A Viewpoint on Prevention of Myocardial Infarction

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Prevention of myocardial infarction has posed a challenge to the medical scientists. The ever-increasing list of coronary risk factors has further confused and obscured the problem. Each proponent of a risk factor has ardent and enthusiastic statistical evidence to prove the correctness of his belief. Heredity, hyperlipidaemia, diabetes mellitus, hypertenson, smoking, obesity, physical inactivity, emtoional conflict and type A personality are the most favoured risk factors finding considerable statistical support. Confusion is further magnified by the belief that atherosclerosis, myocardial infarction and coronary thrombosis are synonymous.

It is submitted that multi-aetiology smacks of ignorance and merely underlines associations. To infer causality from associations is not fair because an effect must find its explanation in terms of one cause which itself may be influenced by several or many factors. Unless we find out the common final path through which various risk factors operate or become manifest, we would be groping in the dark, changing as the fashion demands, our emphasis from one factor to the other.

It is my firm belief that *velocity* of blood flow is the main determinant of the genesis of atherosclerotic plaque. Without blood flow, there would be no atherosclerosis thus defying the cholesterol insudation—intimal muscle cell hyperplasia hypothesis. *Heredity* plays its role by determining the intensity of reaction to intimal trauma and by influencing the angle of branching, the ratio of main vessel lumen to the branch vessel lumen, and size, configuration and morphology of the vessel wall.

Blood pressure influences the compressional and tensile stresses to which a vessel wall is subjected and, hence, may exert a synergistic influence on the effectes of velocity of blood flow on the vessel wall. *Hypoxia*, due to excessive smoking, pulmonary dysfunction and living at high altitudes, may facilitate the adverse effects of velocity of blood flow by causing cell swelling. The atherosclerotic plaque, therefore, is a degenerative process, the rate and intensity of which is influenced by *velocity of blood flow*, *heredity*, blood pressure level and *hypoxia*.

Myocardial infarction is a consequence of catecholamine hyperfunction. The latter may be due to excessive synthesis and/or release of catecholamines (determined by heredity, personality and envionment) and/or due to increased end-organ sensitivity to catecholamines (determined by heredity).

Catecholamine hyperfunction may affect the atherosclerotic plaque by causing shearing movements between the rigid and unyielding atherosclerotic plaque and the elsatic and dilat-

ing coronary artery in three different ways:-

1. Bleeding into the atherosclerotic plaque causing its progressive bulging into the lumen of the affected vessel, ending if unchecked, in complete occlusion of the lumen. The occurrence of intimal bleeding, however, is countered by vasoconstriction initiated by serotonin released from the plateletes adhering and aggregating to close the breach and by catecholamines.

2. Breach of endothelium between the atherosclerotic plaque and the adjacent healthy vessel wall setting the stage for thrombus formation and clottting mechanisms to embark on a progressive odyssey culminating in occlusion of the vessel lumen. This pernicious vicious circle is, however, stemmed by plasminogen-plasmin mechanism and by endogenous heparin.

3. Extrusion of the atherosclerotic plaque into the lumen causing embolism in the distal tributaries of the affected coronary artery leaving behind a raw area triggering the thrombotic and clotting mechanisms and their counter body responses as described above.

It is likely that defence reactions of the body do not permit the progression of thrombus formation or encorachment of the coronary artery lumen by progressive enlargement of the atheromatous plaque by subintimal haemorrhage. This view point finds expression in failure to demonstrate coronary thrombosis in fatal cases of myocardial infarction dying suddenly from dysrhythmias, in those dying from subendocardial myocardial infarction and in 55 percent of fatal transmural myocardial infarctions.

It is probable that excessive liberation of catecholamines by increasing the heart rate (chronotropic effect) and contractility (inotropic effect) enhance cardiac work and myocardial oxygen consumption. The vulnerable areas of myocardium supplied by markedly narrowed atherosclerotic vessels (more than 70 percent encroahment on the lumen of the vessel) suffer from ischaemia. This is especially so in the subendocardium (inner half of the myocardium) which bears the brunt of compromised blood supply. Relative hypoxia thus induced by catecholamines causes cell swelling both of the myocardium and endothelium, most magnified in the subendocardial region. Cell swelling causes encroachment on the vessel lumen occasioning more hypoxia, thus setting in motion a vicious circle which, if unbroken, would end in myocardial necrosis; and if halted, would restore the integrity of the myocardium and the endothelial cell expressed clinically by angina pectoris or myocardial infarction with normal coronary arteriogram or a stage further as ischaemic cardiomyopathy.

Coronary thrombosis would only ocur if hypoxia persisted for a longer period causing marked endothelial swelling or if cardiogenic shock caused slowing of circulation and further aggravation of hypoxia and hence endothelial disruption baring the collagen fibril causing platelet adhesiveness and aggregation and setting in motion the clotting mechanisms. Coronary thrombosis is probably a consequence rather than the cause of myocardial infarction as has been shown by studies with radioactive iodine labelled fibrinogen injected at the onset of myocardial infarction showing radioactivity in the thrombus reflecting its evolution after the

onset of clinical myocardial infarction (Erhardt et al., 1973).

Various risk factors either cause increased release of and/or increased end organ sensitivity to, catecholamines such as in hypertension, diabetes mellitus, heredity, inactivity, obesity, A type personality and emotional conflict or are a consequence of catecholamine overactivity such as in hypertension, hyperbetalipoproteinaemia, raised blood cholesterol, diabetic type of sugar tolerance curve.

Prevention of myocardial infarction should therefore, be based on blocking the action of catecholamines. Unfortunately, there is not much authentic information on catecholamine receptors other than Ahlquist's defining alpha and beta receptors. Recent advances in the action of beta blockers has revealed that beta action may be further split who beta I and beta II action which may be *selectively blocked: sotalol* has no quinidine-like effect, *practolol* has no bronchoconstrictor effect, *butoxamine* does not block the peripheral vascular and lipolytic beta action; *alpranolol* and *oxpranolol* still await the exact delineation of their action.

The lack of more pecise and detailed information on various sympathetic receptors and catecholamine blockers may limit the exploitation of beta blockers to the full in the prevention of myocardial infarction.

More rational and scientific approach to the prevention of myocardial infarction may be briefly presented below. It is based on the premise that catecholamines provide the final common path through which all events leading to myocardial infarction occur. The treatment of associated factors which may be the cause or consequence of catecholamine overactivity should be considered though they may be of secondary importance and may respond to control of catecholamine overactivity.

1. Decrease catecholamine secrection by:-

   (*a*) *Change of personality* effected by healthy bring-up of children indoctrinated to religious, more specifically Islamic, philosophy. Contentment and submission to the will of God does not conflict with ambition and hardwork. It is the frustration culminating from failures in life which blows the catecholamine storm felling the plant of human life. Islamic philosophy teaches us to spare no efforts to study nature and solve the problems of the universe. In fact, Islam has blissful attitude towards science and scientists. The conflict arises only when an unhealthy attitude towards success and failure leads to frustration and disappointment. Islam teaches us that the job of a believer is to work hard and that itself should be an adequate satisfaction and reward. The results are in the hands of God who dictates these in the form of opportunity, intuition and success or failure. Rigid belief in God and concern with the pursuit of ones profession with ones best ability leaving the results to God would minimise stress and mitigate frustration, the harbingers of catecholamine storms.

The characeristics of A type personality described by Friedman and Roseman (Friedman and Roseman, 1959) are:-

A. *Primary traits*

1. Extreme competitiveness.
2. Inordinate ambition.
3. Unexplained restlessness.
4. Profound sense of time urgency.

B. *Secondary traits*

These are somatic manifestations correlating with emotional traits such as first clenching. jaw clenching, facial grimaching, desk pounding and generally keyed-up body movements. The man afflicted with time urgency would tend to move rapidly and would wish to hurry or condense the speech of others.

Such persons are *work addicts* whose ambitions dominate their daily programme. These are the people who would not be easily discouraged and who would avenge all physical and emotional humiliations despite their difficulties and deprivations.

These people through their hypothalmus keep their catecholamine apparatus working at the top gear inflicting physical, hormonal, metabolic and biochemical trauma to their body tissues. The incidence of coronary artery disease in these individuals is six times more than in persons with B type personality which protrays characters just the converse of those exhibited by type A personality indivduals. To stem the onslaught of catecholamine storms, these individuals need change in their attitude towards their environment. This can be best shaped with planned early childhood training of implicit faith in the omnipotence of God in determining the results of our efforts.

(*b*) *Change in environment*

Environment can be made more conducive to healthy mental and emotional growth and to more peaceful and less stressful existence. Honesty, truth, fellow feeling in society and an environment promoting justice merit and appreciation would go a long way in mellowing down the catecholamine mechanisms sparing the body tissues much wear and tear. Such an environment, infact, is the conceptual bliss of God, the Almighty, obtained by strict adherence and obedience to the laws of life as ordained by God in the Holy book, the Quran.

More physical activity with physical conditioning and normal body weight would assure more stable sympathetic nervous system.

(*c*) *Adrenergic blocking drugs*

Though much is still to be learnt about the working and mechanisms of sympathetic nervous system, it would be worthwhile at present to use beta blockers to maintain heart rate and blood pressure within reasonably normal limits. Their antilipolytic potential would facilitate normalisation of blood betalipoproteins. It is suggested that propranolol should be used as a routine in individuals showing coronary risk traits always insisting that pulse and blood pressure are lowered to the lowest possible limits compatible with normal living.

2. *Decrease end-organ Sensitivity*

This can be achieved by:

(*a*) Physical activity and physical conditioning.

(*b*) Reduction of weight to within normal limits, peferably on the lowest side of normal.

(*c*) Control of diabetes mellitus may delay the onset and prevent and retard the progress of neuropathy precluding denervated end-organ hypersensitivity to the neurotransmitters viz. catecholamines.

3. *Control of hyperlipidaemia*

Advances in electrophoresis have revealed that there are five types of hyperlipidaemias. Of these only tye IIa, IIb and type IV are believed to be associated with atherosclerosis.

Though hyperlipidaemia (type II) may be caused by catecholamine overactivity, diabetes mellitus, hypothyroidism, nephrotic syndrome, chronic obstructive jaundice, pancreatitis, hepatoma, dysproteinaemias, glycogen storage disease and contraeeptives, it is the *primary hyperlipidaemias* which pose a greater risk because of their occult nature discerned only by biochemical studies. Though there is no definite and authentic evidence that control of hyperlipidaemias may protect against angina pectoris or myocardial infarction, it is quite physiological to correct this metabolic abnormality. It is probable that hyperlipidaemia is merely a marker of more complex metabolic abnormalities underlying the evolution of coronary artery disease.

Type II hyperlipidaemia (hyperbetalipoproteniaemia) may be controlled in *heterozygot* by low cholesterol (100 to 150 mg. a day) diet containing a high polyunsaturated fatty acids to saturated fatty acids ratio (2:1) and cholestyramine (250 to 800 mg/kg per day). In the *homozygot*, low cholesterol (100 to 150 mg. a day) diet with high polyunsaturated fatty acids to saturated fatty acid ratio (2:1) may be combined with drugs such as cholestyramine (0.5 to 1.5 gm/kg a day), and nicotinic acid (25 to 75 mg/kg. a day) The effect of clofibrate and d-thyroxin on type II hypertetalipoproteniaemia is not consistent. Secondary hyperlipidaemia may be controlled by the treatment of underlying disease.

Beta blockers may be helpful in both primary and secondary hyperlipidaemias.

4. *Control of Blood Pressure*

Blood pressure is a quanity and as such every effort should be made to keep it as low as is compatible with normal healthy living. To regard blood pressure abnormal only if it exceeds the arbitrarily described normal limits of 140/90 mm. Hg. would leave much to be desired. There is no acceptable definition of normal blood pressure; for diastolic blood pressure, whether to record diastolic blood pressure at phase IV or V, is itself controversial. Since catecholamines raise the blood pressure both *directly* by causing peripheral vasoconstriction, raising the peripheral vascular resistance and *indirectly* by promoting the release of renin with increased elaboration of angiotension II. The latter would cause direct peripheral vasconstriction raising the peripheral vascular resistance and systemic blood pressure and indirectly by stimulating the secretion of aldosteron with consequent salt and water retention with resulting hypervolaemia and thickened and swollen arterial walls, more sensitive to the vasoconstrictive potential of catecholamines and angoitensin II. It has recently been reported that hypertensive patients with raised blood renin levels are more prone to coronary and cerebral arterial disease.

With such overwhelming evidence incriminating hypertension and raised blood renin as determinants of coronary artery disease, it is advisable to contain both hypertension and hyperreninaemia with beta blockers.

5. *Improve lung function*

Since lung is a rich source of plasminogen activitor and heparin and because it inactivates about 30 percent of norepinephrine, a diseased lung poses a potential threat of coronary artery disease.

It would be a sensible thing to treat, and if possible avoid, pulmonary dysfunction. This may be done by avoiding or giving up smoking, reducing weight, promoting physical activity and treating lung disease if present. In chronic obstructure pulmonary disease, it is worthwhile to prescribe oxygen therapy to forestall and treat hypoxia.

6. *Counter platelet adhesiveness and aggregation*

This can be achieved by reducing catecholamine activity by adrenergic blockers, reducing blood lipoproteins and controlling diabetes mellitus. Aspirin and dipyridamole. (Persantin) are believed to be useful due to their anti platelet effect.

7. *Minimising the formation and size of atheromatous plaque*

This may be achieved by countering genetic susceptibility by avoiding consanguinous marriages and by avoiding marriages between the members of families showing coronary risk factors.

Smoking should be avoided or given up to forestall cell swelling.

Pulmonary dysfunction causing hypoxia should be appropriately treated.

Blood velocity should be kept within reasonable limits especially in those with type A personality or during emotional stress by the exhibition of beta blockers.

Blood lipoprotein levels should be kept within normal limits by instituting measures already described.

It is obvious that the central and focal aspect of coronary prevention is containment of adrenergic activity which finds expression under different circumstances by compromising haemodynamic and biochemical homeostasis of the body.

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