Pharmacological Intervention For Cardiovascular Disease: Current Strategies And Future Directions.

[1]Ms. Dipali pandharinath khillare ,[2]Mr. Kuldeep Sukhdeo Kanadje, [3]Dr. D.K.Vir , [4]Ms.Tanushri popat Gawande , [5]Ms.Nikita Ganesh kakde

[1 4 5]Student, [2]Assistant professor ,[3]Principal,

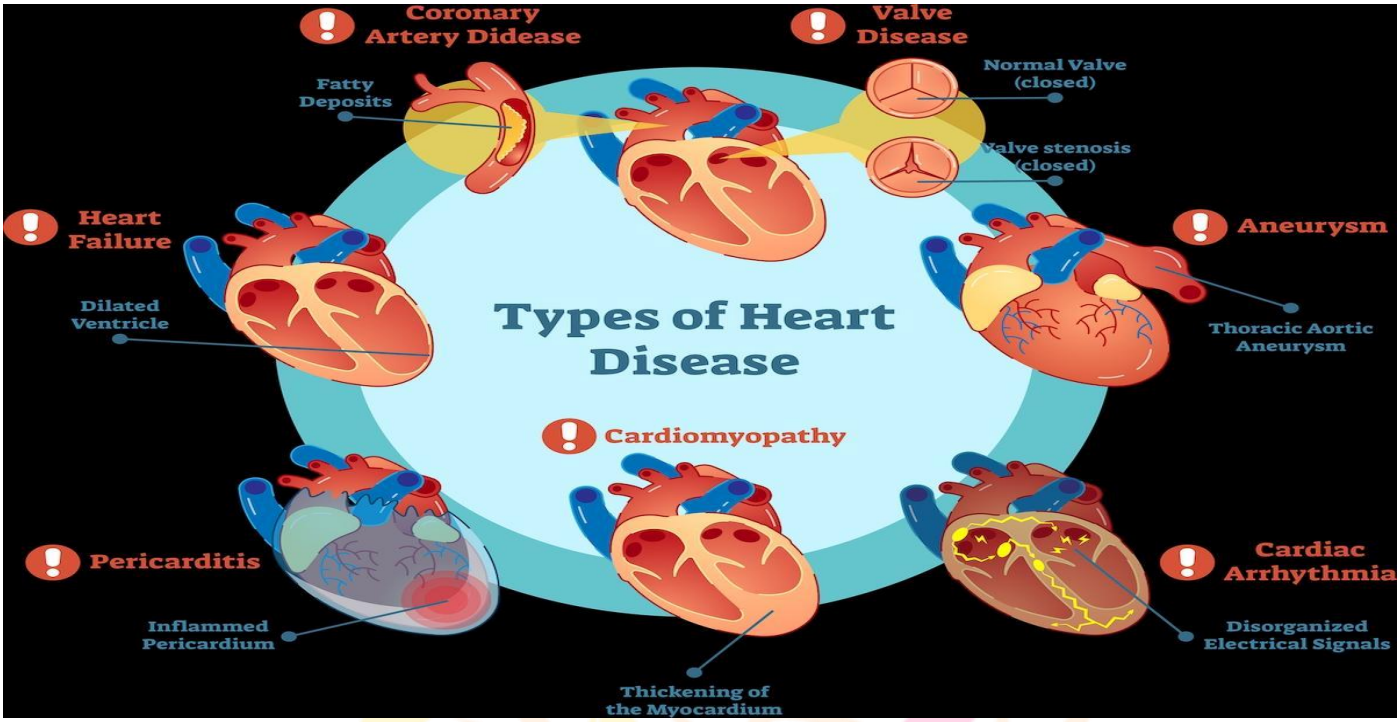
SHREE GORAKSHA COLLEGE OF PHARMACY & RESEARCH CENTRE Khamgaon- 431151

***Abstract*—**Cardiovascular disease (CVD) presents a significant burden to the UK. This review presents data from nationally Representative datasets to give up- to- date statistics on mortality, frequency, treatment and costs. Data concentrate On CVD as a whole, coronary heart complaint(International Bracket of conditions(ICD) I20 – 25) and Cerebrovascular complaint(ICDI60 – 69); still, where available, other cardiovascular conditions are also presented. In 2012, CVD was the most common cause of death in the UK for women (28 of all womanish deaths), but not for Men, where cancer is now the most common cause of death (32 of all manly deaths). The highest age- standardized CVD death rates are seen in Scotland (347/100000) and the North of England (320/100 000 in the North West), with Mortality from CVD varying greatly across the United Kingdom. The North of England (4.5 in the north East) and Scotland (4.3) have the highest rate. Of coronary heart disease.

Keywords - Cardiovascular disease, Pharmacological interventions, Antihypertensive drugs, Lipid-lowering therapy, Antiplatelets, Future therapies.

I. INTRODUCTION

Worldwide, cardiovascular disease (CVD) is the leading cause of death. According to the 2010 Global Burden of Disease report, CVD was responsible for 15.6 million deaths globally, or 29.6% of all fatalities. This was more than all communicable, maternal, neonatal, and nutritional disorders combined,[1]. And it was twice as many deaths as cancer. One According to statistics published in this journal over the past two years, cardiovascular disease (CVD) is the leading cause of death in Europe. Despite consistent declines in CVD mortality rates throughout the continent, 0.4 million Europeans lose their lives to CVD each year.[2]. This review provides information describing the burden of cardiovascular disease (CVD), namely coronary heart disease (CHD) and stroke, throughout Europe, updating previously published work .It also introduces new information regarding mortality, morbidity, and treatment across European countries, and for the first time in this series, we compute Age standardized mortality rates using the updated European Standard Population (ESP).[3] Several effective approaches to support CVD patients in adopting These preventive behaviors have been established, including engagement in lifestyle modification programmed, use of technology-based Interventions (e.g., telehealth, mobile health applications) and cardiac Rehabilitation.5 However, despite good evidence for their effectiveness, These programmed are not always well-utilized or accepted by the target Population. For example, the benefits of cardiac rehabilitation are well-recognized and include lower mortality rate, reduced risk of hospital Admissions and improved health-related quality of life.10,11 However, Cardiac rehabilitation continues to have poor attendance rates, with only 15%–30% of eligible patients engaging with the programmed .To Address poor uptake, policymakers and healthcare providers need to Ensure that interventions are well-accepted and adapted to the specific Needs and perceptions of the target population. One way to achieve This is for researchers to work with end-users and nonacademic Stakeholders in the development of interventions; this is known as Co-design.



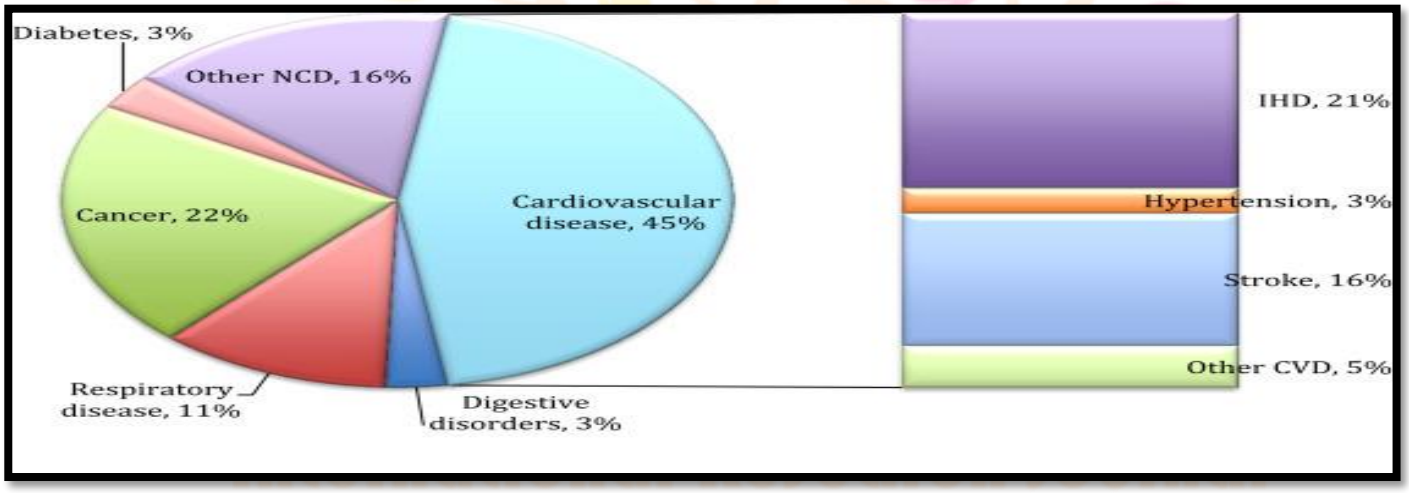
II. Epidemology

CVD is the primary cause of mortality globally, responsible for approximately 16.7 million fatalities annually, primarily due to heart attacks and strokes.[3] This figure is expected to rise to around 25 million deaths by 2020, assuming that current trends persist.[4]. In 2004, ischemic heart disease led to approximately 7.2 million fatalities, while cerebrovascular disease resulted in 5.5 million fatalities, representing 22% of total worldwide deaths.[5]. However, these deaths merely signify the surface of the cardiovascular issue. A significantly greater percentage of individuals experience asymptomatic disease and target organ damage due to undetected high blood pressure and the existence of additional risk factors Present estimates indicate that the worldwide impact of CVD vastly surpasses its mortality rates, impacting approximately 128 million individuals, which is nearly eight times the figure for cardiovascular deaths [6]. In the United States, 71.3 million adults—or 1 in 3— are affected by at least one form of CVD.[7]. Consequently, the heavier load of CVD is due not to death rates but to nonfatal cardiovascular incidents and their lasting effects Moreover, the worldwide prevalence of CVD is rising due to the aging population and the fact that lifestyles (and thus, risk factors) in lower- and middle income countries are increasingly resembling those of affluent nations. The future cardiovascular burden is expected to worsen not only due to the aging population but also because of the growing epidemic of obesity and associated cardiovascular risk factors, both of which are rising in prevalence. The recently released Reduction of Atherothrombosis for Continued Health (REACH) Registry, which gathered worldwide data on atherosclerosis risk factors from 67,888 patients aged 45 in 44 countries, revealed that traditional cardiovascular risk factors (hypertension, elevated cholesterol, diabetes, obesity, and smoking) support the results from the INTERHEART study and are prevalent and consistent across various ethnic groups, even though the Are often inadequately treated and poorly managed in numerous areas globally Even though the issue of CVD may be widespread, prevention can rely on the same principles globally. REACH also identified regional variations in the prevalence of various types of CVD (coronary artery disease. [CAD], cerebrovascular disease, and peripheral arterial disease).[8]. Early studies indicated that the prevalence of depression ranged from 18 to 60 in CAD cases.Subsequently, later studies reported more consistent prevalence rates of depression in CVD cases,ranging from 16 to 23 (mean, 19; standard, 18)

CVD Mortality Measurement :

In Developed Countries In the United States, the National Vital Statistics System uses Death certificates to collect mortality data under the jurisdiction of each state.[9]. Diagnoses on the death certificates are then Converted to a diagnostic code from the International Classification of Diseases (ICD), which is the standardized classification of diagnoses developed by the World Health Organization (WHO). Vital record

systems using death certificates are also Used in other developed countries such as the United King-Dom, Sweden, and Italy. In reality, death certificate diagnoses are often inaccurate as A result of either erroneous clinical diagnoses or incorrect or Inadequate coding of the diagnosis.[10]. This has been a long Standing problem.[11]. In 1955, James et al Found that in a comparison of 1889 death certificates with corresponding autopsy Reports, only 52% of cases had full agreement between 3-digit ICD codes A 1980 series of 257 autopsied cases found that 42% of cases had improper recording of the underlying cause Of death.[12]. Malignant neoplasms were underreported by 10%, And vascular diseases were over reported by 10%.More recently, Roulson [13]. The Authors found that the rate of misdiagnosis has not significantly Improved since the 1960s: At least one third of death Certificates are likely to be incorrect, and 50% of autopsies Produce findings unsuspected before death, underlining the importance of autopsy. These studies show that the inconsistencies and inaccuracies of causeofdeath reporting have Been an issue over the past several decades and continue to Present a major problem. It can be argued that autopsy discrepancy studies such as Those outlined above are biased because the autopsied cases May have been those in which the cause of death was particularly obscure clinically. However, in a 1980 study by Cameron [14]. An autopsy rate of 65% was reached for 6 months to Try to diminish the effect of selection bias. They found that in 38% of cases the cause of death was still discrepant between The autopsy findings and the death certificate, even when clinician were “certain” or “fairly certain” about their diagnoses. Interestingly, in cases in which clinicians indicated that they Would not normally have requested an autopsy, the discrepancy rate was similar to those cases in which they would have. This finding indicates that it is difficult for a clinician to predict which cases will have discrepant diagnoses.[15].

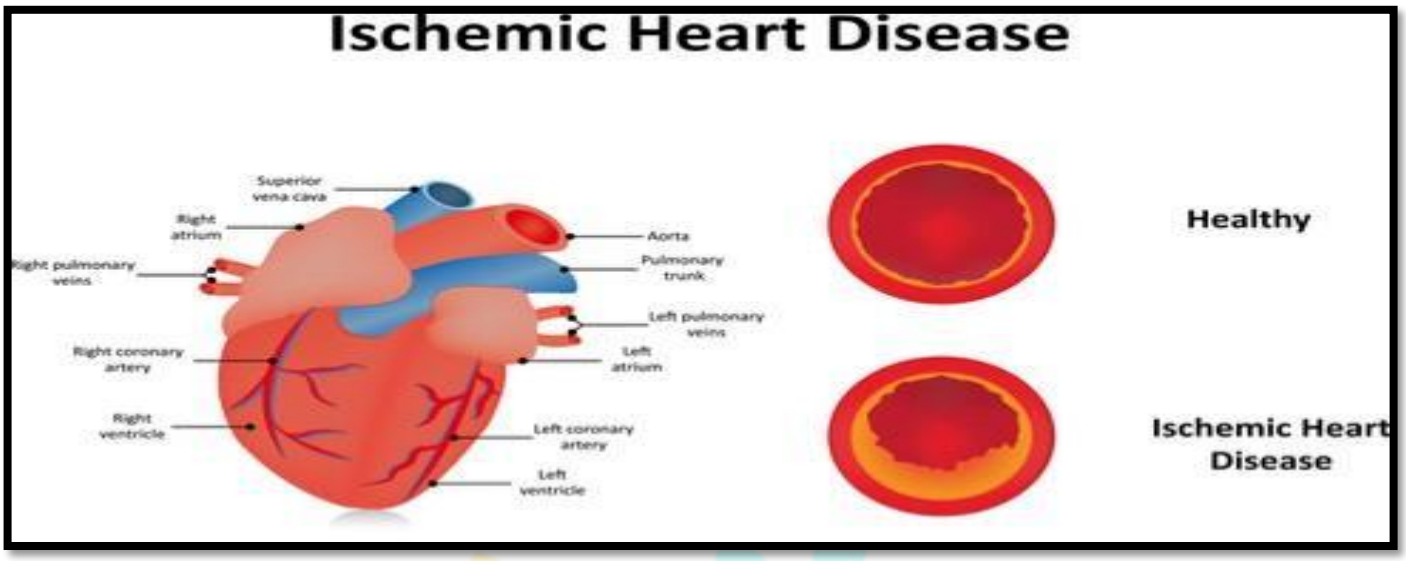


Cardiovascular disease *:*

Cardiovascular disease (CVD) is a broad term describing disorders of the heart and blood vessels. The major conditions under CVD include coronary artery disease, cerebrovascular disease, heart failure, rheumatic heart disease, congenital heart defects, and arrhythmias.

i. **Ischemic heart diseases *:***

Ischemic heart complaint characterized by reduced blood force to the heart muscle is the most common cause of death in utmost western countries. It results from the blockage in coronary highways by atherosclerosis and thrombus. Ischemic heart complaint presents with symptoms similar as temporary pain(angina), irregular heart beat(arrhythmia), endless heart muscle damage(myocardial infarction) and loss of muscle exertion(heart failure). Cardiac redoing is the global and cellular change in the ventricular shape and function following chamber dilation and interstitial and perivascular fibrosis. The redoing leads to the habitual heart failure. The redoing includes neurochemical responses, cytokine activation, loss of cardiomyocytes due to necrosis or apoptosis, cardiomyocytes hypertrophy, dislocation of extracellular matrix(ECM) and collagen accumulation followed by scar conformation[16].



1.1. Conventional medical treatments :

• Percutaneous coronary intervention (PCI)

PCI is a medical procedure which involves the inflation of a balloon Within the blocked coronary artery to crush the plaque into the walls of The artery and restores normal blood flow to the heart muscle. While Balloon angioplasty has been performed as a part of nearly all Percutaneous coronary interventions, sometimes a stent, recently drug Eluting stent is often introduced into the blood vessel or artery. Stenting Is an alternative to heart surgery for some forms of non-severe coronary artery disease. This procedure is effective in mostly acute heart attack and reduces mortality of coronary artery disease compared with a Common medical treatment administrating thrombolytic agent [17]. Other procedures that are done during a percutaneous coronary Intervention include rotational or laser atherectomy, brachytherapy (use of radioactive source to inhibit restenosis) in addition to balloon Angioplasty and implantation of There have been enormous advances in percutaneous coronary intervention(PCI)(preliminarily called angioplasty, percutaneous transluminal coronary angioplasty(PTCA) or balloon angioplasty) ways, bias and specifics since Andreas Grutzig first performed in 1977. In particular, medicine- eluting stent(DES) has been vulgarized as an effective intervention tool inhibiting overgrowth of scar towel that can narrow the roadway and block blood inflow to the heart, a complication called restenosis. still, it should be emphasized that although the coronary roadway intervention has remarkably reduced restenosis, the prevalence of myocardial infarction and heart related deaths was not specially dropped. This fact suggests that it's important to discourage the complaint progression and help the rush with the applicable medicine treatment furnishing defensive goods at the cellular position of myocardium.[18].

Coronary-artery bypass-graft surgery (CABG)

Coronary roadway bypass graft surgery is a general surgical procedure performed to reduce the threat of death From coronary roadway complaint. In utmost cases, coronary bypass surgery requires a general anesthesia and Median sternotomy. Highways or modes began from the case's body are grafted to the coronary highways to Bypass atherosclerotic narrowings and increase the blood force to the coronary rotation supplying the Myocardium. The representative blood vessels that are used for coronary bypass surgery include saphenous Tone and internal thoracic roadway. Saphenous tone has been reported to have some disadvantages including a Time-dependent restenosis threat(19). The administration of anti-platelet medicines or lipid- lowering agents Averted the progression of arthrosclerosis and reduced the progression of restenosis. When the saphenous tone Was used, the long- term follow- up results weren't satisfactory.

1.2. Protein, cell and gene therapy

• Protein therapy :

Proteins with other bio-macromolecules similar as polysaccharides And nucleic acids are essential composition Of organisms and share in pivotal process in cells. Proteins are potent hormones, Antibodies, enzymes that Beget biochemical responses, structural or Mechanical functions, involved in cell signaling, vulnerable Responses, And cell cycling, and energy source. Colorful mortal conditions are nearly related to the Malfunctioning of particular proteins. A variety Of therapeutically important mortal proteins can be produced With Relative ease by means of the recombinant DNA technology in Mammalian cells, incentive or bacteria.

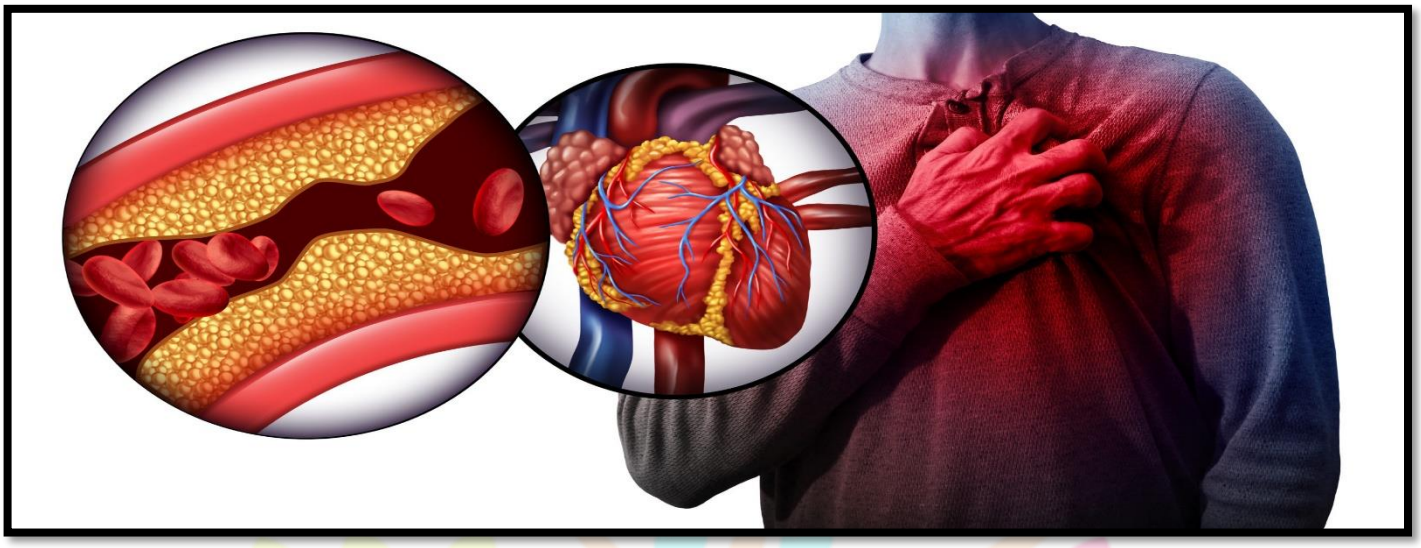
• Gene therapy:

Recent achievements in the cardiovascular area have been made with viral Andon-viral gene curatives. A Variety of catheter or surgical approaches for in vivo cardiac gene transfer showed promising results in beast And clinical studies. Transgene expression would be needed only during a period of defined threat, similar as Redoing after myocardial infarction. In common with the antigenic protein remedy, antigenic gene remedy is Getting important interest as an volition remedy to ameliorate the ischemic heart failure. An beast model with Habitual ischemic myocardium showed an increase in contributory blood inflow and an enhancement of cardiac Function by an injection of plasmid VEGF or FGF(20,21). The antigenic gene remedy intensely studied in Mortal clinical trials. The administration of plasmid VEGF into mortal ischemic myocardium through a small Left anterior thoracotomy redounded in bettered heart responses, demonstrating the remedial efficacy of this Approach(22). Colorful isoforms of VEGF have been delivered to case in clinical studies by different delivery Styles. VEGF165 delivered by myocardial injection and intramyocardial transfection to case demonstrated the Significant enhancement of ischemic myocardium area with increased perfusion and the reduced angina, Independently.[23,24].

ii. Angina Pectoris :

When atherosclerosis affects the coronary arteries (i.e.,CAD) the clinical manifestations of the disease reXect Both the chronic and the Acute effects of luminal narrowing on coronary blood Xow. Coronary blood Xow that Inadequately meets metabolic demands results in myocardial ischemia, with angina pectoris being the Pathognomonic symptom. More abrupt or Severe disruption of the blood supply that is due to a rupture of an Athermanous plaque or to a superimposed thrombus can result in an acute myocardial Infarction (see chap. 8). The clinical manifestations of CAD include asymptoMatic silent myocardial ischemia, angina, unstable angina, Myocardial infarcTion, arrhythmias, heart failure, and death. Sequelae of CAD and myocardial Infarction Include cardiomyopathy, congestive heart failure, left ventricular an Eurysms, mitral valve regurgitation, Arrhythmias, and other abnormalities in The conduction system. The presenting cardiac event is more likely to Be a myocardial infarction or sudden death in men and angina in women. More than half Of all coronary events Are sudden events. Approximately 300,000 people die sudDenly in the United States each year, and many of These people are in apparently Good health without a prior history of symptomatic heart disease. Data from The Framingham Heart Study demonstrate that in one third of patients the Wrst, Only, and last symptom of CAD is Sudden death (Schatzkin et al., 1984). Angina pectoris classically refers to chest pain or pressure produced by Myocardial ischemia. It typically occurs in the setting of exertion resulting in inCreased demand that cannot be Met adequately by diseased coronary arteries, Thus leading to ischemia. Angina pain typically leads to a Pressure like sensation In the chest, but the pain may radiate to the left arm, jaw, teeth, or throat. Some Patients Describe a burning sensation. Accompanying symptoms often include Dyspnea, tachycardia (rapid heart rate), And diaphoresis (sweating). The symptoms usually begin at a low intensity, increase over 2 to 3 minutes and last Less Than 15 minutes. The pathophysiology of the pain is uncertain, because Studies that have used Holter Monitors to examine ischemia during activities of Daily living demonstrate that the majority of ischemic Episodes are clinically Silent. The most common cause of angina is atherosclerosis of the coronary arteries. Signs and symptoms of angina pectoris appear when one or more coronary arteries are more than 75% blocked. Angina pectoris is derived from the Greek word meaning

chest compression. The presence of angina indicates Cardiac ischemia. Ischemia was associated with short-term angina. It does not lead to permanent damage to the Heart muscle tissue, but it is nevertheless a life threatening factor and can further lead to dysrhythmia and Myocardial infarction. Angina pectoris is caused by a temporary ischemia caused by an imbalance between the Supply and demand of oxygen required by the heart muscle. Angina pain is often relieved by rest and Consumption of nitroglycerin and its accompanying symptoms include: shortness of breath, tachycardia, Palpitations, nausea, vomiting, fatigue, sweating, paleness, weakness and syncope may be associated with Angina to be seen.



Angina pectoris is classified according to clinical Signs asfollows:

A. Stable angina: This angina is caused by Activity. Exercise increases the oxygen Consumption of the heart muscle. This Pain is relieved by resting, lowering blood Pressure, and lowering the number of Heartbeats . . Eventually each stable Angina Becomes unstable and eventually MI, but This time varies greatly .

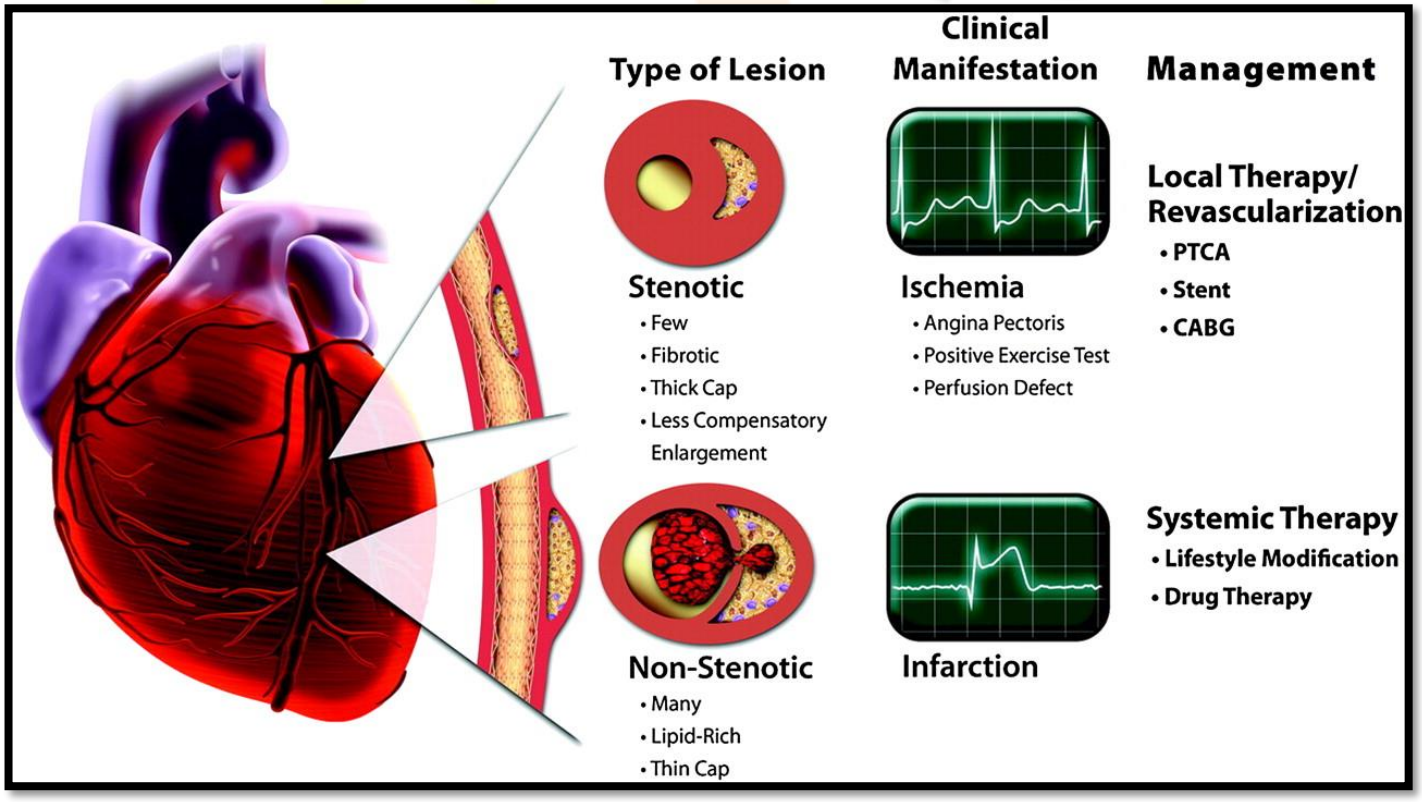
B.Unstable angina: In the past, this type of Angina was called angina before a heart attack.Angina, which used to be caused by a specific Activity, does not require much activity Now and Occurs at rest and even at night while sleeping .The characteristics of Angina pain have changed, its severity and duration have Increased, i.e., the patient used To have pain Every few months or every few weeks, but now He does not need much Activity to cause pain and Pain occurs every day. After a long rest, It takes some time For the pain to heal. There is Also pain at night and it wakes the patient. There Is pain Almost all day and all night .Previously, he did not have nausea, vomiting and Cold sweats when he was in pain, but Now, with The onset of heart pain, he has nausea, vomiting And cold sweats . On the Other hand, Sometimes taking 4-5 tablets of sublingual Nitroglycerin takes a quarter to Half an hour to Reduce the pain a little In some patients, The transition from stable to Unstable angina May take years, but in some it may take less than A month.

C.Nocturnal angina: In this angina, the patient Wakes up at night due to pain and mentions The Specific symptoms of frontal chest pain with spread to the neck, left hand, right hand And epigastrium. Angina usually occurs in the REM phase of sleep with dreaming . At this stage, due to the sympathetic increase, the number of pulses and blood pressure Increases. In other patients, the cause of the abnormal decrease in aortic diastolic pressure And increased venous return due to increased fluid during sleep is the result of increased Heart diameter and increased myocardial oxygen consumptstage, which is the most Important cause of nocturnal angina.

D. Angina pectoris: Angina, in which pain attacks occur when bending or lying down, is a Similar cause to nocturnal angina. It occurs mostly at night when sleeping, causing the Person to wake up, and is now accompanied by shortness of breath , nocturnal Attacks, and resolves shortly after sitting or standing. The cause of this type of angina is Increased venous return to the heart.

PATHOPHYSIOLOGY :

Preliminarily considered a cholesterol storehouse complaint, we presently understand atherogenesis as a Complex Commerce of threat factors including cells of the roadway wall and the blood and molecular Dispatches that they change. A useful organizing theme, which surfaced first from laboratory studies and has Now gained currency in the clinic, accords Inflammation a major part in all stages of Atherogenesis.Inflammation also participates in the original, myocardial, and Systemic complications of Atherosclerosis When the arterial endothelium encounters certain bacterial products or threat factors as different As dyslipidemia, Vasoconstrictor hormones inculpated in hypertension, the products of glycoxidation associated With hyperglycemia, or pro Seditious cytokines deduced from redundant adipose towel, these cells compound The expression of adhesion motes that Promote the sticking of blood leukocytes to the inner face of the arterial Wall. Transmigration of the disciple leukocytes Depends in large part on the expression of chemoattractant Cytokines regulated by signals associated with traditional and Arising threat factors for atherosclerosis. Once Occupant in the arterial intima, the blood leukocytes substantially Mononuclear phagocytes and T lymphocytes Communicate with endothelial and smooth muscle cells, the Endogenous cells of the arterial wall. Major Dispatches changed among the cell types involved in atherogenesis depend on Intercessors of inflammation and Impunity, including small motes that include lipid intercessors similar as prostanoids And other deriv atives of Arachidonic acid, eg, the leukotrienes Other autacoids, similar as histamine, classically regulate Vascular tone And increase vascular permeability. Lately, important attention has concentrated on protein intercessors of Inflammation and impunity, including the cytokines and complement factors. Nearly unknown by cardiologists A bare Decade agone the cytokines have joined the mainstream of our specialty. As a major consequence of the Seditious raise afoot in the early atheroma, SMCs resettle from the tunica media into the Intima. In musicale With endothelial cells and monocytes, They cache matrix metalloproteinases in response to colorful oxidative, Hemodynamic, seditious, and Autoimmune signals. MMPs, in balance with their endogenous towel Impediments, modulate multitudinous functions of Vascular cells, including activation, proliferation, migration, And cell death, as well as new vessel conformation, geometric Redoing, mending, or destruction of extracellular Matrix of highways and the myocardium.



TREATMENT :

Although some stress operation or behavioral comforting programs with CVD cases have been associated with Reduced Threat of intermittent cardiovascular eoverdo8 And increased rates of long- term(5- time)-4 more Recent studies report no Benefit to cases 9, or an indeed worse outgrowth for women in comparison with usual Care.10 Because of smaller implicit Adverse goods on the cardiovascular system and the lack of lethality in Overdose, physical treatment with picky serotonin Reuptake impediments(SSRIs) or other atypical Antidepressants may offer significant advantages in depressed cases with CVD. The cardiac poisonous goods of The TCAs and affiliated antidepressants limit their clinical use in cases with CVD. The anthology is directed Toward excellent reviews on the safety and efficacity of TCAs in cases with CVD.11,12Monoamine oxidase Impediments and trazodone are generally free of goods on cardia conduction, but, like the TCAs, may beget Postural hypotension.13Because the SSRIs are newer than TCAs, little methodical exploration on their Efficacity in senior or CAD cases has been performed, including large- scale, randomized, treatment trials of Post-MI cases With comorbid major depression.12A recent randomized, double-eyeless multicenter study Compared the efficacity of Nortripty line and paroxetine in depressed cases with ischemic heart Complaint.14Both antidepressants were effective in the Treatment of depression but, not unexpectedly, there Were further dropouts because of adverse goods and further cardiacAffiliated goods with the TCA.

FUTURE DIRECTIONS :

Prevention of CVD remains one of the major pretensions for the scientific and healthcare community. Thus, CVD Forestallment requires devoted attention and training. Still, preventative cardiology is a Subspecialty That's at times, lost between clinical internal drug, endocrinology, and cardiology with no clear champion. Coffers and homogenized structure in CVD forestallment training are spare. Although the ACC COCATS Guidelines give A general frame and recommendations for introductory training in CV forestallment that's Needed of all training programs In cardiovascular drug, several programs still warrant the conditions for Introductory training in CVD forestallment. Moving forward, it's important for central educational bodies like The ABIM to fete CVD forestallment as a subspecialty Of cardiovascular complaint training. LeadingProfessional associations like the American College of Cardiology And American Heart Association(AHA) can Unite with other associations concentrated on CVD forestallment to give Coffers and help develop CVD Forestallment training programs.[22]

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