincidence of coronary heart disease and stroke. Thosewho have slightly elevated blood sugar levels but donot have detectable diabetes also have an increasedrisk of developing these problems. Many individualswhose diabetes begins after age 40 or 50 (so-calledadult-onset or Type II diabetes) often have higherthan normal levels of circulating insulin. The primaryrole of insulin, a hormone produced by the pancreas,is to maintain blood sugar at normal levels and toassist this body fuel in entering each of the body'scells. For some reason, some individuals do not respondas readily to insulin, and more is required todo the job; they have insulin resistance. Elevated levelsof insulin can raise blood pressure and assist inthe deposition of and reduce the removal of cholesterolfrom plaques in the arteries. Both these actionsincrease the likelihood that atherosclerosis and itscomplications will develop.Weight reduction and exercise canimprove the burning up of blood sugar (glucose) andprevent or slow down the onset of diabetes.Individuals who develop diabetes in childhood (socalledjuvenile-onset or Type I diabetes) are morelikely to develop kidney and eye problems than coronaryheart disease or strokes. In this type of diabetes,insulin is absent due to disease in the pancreas.

7) Fibrinogen:

Serum fibrinogen is a component of the blood thatplays a central role in the clotting process. The level of fibrinogen is anindependent cardiovascular factor. Individuals with higherlevels may be more prone to develop clots in theirarteries, thereby increasing the risk of a heart attackor stroke. Fibrinogen levels rise with age, and in thatsense are not a risk factor that can be modified. However,fibrinogen levels are also adversely affected bycigarette smoking, which can be controlled.

8) Alcohol:

Drinking four or more drinks per day can have deleterious effects. It raises blood pressure and puts the individual at significant risk of liver damage, central nervous system complications, and a number of other serious problems, some of which are cardiovascular.

9) Behavioral Factors:

Coronary-prone behavior, sometimes referred to as"Type A behavior, is felt by some, but not all, expertsto be an important risk factor for coronary heart disease. Current definitions of Type A personality includea sense of time pressure and chronic impatienceas well as excessive hostility. Contrary to popular belief, working hard or long hours is not necessarily afeature of the Type A or coronary-prone personality.Type A individuals tend to become upset easily, oftenfor little cause, and are always in a hurry. They areconstantly trying to do yet one more thing. Thoughmany individuals who have heart attacks fit this personalitydescription, current studies have not conclusivelyproved that a Type A personality is a truecardiovascular risk factor.

iii)Protective Factors:

1) Left Ventricular Hypertrophy (LVH):

The left ventricle is the chamber of the heart thatpumps blood to all parts of the body except the lungs.The majority of persons with an enlarged left ventricle either has hypertension or has alreadyhad a heart attack. Successful treatment of hypertension will not only reduceblood pressure but will also reduce the size ofthe left ventricle and probably lower the risk associatedwith ventricular enlargement.

2) Cocaine:

Cocaine constricts the coronaryarteries, decreasing blood flow to the arteriesof the heart, and reduces the amount of oxygen availableto the heart while increasing the heart rate andits demand for oxygen. This combination of effectscan precipitate a cardiac crisis and sometimes death,even upon the first use of the drug.Cocaine is also a risk factor for congenital heartdisease. Babies born to women who took cocaineduring pregnancy are at increased risk of atrial-septaland ventricular-septal defects, as well as other congenitalanomalies and adverseeffects, such as lowbirth weight, that are directly related to the drug'saction on the mother's cardiovascular system.

3) Exercise:

Exercise also seems to have a positiveeffect on a number of other risk factors. Regular exercise can lower cardiovascularrisk and it should be encouraged foreveryone within the limits of each individual.

4) Estrogen:

Estrogen (the major female sex hormone) protectsagainst heart attacks and other forms of cardiovasculardisease. Estrogen increases HDL cholesterol,which may explain how the hormone reduces the incidenceof heart attacks in premenopausal women. Itis now clear that once menopause occurs, women areat the same risk for heart attacks as are men. Thus,it is reasonable to advise that postmenopausalwomen receive estrogen replacement therapy unlessit is medically contraindicated. Although it is likelythat estrogen replacement therapy reduces the frequencyof heart attacks, such therapy may increasethe risk of cancer of the uterus. This risk can be reducedor eliminated by combining estrogen with progesterone,another female sex hormone. As an added advantage, postmenopausalestrogen replacement reduces the severity ofosteoporosis—the bone thinning that is a leadingcause of death and disability in older women.

PROGRAMME FOR CARDIOVASCULARRISK FACTOR MODIFICATION:

For those who are freeof cardiovascular risk factors or clinical vascular disease,certain simple steps can always help, and willdo little if any harm:

Eat a heart-healthy diet—onelow in saturatedfats and cholesterol. Use monosaturated or polyunsaturated fat.

Reduce weight if it is elevated.Even a smallamount of weight loss can be helpful if you areoverweight.

Moderate your salt intake.Many people are notsensitive to salt and their blood pressure willnot rise even if their intake of table salt andother forms of sodium is high. The problem is,we cannot distinguish who is and is not saltsensitivewithout complex testing. Most of useat more salt than we need. Many foods arenaturally high in sodium and others have saltadded in processing. Simple measures such asnot adding salt to the food as it is cooked or atthe table will reduce sodium intake to a reasonableamount. This degree of salt restrictionis absolutely safe and does not rob food of itstaste, especially if herbs and spices are used asalternative flavorings.

Start a regular exercise program.Virtually everyonecan benefit from regular exercise. To behelpful, the program need not be too strenuousand can be tailored to an individual's preferences,schedule, and physical capabilities. Regularwalking may be all that is necessary.

If you smoke, stop.Nothing will be more beneficial.

If you drink alcohol, do so in moderation.

Learn stress-reduction techniquesand avoid reactingto stressful situations in ways that willonly serve to aggravate the problem.

Have your risk factor status assessed on a regularbasis.A clean bill of health on one occasiondoes not guarantee a lifetime of protection.Blood pressure, if normal, should be checkedevery two years or so, and cholesterol, if normal,should be checked every five years[19] .

ATHEROSCLEROSIS TREATMENT PROGRAM OVERVIEW:

1.The diagnostic and therapeutic focus for patients with coronary artery, other vascular disease, and diabetes should shift to address the underlying atherosclerosis disease process.

2. Patients with coronary artery, other vascular disease, and/or diabetes should be treated with therapies that have been demonstrated in randomized clinical trials to alter the natural history of atherosclerosis, decrease cardiovascular events, and improve survival.

3. Patients should be treated regardless of whether they have undergone or are undergoing a revascularization procedure and regardless of whether they have symptomatic angina, silent ischemia, or atherosclerosis without ischemia.

4. Antiplatelet agents, beta blocker, ACE inhibitor, statin, omega-3 fatty acids, diet, and an aerobic exercise program should be considered initial and fundamental therapy for all patients with clinical manifestations of any atherosclerotic vascular disease (coronary artery disease, peripheral vascular disease, and/or carotid artery disease) and/or diabetes, irrespective of presence or absence of known vascular disease.

5. Patients with documented atherosclerosis or diabetes should not be discharged from the hospital or leave their outpatient encounter without initiation of treatment, unless contraindicated.

6. Therapies such as type I anti-arrhythmic agents that have been shown to potentially increase the risk of an adverse outcome should, in general, be avoided in patients with AVD.

7. Therapies such as nitrates and calcium channel blockers that provide symptomatic benefit but have not been shown to impact mortality or the incidence of coronary events should, in general, be reserved for patients who remain unacceptably symptomatic despite therapy with ASA, statin, ACE inhibitor, beta blocker, and an exercise program [20].

CONCLUSION:

Our understanding of atherosclerosis has progressedremarkably over the past few years. All phases of atherosclerosis are regulated by inflammatory mechanisms that provide overlapping networks of pathways involved in the regulation of immune cell functions, activation of endothelium, and alteration of metabolic parameters. Lp(a) lipoprotein, cholesterol ester transfer protein,apolipoprotein A (the principal apoprotein of highdensitylipoprotein), and other molecules have little effect on atherogenesis. Thus, although hypercholesterolemia is importantin approximately 50 percent of patients with cardiovasculardisease, other factors need to be taken intoconsideration. Atherosclerosis is clearly an inflammatorydisease and does not result simply from the accumulationof lipids. If we can selectively modify theharmful components of inflammation in the arteriesand leave the protective aspects intact, we

may createnew avenues for the diagnosis and management ofdisease in the 50 percent of patients with cardiovasculardisease who do not have hypercholesterolemia. In children and adolescents with a family history of premature coronary artery disease,early identification of the risk factors for atherosclerosis is essential to allow the implementation ofpreventive measures. Therapeutic lifestyle change (TLC) is an effective approach to lipid managementthat accommodates opportunitiesfor other types of health risk counseling.

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