



## HYPERLIPIDEMIA DEVELOPMENT AND CONSEQUENCES

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### ABSTRACT

*Hyperlipidemia (hypercholesterolemia) is a major risk factor for development of CHD. Thus, it is not surprising that cholesterol is the most “decorated” molecule in history, having contributed to as many as 13 Nobel prizes. In the past 20 years, major strides have been made in the understanding and treatment of hypercholesterolemia and other dyslipidemias. Since its inception in 1985, the National Cholesterol Education Program (NCEP) has battled to reduce the prevalence of high blood cholesterol through educational campaigns and science-based practice guidelines. However, cholesterol levels are still under treated.*

**KEY WORDS:** Hyperlipidemia, Cholesterol, Triglyceride, HDL, LDL, IHD, CHD

### INTRODUCTION

Cardiovascular and related illnesses are one of the most common disease prevalent in many parts of the world, including Pakistan. An increased risk of coronary heart disease is primarily associated with a high serum total cholesterol and low density lipoprotein (LDL) concentration and a decrease in high density lipoprotein (HDL). Hyperlipidemia is a condition characterized by increased concentration of lipids (fats) in the bloodstream. The major lipids reported to be present in the plasma are, fatty acids, triglycerides, cholesterol, cholesterol esters (compounds), and phospholipids. Other lipid soluble substances, present in much smaller amounts but of considerable physiological importance, include steroid hormones and fat-soluble vitamins<sup>1-2</sup>. Another related condition, dyslipidemia indicates disorders of lipoprotein metabolism, including lipoprotein overproduction or deficiency. These disorders may manifest with the elevation of serum total cholesterol, low-density lipoprotein (LDL), triglyceride concentrations, and a decrease in the high-density lipoprotein (HDL) concentration<sup>3</sup>.

### CLASSIFICATION AND CLINICAL PRESENTATION

**Primary Hyperlipidemia:** This occurs as a result of high intake of diet, rich in saturated fats and cholesterol or because of some genetic defect and heredity factor<sup>2,4-5</sup>.

**Secondary Hyperlipidemia:** This occurs as a result of some other illnesses or metabolic disturbances, e.g., diabetes mellitus, hypothyroidism, obstructive liver disease<sup>2,4-5</sup>.

When hyperlipidemia is defined in terms of a class or classes of elevated lipoprotein in the blood, the term “**Hyperlipoproteinemia**” is used. “**Hypercholesterolemia**” is the term for high cholesterol levels in the blood (*desirable*: < 200 mg / dl; *borderline*: 200 to 239 mg / dl; *high*: > 240 mg / dl). “**Hypertriglyceridemia**” refers to high triglyceride levels in the blood (*desirable*: < 200 mg / dl; *borderline*: 200 to 400 mg / dl; *high* 400 to 1000 mg / dl; *very high*: > 1000 mg / dl), while the “**Mixed Hyperlipidemia**” is used to indicate increased cholesterol and triglyceride levels<sup>4-6</sup>.

The predisposing factors relating to hyperlipidemia<sup>2,4</sup> include:

- Age (males > 45 years; female > 35 years).
- Heredity.
- Sedentary life style.
- Diet rich in saturated fats and cholesterol.
- Associated medical conditions, e.g., diabetes mellitus, nephritic syndrome, hypothyroidism, alcoholism, obstructive liver disease.

### CONSEQUENCES

Hyperlipidemia is a major risk factor for “**Atherosclerosis**” leading to heart attack and

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stroke. Less severe degrees of hypercholesterolemia nevertheless can impart some degree of risk for “**Ischemic Heart Disease**” (IHD). Low density lipoprotein (LDL) is pro-atherogenic. Hence high levels of LDL increases “**Coronary Heart Disease**” (CHD) risk. High density lipoprotein (HDL) is anti-atherogenic. Hence low levels of HDL also increases CHD risk <sup>6-8</sup>. The overall development of hyperlipidemia and its associated illnesses are shown in Figure – 1.

**EFFECTS OF CHOLESTEROL ON ARTERIES**

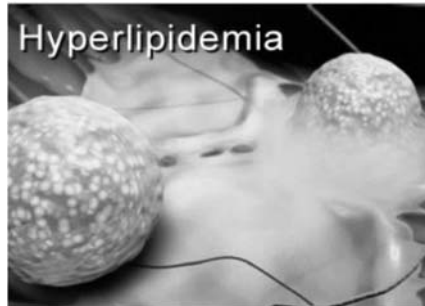
The human is created with many types of arteries, each functions to pump blood. The main artery is called the “**Dorsal Aorta**”, which branches out into many smaller arteries. Each system of the body has its own arteries responsible for providing oxygen-rich blood <sup>9</sup>. The way the arteries are constructed is that they are tough on the exterior and soft and smooth on the interior. Each artery has three specific layers comprising of the outer layer (*Tunica adventitia*), the middle muscular layer (*Tunica media*), and the inner layer (*Tunica intima*) made up of epithelial cells (Figure – 1E). The middle layer is strong and elastic and helps to pump the body’s blood while the inner layer is smooth as a way to allow the blood to flow through easily <sup>9</sup>.

As the heart beats, arteries expand as they are filled with blood. Once the heart relaxes, it produces enough force to push the blood through (Figure – 2, Stage – 1). In cases of high cholesterol (high LDL & triglycerides), the risk for coronary heart disease is at much higher side. This disease (atherosclerosis) fills the arteries with fatty deposits that act as obstacles. In other words, the artery becomes clogged (Figure – 2, Stage - 2), gradually become hard and narrow (Figure – 2, Stage – 3) and thus required quantity of blood can not get past these obstacles to adequately reach the heart (Figure – 2, Stage - 4). Eventually, this lack of blood flow causes disorders as under:

Development of plaque which slows down the blood flow (Figure 1E ). As the plaque development progresses, blood flow partially blocked.. Finally the plaque ruptures leading to clot formation and the blood flow blocked. If the obstruction occurs in the coronary arteries it could result in a heart attack (Figure – 1F) and if the obstruction occurs in arteries of the brain it could lead to a stroke (Figure – 1G). The over all process of atherosclerosis is given in figure – 2, while the summary and end result is

**FIGURE – 1**  
**HYPERLIPIDEMIA, ITS DEVELOPMENT AND CONSEQUENCES**

**A - HYPERLIPIDEMIA**



**B – COMPONENTS OF BLOOD**



Blood has many life-sustaining responsibilities, including transporting oxygen, Carbon dioxide, nutrients, and hormones throughout the body. Blood is composed of red blood cells, white blood cells, platelets and nutrients. Also circulating in blood is cholesterol. The two major forms are LDL, the ‘bad cholesterol’, and HDL ‘good cholesterol’.

**FIGURE – 1 (Continued)**  
**DEVELOPMENT OF HYPERLIPIDEMIA**

**C – Deposition of LDL**

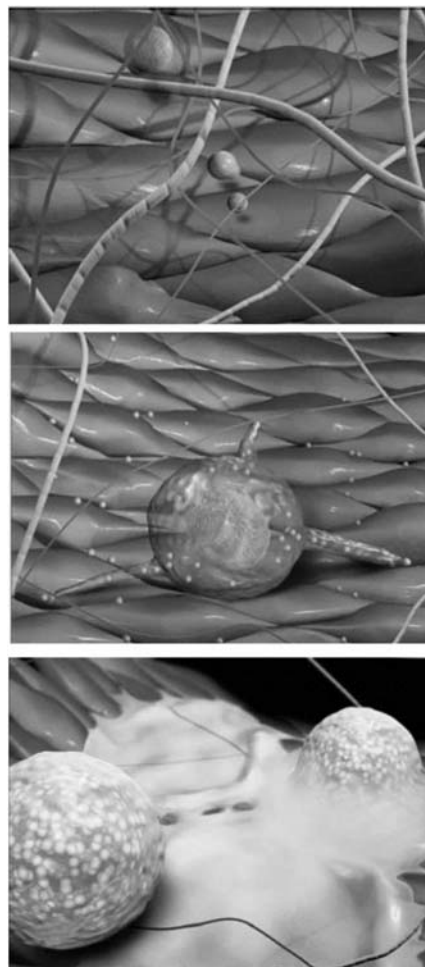
Hyperlipidemia occurs when an higher amount of LDL than the normal LDL travels out of the blood and is deposited between the smooth muscle cells of artery.

**D – Formation of foam cells**

White blood cells called macrophages eat the LDL and become foam cells.

**E – Formation of plaque leading to development of hyperlipidemia**

These cells eventually rupture and begin to form al lipid layer called plaque.

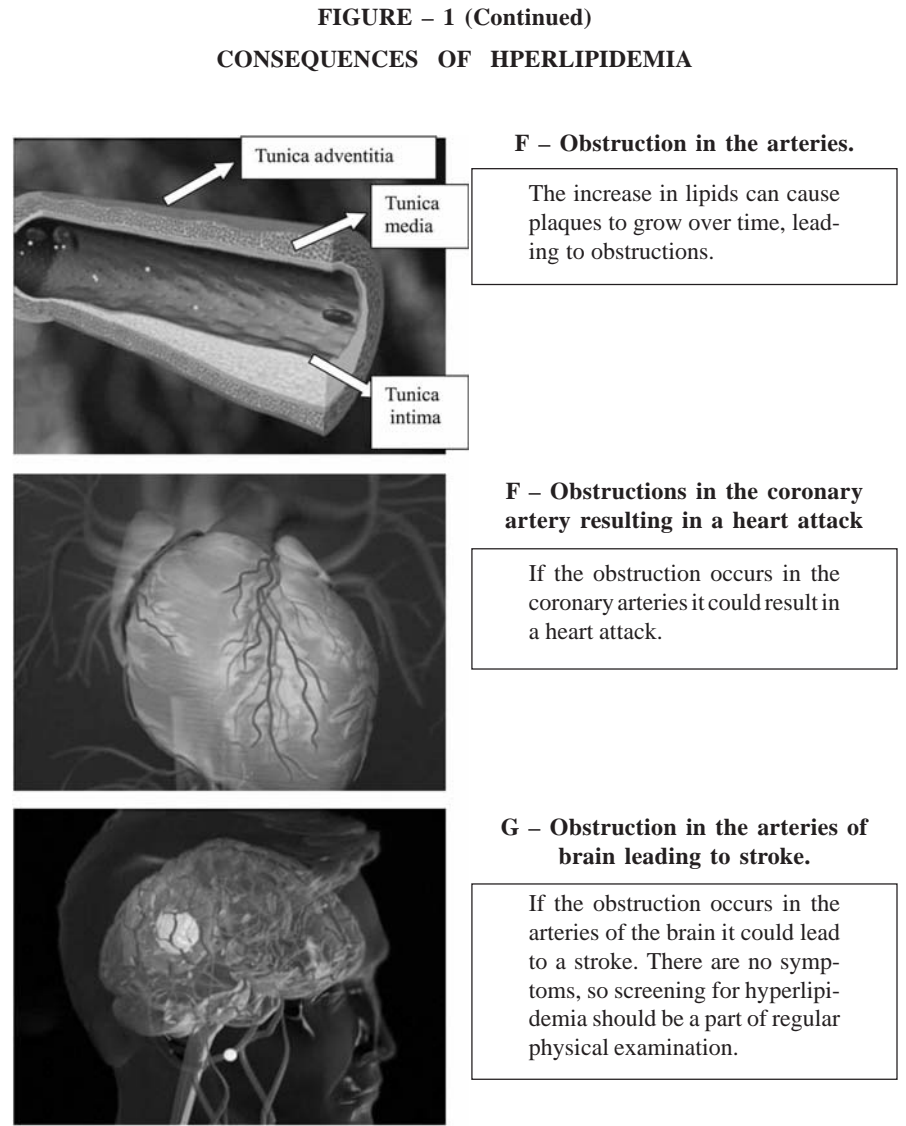


presented in figure – 3.

## DISCUSSION AND CONCLUSION

In the developing and developed countries, coronary and associated circulatory diseases now constitute the principal cause of human mortality. Not surprisingly, therefore, this is an area of intensive research, not entirely devoted to treatment, but also to the prevention of these diseases. With increased public awareness of the importance of the latter, healthier living focused on diet, supplementary food factors, exercise, etc., has taken on a more important role, not least in the mind of the commercial world where health food stores now supply many dietary supplements products which overlap the traditional pharmaceutical range <sup>1</sup>

In recent years much prominence has been given to the association of high levels of blood cholesterol and plasma triglycerides with atherosclerosis and ischemic heart disease (IHD). Treatment of Hyperlipidemia is preferably dietary accompanied by other regimes. Drug therapy is reserved for more intractable conditions <sup>1</sup>. Thus, foremost in the prevention and treatment of atherosclerosis is the reduction of serum cholesterol levels. The overwhelmingly associates elevated cholesterol levels with heart disease. In men and women 33 to 44 years of age, the serum cholesterol levels of 256 mg / dL or over have a five times greater risk of developing coronary artery disease than those whose levels are below 220 mg / dL <sup>7-9</sup>. Further analysis of serum lipoproteins ( fat-carrying proteins) has refined this risk to show that the serum levels of “ Low Density Lipoproteins” (LDL) and “ Very Low Density Lipoproteins “ (VLDL) are directly related to risk in both men and women, while “High Density Lipoproteins” (HDL) are protective against atherosclerosis. LDL transports cholesterol to the tissues. HDL, on the other hand, transports cholesterol to the liver for metabolism and excretion. Therefore the HDL-to-LDL ratio largely determines whether cholesterol is being broken down or deposited in tissues. The HDL-to-LDL ratio also affects other balances in the body; for instance, as the HDL / LDL ratio increases, platelet aggregation decreases proportionally<sup>7- 9</sup>. Reduction of LDL results in a decrease in progression of atherosclerosis in humans and other primates. Several controlled trials of different diets which have been accompanied by a fall in mean cholesterol levels in small test populations have shown a favourable effect on incidence of the overall complications of IHD. The American College of Cardiology / American Heart Association (ACC / AHA)



guidelines recommend that lipid lowering therapy be initiated in all Coronary Artery Disease (CAD) patients with a baseline LDL cholesterol level greater than 130 mg / dL, with a target LDL cholesterol goal of less than 100 mg / dL <sup>10</sup>. The association of Hyperlipidemia with the development of atherosclerotic lesion has also promoted widespread search for dietary supplement which safely and effectively control the concentration of cholesterol and triglycerides in the blood and hopefully in the tissues with least or no toxic effect.

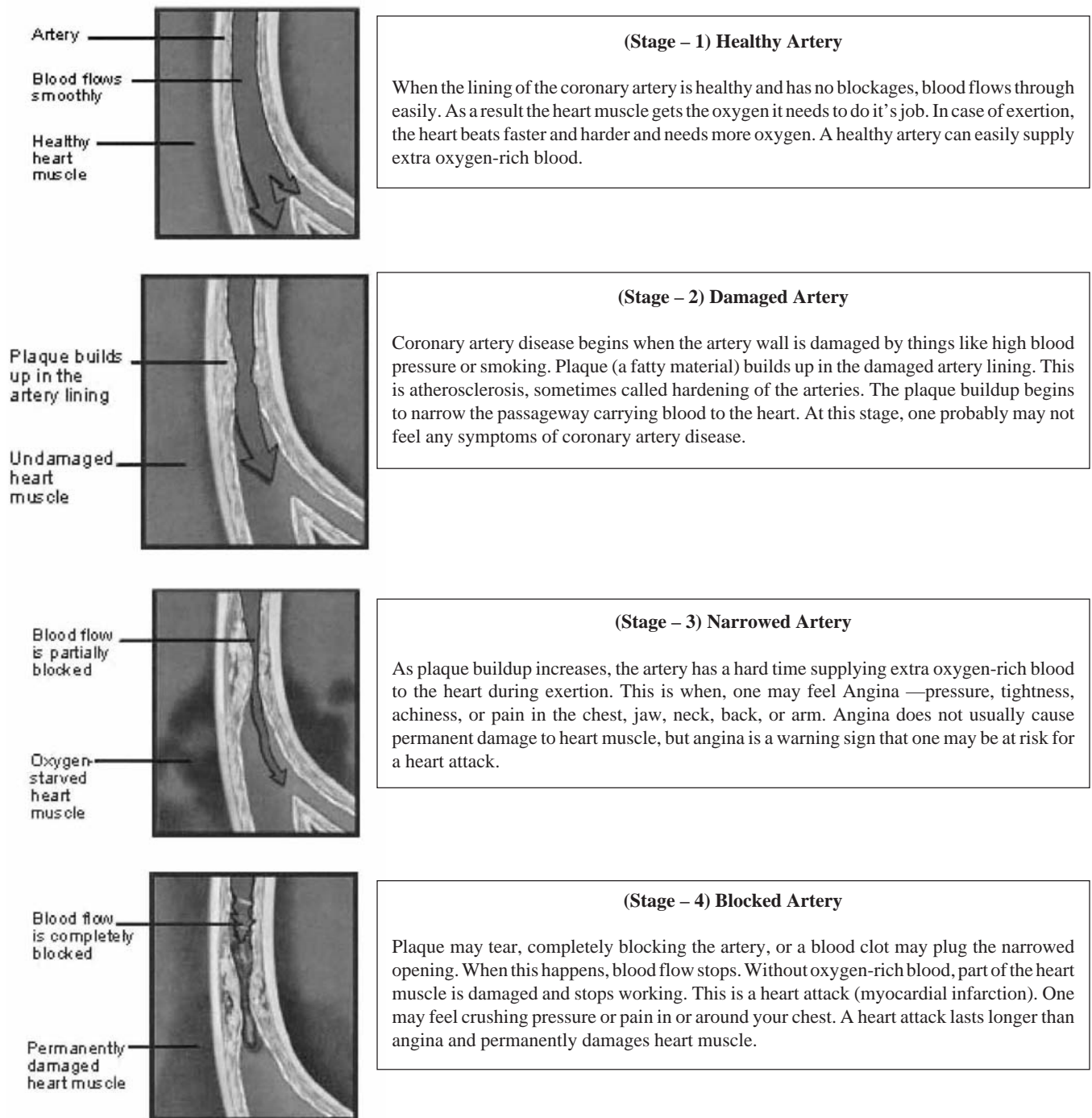
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**FIGURE - 2  
PROCESS OF ATHEROSCLEROSIS**



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