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The effect of consumption sugar on cardiovascular disease

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I thank Allah almighty for having given me the privilege, the chance to study and follow the path of science, as I always wanted and desired..

Special thanks to my parents ***Naziha*** *and* ***Mountasser*** *who supported me all along my journey by their blessings.*

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thank you for your help and for all good and bad moment we spent together.

Bouchra

Dedication

*Thanks to **ALLAH** who have lightened my path and who granted me the ability to accomplish this work and the force to overcome all difficulties.*

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*Thank you **Bouchra** for being my friend and partner since ours five years in ENS*
thank you for your help and for all good and bad moment we spent together.

Djihane

Table of contents

CHD: Coronary heart disease

CRP: C-reactive protein

CV: Cardiovascular

CVD: Cardiovascular disease

Cx: Circumflex

ECM: Extracellular matrix

FFA: Free fatty acids

HDL: High density lipoproteins

HFCS: Honey and high fructose corn syrup

hs-CRP: High-sensitivity C-reactive protein

IgG: Immunoglobulin G

LAD: Left anterior descending

LDL: Low density lipoprotein

MCP-1: Monocyte chemoattractant protein-1

MetS: Metabolic syndrome

PGS: Proteoglycans

RCA: Right coronary artery

SMC: Smooth muscle cells

T2DM: Type 2 diabetes mellitus

TF: Tissue factor

VCAM-1: Vascular cell adhesion molecule-1

Liste of figures

The term sugar is used to designate the different carbohydrates which are characterised by having a sweet taste **(Jana et al., 2015).**

Researchers have concentrated on the properties of sugar, and in particular in fructose. This monosaccharide forms with glucose the sucrose, a disaccharide more commonly known as "table sugar" **(Thornley et al., 2012).** Sugar is considered one of the most elemental nutrients for humans; it may lead to disruption of signaling network and could be associated with some pathological stats, such as cancer, cardiovascular and similarly with inflammatory complication **(Jana et al., 2015).** Increased fructose consumption can lead to increase in inflammatory biomarkers (**Aeberli et al., 2011).**

Cardiovascular diseases are still the primary cause of mortality worldwide, with high blood pressure and type 2 diabetes. In parallel with the rise in cardiovascular disease incidence, the consumption of sugar has increased. Sugar is potential contributors to weight gain and increase the risk for elevations in blood pressure, type 2 diabetes, coronary heart disease, stroke, prevents triglycerides (a type of blood fat associated with cardiovascular disease) from being broken down and lowers the level of HDL cholesterol the "good" cholesterol in the body while raising LDL "bad" cholesterol levels **(Thornley et al., 2012).**

Atherosclerosis is a dominant cause of cardiovascular. It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, in large part due to the accumulation of macrophage cells and promoted by low density lipoproteins LDL is commonly referred to as a hardening or furring of the arteries. It is caused by the formation of multiple plaques within the arteries **(Jagdish, 2009).**

In this thesis we analyse the relationship between sugar and cardiovascular disease, to answer the following question: is the consumption of sugar, in large quantities, associated with a higher risk of suffering from a cardiovascular disease?

Chapter 1: Sugar and inflammation

I.Sugars

I.1.Definition of Sugar

Sugars are white crystalline carbohydrates that are soluble in water and generally have a sweet taste. The commercial sugar is the disaccharide sucrose (white sugar or table sugar) **(Kamal and Klein, 2011),** and it is ever present in the modern world and is estimated to be found in 75% of packaged foods **(White, 2018).**

The simplest sugars consist of a single monosaccharide. They include glucose, fructose, and galactose **(Asif et al., 2011).** Glucose is the major sugar that is mobilized from mammalian energy reserves **(Manolescu et al., 2007).**They are important for every-day life biological functions such as provide in energy for running vital roles of the living body **(Kamal and Klein, 2011).**

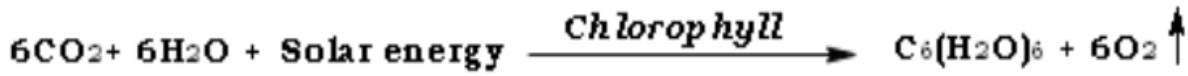
I.1.1.Carbohydrates

I.1.1.1.Definition

Carbohydrates are the main source of energy that is ingested by the human body **(Jéquier, 1994)**.They are biological molecules made of carbon, hydrogen, and oxygen in a ratio of roughly one carbon atom (C) to one water molecule (H2O).This composition gives carbohydrates their name: they are made up of carbon (*carbo-*) plus water (*-hydrate*) **(Raven et al.,2014).**

The formula for carbohydrates is $(CH_2O)n$. Structurally carbohydrates are polyfunctional compounds. They contain two types of functional groups hydroxyl and carbonyl. They may be polyhydroxy aldehydes or polyhydroxy ketones **(Mondal, 2017).**

Formation of carbohydrates in nature occurs in green plants by a process called photosynthesis, plant containsthe green pigment chlorophyll, which catalyses the conversion of carbon dioxide and water into sugar **(Mondal, 2017).**



I.1.1.2.Chemical structure of carbohydrate

Carbohydrates chains come in different lengths, and biologically important carbohydrates belong to three categories: monosaccharides, disaccharides, and polysaccharides **(Raven et al., 2014).**

A. Monosaccharides

The basic building block of carbohydrates is the monosaccharide, which consists of six carbon atoms **(Wakim and Grewal , 2021)**, (mono = one, saccharide = sugar) are simple sugars, the most common of which is glucose. Monosaccharides have a formula of $(CH_2O)n$. from which disaccharides, oligosaccharides, and polysaccharides are constructed **(Khowala et al., 2008).**

Simple monosaccharides ($C_n(H_2O)_n$) are classified according to the number of their C atoms (n) **(Neuman, 2013).** Monosaccharides contain a single polyhydroxy aldehyde or ketone unit.

- If the sugar has an aldehyde group, meaning that the carbonyl C is the last one in the chain, it is known as an aldose.

- If the carbonyl C is internal to the chain, so that there are other carbons on both sides of it, it forms a ketone group and the sugar is called a ketose.

Sugars are also named according to their number of carbons, some of the most common types are trioses (three carbons), pentoses (five carbons), and hexoses (six carbons) **(Mondal, 2017) (Figure 1).**

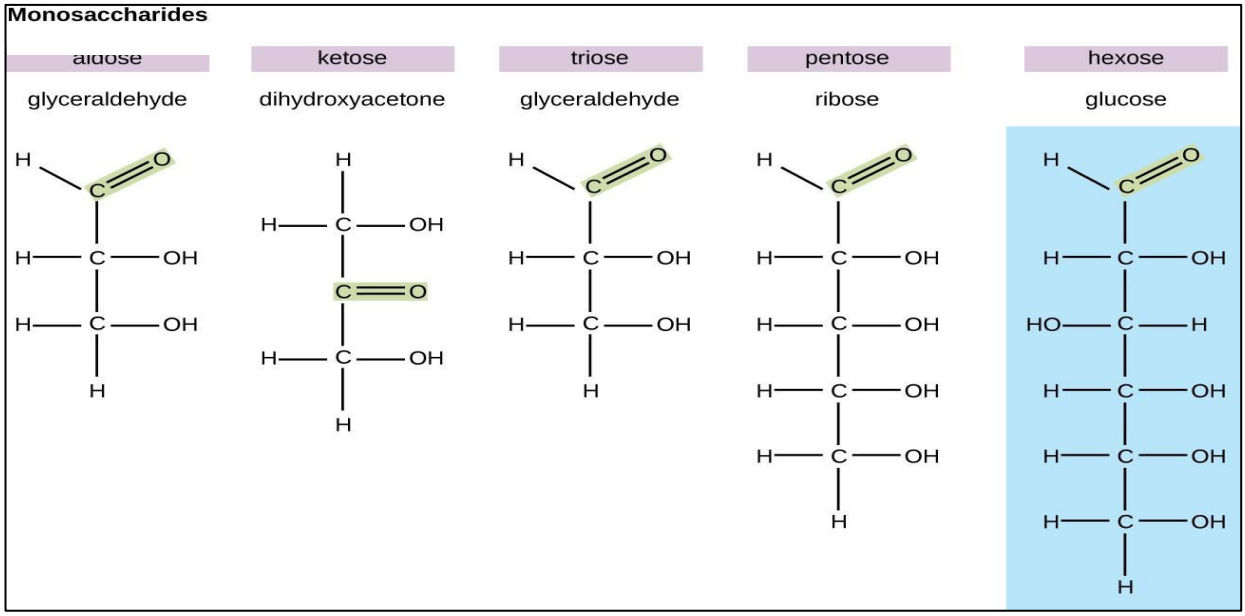


Figure 1: Monosaccharides are classified based on the position of the carbonyl group and the number of carbons in the backbone **(web site1).**

B. Disaccharides

A disaccharide is a carbohydrate formed by the joining of two monosaccharides **(Wakim and Grewal, 2021)**. They have 12 carbon atoms, and their chemical formula is $C_{12}H_{22}O_{11}$ **(Neuman, 2013).**The most common disaccharide is sucrose, or table sugar, which is composed of the monomers glucose and fructose. Other common disaccharides include lactose and maltose **(Wakim and Grewal, 2021) (Figure 2).**

C. Polysaccharides

Polysaccharides are composed of chemically bonded monosaccharides, they are considered as vital bio-macromolecules for all living organisms, which are structurally comprised of homo or hetero monosaccharides and uronic acids connected with glycosidic linkages **(Zhang and Wang, 2015).**

They are also referred to as complex carbohydrates, they are found in living things**,** they serve as energy storage such as starch and glycogen and as structural components (chitin in insects and cellulose in plants) **(Wakim and Grewal , 2021)**.

II. Inflammation

II.1.Definition

The word inflammation comes from the Latin "inflammo", meaning "I set alight, I ignite» **(Christian, 2015)**,it is derived from the Latin "inflammare" meaning « to burn ». Inflammation is a local response (reaction) of living vascularized tissues to endogenous and exogenous stimuli **(Altameemi and Mohammed, 2019).**

Inflammation underlies a wide variety of physiological and pathological processes **(Ruslan, 2008).** It is a biological reaction to a disrupted tissue homeostasis **(Noah et al., 2012),** and it is critical for the development of many complex diseases and disorders including auto-immune diseases, metabolic syndrome, neurodegenerative diseases, cancers, and cardiovascular diseases **(Masaaki and Toshio, 2012).**

II.2.Mechanism of the inflammation

The inflammatory response (inflammation) occurs when tissues are injured by bacteria, trauma, toxins, heat, or any other cause. They are essential for the maintenance of normal tissue homeostasis**.** The primary purpose of the inflammation response is to eliminate the pathogenic insult and remove injured tissue components **(Fantone and Ward, 1999).**

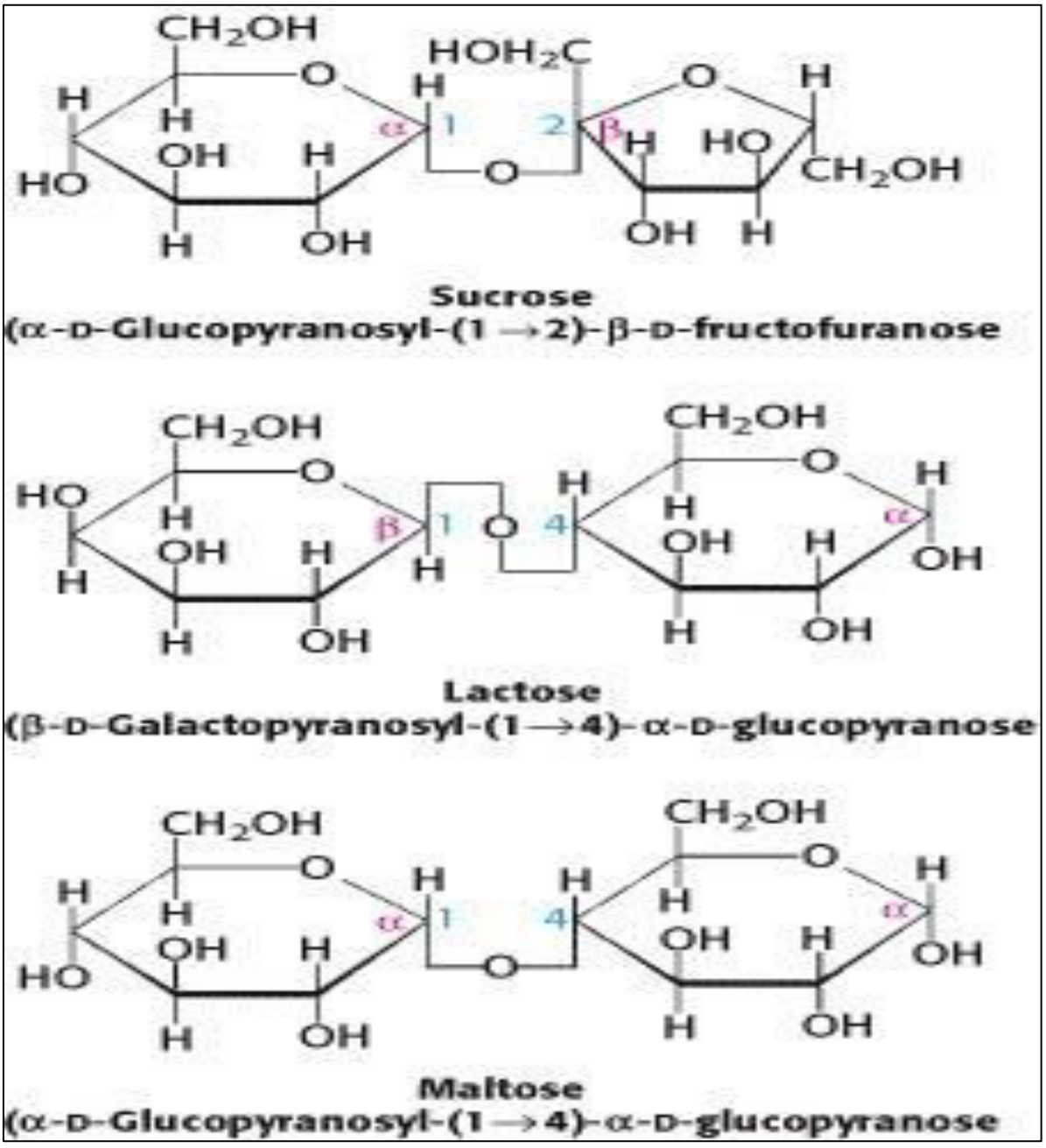


Figure 2: Common disaccharides include maltose (malt sugar), lactose (milk sugar), and sucrose (table sugar) **(Berg et al., 2002).**

II.3.Types of inflammation

A. Acute inflammation

Acute inflammation is the immediate and early response to injury designed to deliver leukocytes to sites of injury **(Mitchell and Cotran, 2003).**

Vijay, 2018 reported that, acute inflammation is initiated by cells, such as mast cells that recognize pathogen-associated molecular patterns (PAMPs) with toll-like receptors, but other cells like natural killer (NK) cells can trigger inflammation as well **(Vijay, 2018)**.

Mast cells detect injury to nearby cells and release histamine, initiating an inflammatory response. Histamine increases blood flow to the wound site, and increased vascular permeability allows fluid, proteins, phagocytes, and other immune cells to enter infected tissue **(Vijay, 2018)(Figure3)** and **(Figure 4).**

II.4. The vascular and cellular response to inflammation

A. vascular response

The vascular phenomena are transient vasoconstriction mediated by thromboxane to prevent possible bleeding and it is stimulated by vasoactive agents such as catecholamines, serotonin, bradykinin, and prostaglandins that are released from surrounding tissues and by norepinephrine released by the sympathetic nervous system **(Lawrence, 1998)**. Within minutes, vasodilation mediated by vasoactive amines such as (histamine), nitric oxide (NO) **(Maiorana et al., 2003)**, prostraglandin as, kinins and fragments complement (C3a and C5a) to keep the blood concentrated, and thus have a greater number of leukocytes to the inflammatory process and increase the permeability to assist in the output cells of the immune system **(Lawrence and Gilroy, 2007)**.

During inflammation, large proteins in the bloodstream, such as serum albumins, can leak out and into the tissues. Water follows these proteins due to the force of oncotic pressure that the proteins exert **(Scallan et al., 2010).** This is called exudate, a form of edema. As exudate accumulates within the tissues, they become swollen. The exudate may carry antimicrobial proteins and antibodies into the tissues, and stimulates lymphatic drainage **(Altameemi and Mohammed, 2019) (Figure 5).**

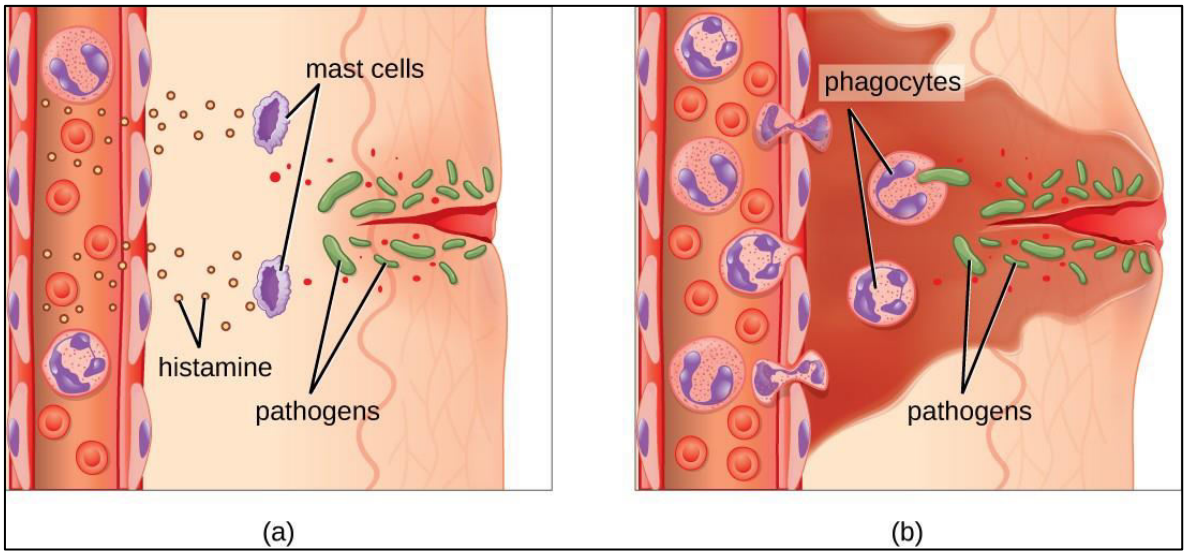


Figure 3: Mast cells in acute inflammation **(Kumar et al., 2009).**

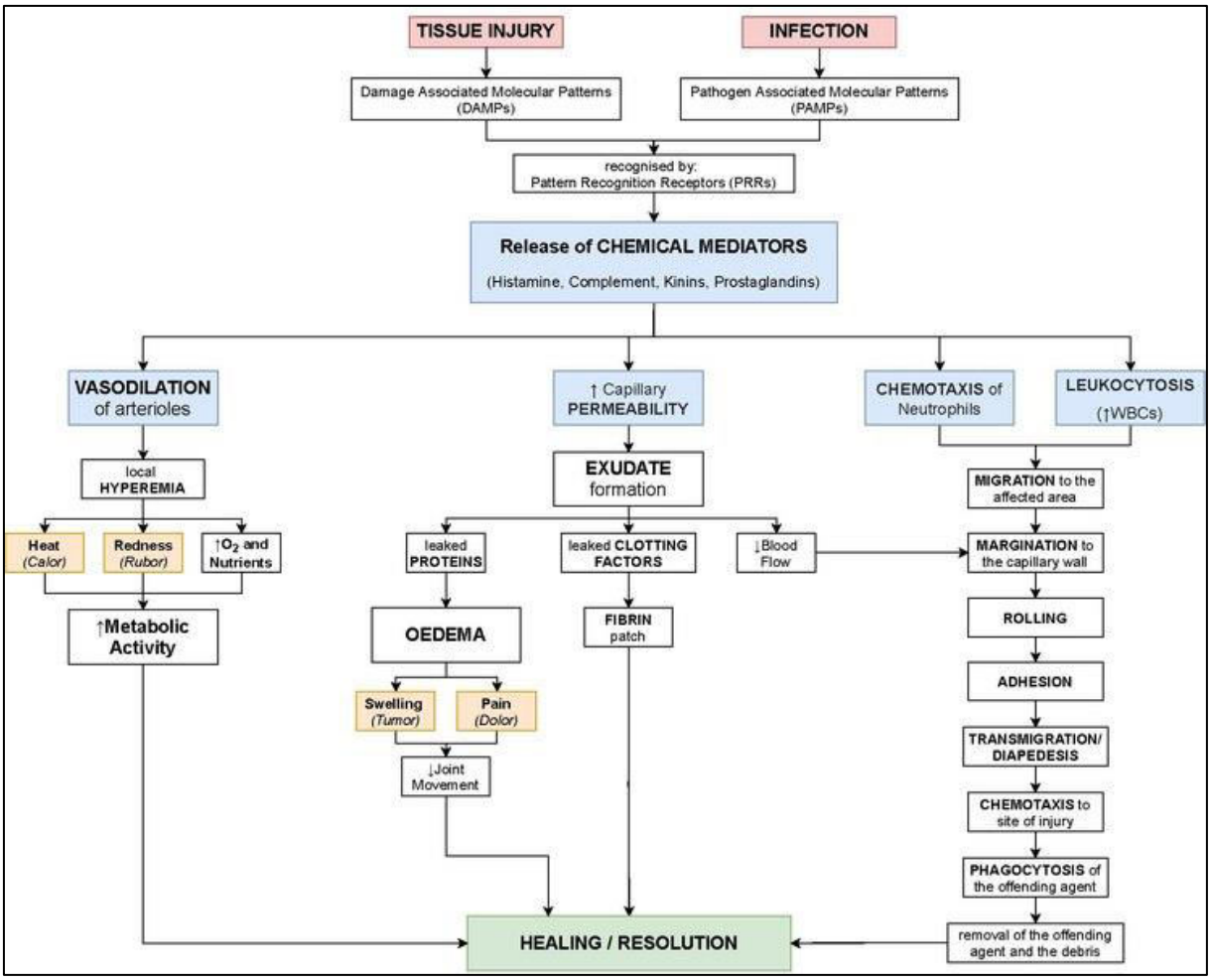


Figure 4: A flowchart depicting the events of acute inflammation **(Robbins et al., 2020).**

B. Cellular response

The predominant cell of acute inflammation is the neutrophil. They are attracted to the site of injury by the presence of chemotaxins, the mediators released into the blood immediately after the insult **(Herrington, 2014).**

The migration of neutrophils occurs in four stages **(Figure 6):**

• Margination : cells line up against the endothelium.

• Rolling : close contact with and roll along the endothelium.

• Adhesion : connecting to the endothelial wall.

• Emigration : cells move through the vessel wall to the affected area.

Once in the region, neutrophils recognise the foreign body and begin phagocytosis, the process whereby the pathogen is engulfed and contained with a phagosome. The phagosome is then destroyed via oxygen-independent (e.g. lysozymes) or oxygen-dependent (e.g. free radical formation) mechanisms.

Following the process of acute inflammation, there are several possible results:

• Complete resolution with total repair and destruction of the insult

• Fibrosis and scar formation occurs in cases of significant inflammation

• Chronic inflammation from a persisting insult

• Formation of an abscess **(web site 2).**

II.5. Diagnosis of inflammation

Pathology exam is the gold standard for disease diagnosis. The pathological characteristics of acute and chronic inflammation are clear. (Figure 7 and Figure 8 are respective slides for inflammation) **(Mitchell and Cotran, 2003).**

In addition to local symptoms, such as edema, pain, reddish, inflammation also has systemic symptoms. Some of them can be used as diagnosis index **(LeiYu, 2003).**

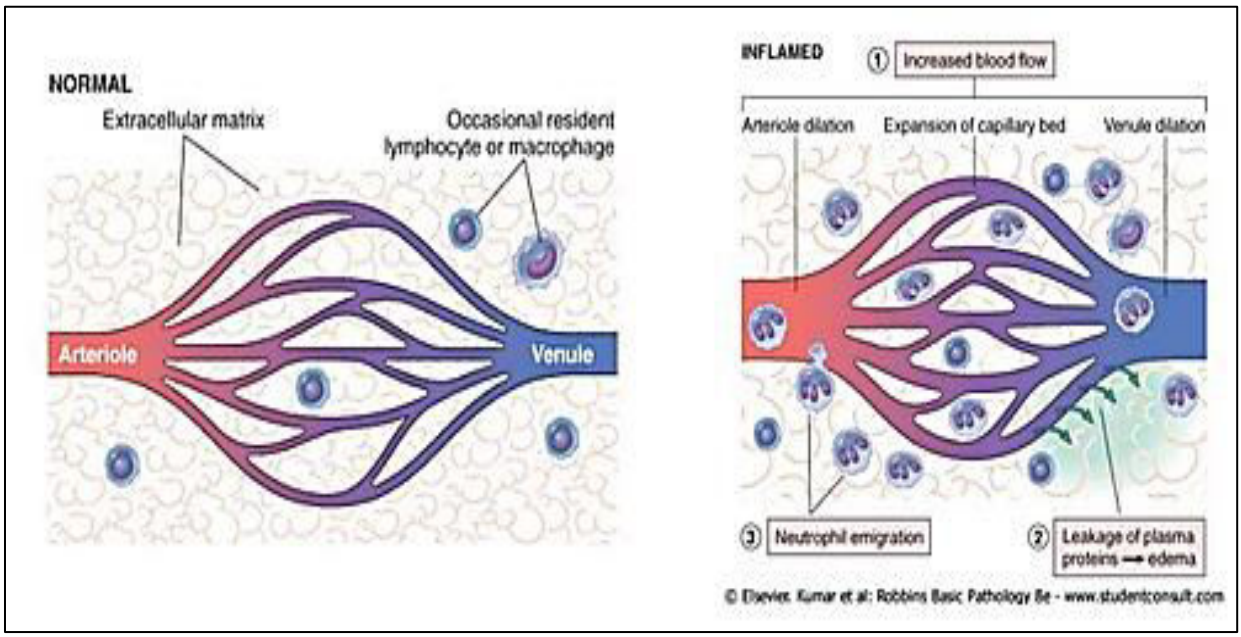


Figure 5: Vascular phenomena of inflammation **(Kumar et al., 2009).**

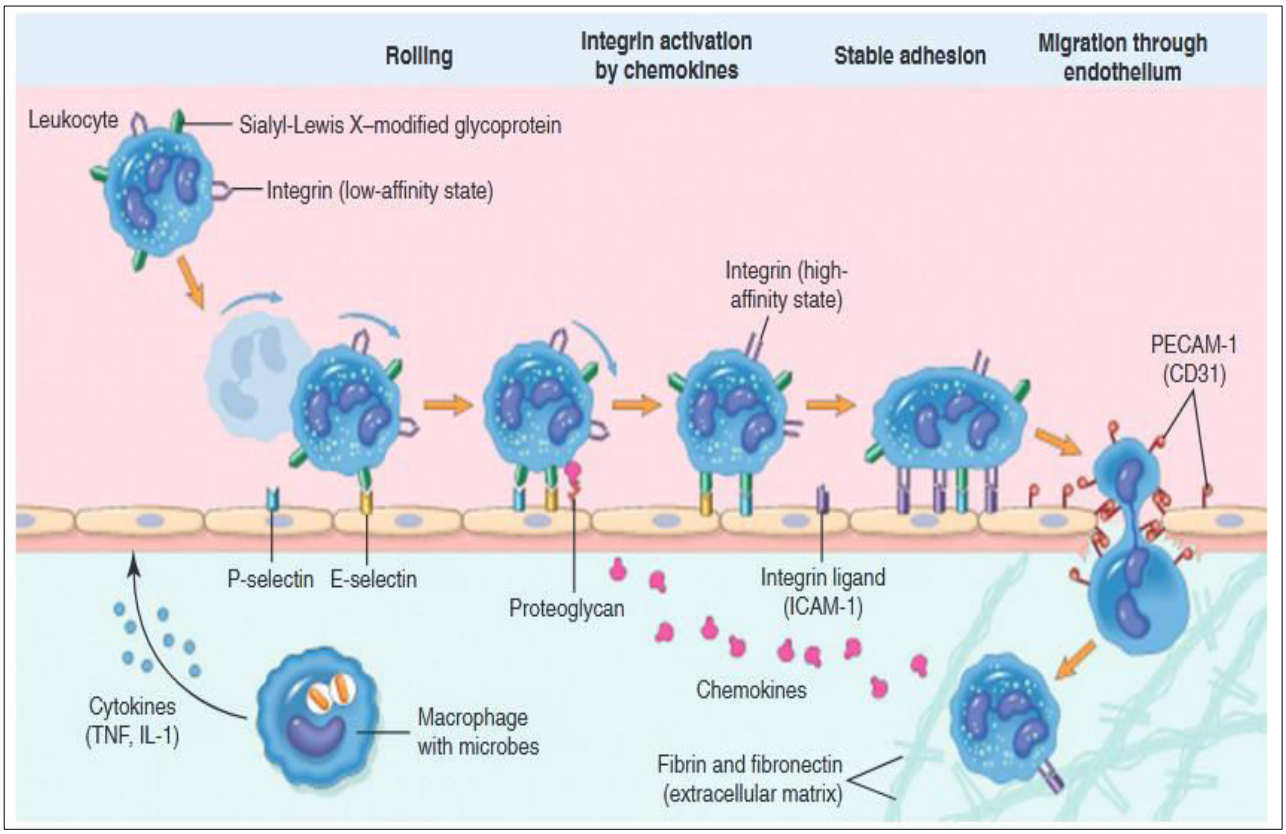


Figure 6: Neutrophil extravasation (Leukocyte extravasation is a multistep process orchestrated by both hemostatic and cell–cell interactions) **(Kumar et al., 2009).**

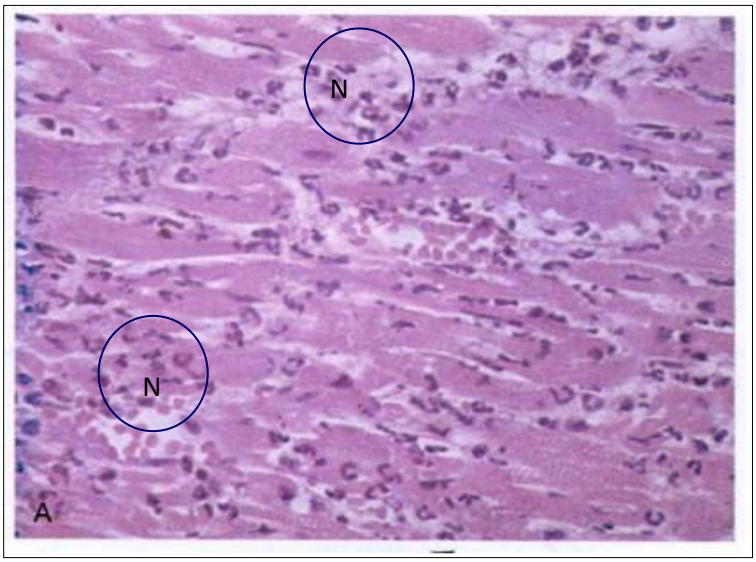


Figure 7: Acute inflammation, showing the multilobed polymorphonuclear cell infiltrate (myocardium) **(Mitchell and Cotran, 2003).**

N: Neutrophil cells

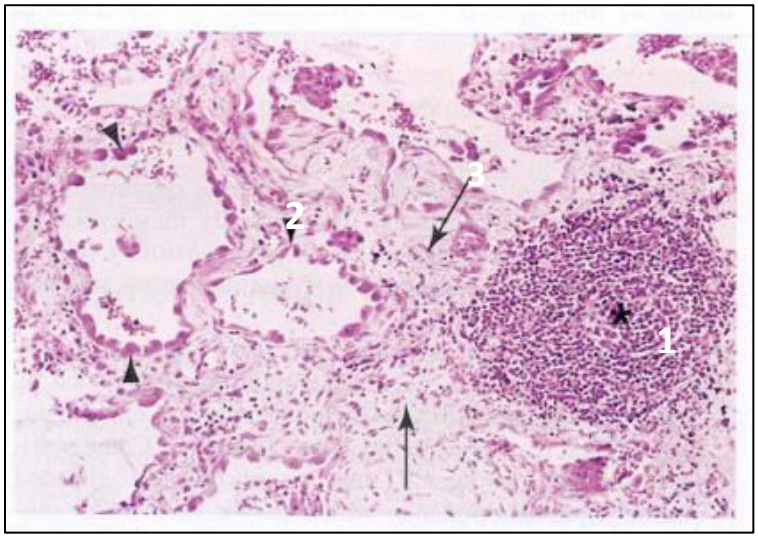


Figure 8: chronic inflammation in the lung, showing the three characteristic **(Mitchell and Cotran, 2003).**

(1) Collection of chronic inflammatory cells (*) , (2) Destruction of parenchyma (normal alveoli are replaced by spaces lined by cuboidal epithelium [arrowheads]) (3) Replacement by connective tissue (fibrosis) (arrows) **.**

Clinically, higher temperature means there is inflammatory response in patient's body. The changes in the body fluid including blood are indexes of inflammation. For example, in bacteria infection induced inflammation, the number of leukocyte multiply while the percentage of neutrophils increases to more than 90% **(LeiYu, 2003).**

Another index of inflammation in body fluid is C- reactive protein (CRP); this protein level increases during acute inflammation. But we can see here, all the indexes mentioned above are general, and no one is pathogenically specific. So when make diagnosis of inflammation, the reason that induces the inflammatory response should be identified. Thus, the correct therapy can be delivered **(LeiYu, 2003).**

III.C-reactive protein

III.1. Definition

C-reactive protein (CRP) is one of the common test parameters used in clinical practice, to assess, diagnosis, and prognosis inflammation. The C-reactive protein (CRP), belonging to pentraxin family of proteins shows a 1000-fold or more increase in concentration during the occurrence of an injury, inflammation or tissue death **(Hirschfield and Pepys, 2003).**

The C-reactive protein was first discovered as a substance in the serum of patients with acute inflammation that reacted with the C- (capsular) polysaccharide of pneumococcus **(Séverine et al., 2004) .**The plasma half-life of CRP is about 19 hours and is constant under all conditions of health and disease **(Srikantiaha, 2014)**.

III.2. Production of C-reactive protein

C-reactive protein is produced in many sites within the human body, such as the liver in response to IL-6. It is also produced in very limited concentration by non-hepatic cells like neurons, atherosclerotic plaques, monocytes, Kupffer cells and lymphocytes **(Hirschfield and Pepys, 2003) (Jialal et al., 2004) and (Kuta and Baum, 1986).**

Studies have shown that epithelial cells of both respiratory tract and renal epithelium can also produce CRP under certain circumstances **(Gould and Weiser, 2001).**

Cogent data have indicated that the protein is also produced by the atherosclerotic lesions (especially by smooth muscle cells and macrophages), kidneys, neurons, and alveolar macrophages **(Venugopal et al., 2005)**.

III.3. Structure of C-reactive protein

C-reactive protein consists of five identical, non covalently associated ~23-kDa protomers arranged symmetrically around a central pore. The term "pentraxins" has been used to describe the family of related proteins with this structure. Each protomer has been found by x-ray crystallography to be folded into two antiparallel β sheets with a flattened jellyroll topology similar to that of lectins such as concanavalinA **(Shrive et al., 1996)** and **(Thompson et al., 1999).**

It has a recognition face with a phosphocholine binding site consisting of two coordinated calcium ions adjacent to a hydrophobic pocket. The co-crystal structure of CRP with phosphocholine demonstrated that Phe-66 and Glu-81 are the two key residues mediating the binding of phosphocholine to CRP **(Thompson et al., 1999)**. The amino acid Phe-66 provides hydrophobic interactions with the methyl groups of phosphocholine whereas Glu-81 is found on the opposite end of the pocket where it interacts with the positively charged choline nitrogen **(Black et al., 2004) (Figure9).**

III.4. Dosage and detection of C-reactive protein

In the beginning, CRP plasma levels were determined by serum-agglutination performed in latex particles in a slide. This assay allowed a semi-quantitative determination, with a subjective interpretation. Later, quantitative methods for CRP quantification were developed through immunoturbidimetry and nephelometry **(Lima et al., 2000).**

Due to the low sensitivity of these methods on detection of low levels of inflammation, in the 90s a high sensitivity nephelometry method for detection of very low levels of serum CRP was developed, called high sensitivity CRP (hs-CRP). This is the ideal laboratory method in use to determine cardiovascular risk linked with chronic systemic vascular inflammation of atherosclerosis, having a detection limit of 0.3 mg/l **(Silva and Lacedra, 2012).**

III.5. Functions of C-reactive protein

C-reactive protein levels are known to increase dramatically in response to injury, infection, and inflammation **(Pradhan et al., 2001)** Furthermore, soluble and immobilized CRPs have been demonstrated to mediate the uptake of native low density lipoprotein (LDL) into macrophages. The main role of CRP in inflammation tends to focus around the activation of the C1q molecule in the complement pathway leading to the opsonization of pathogens **(Baumeister et al., 2016)**.

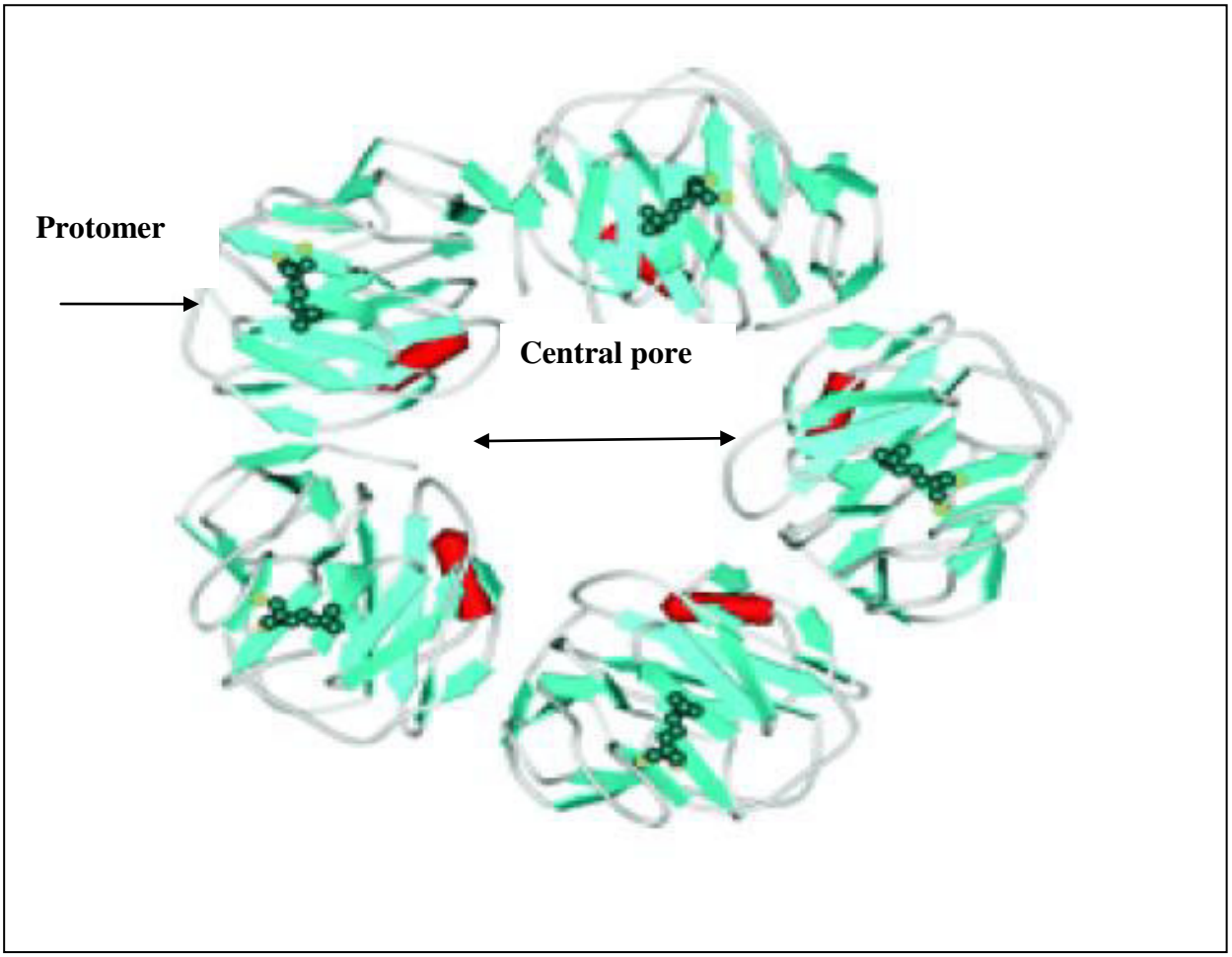


Figure 9: Crystal structure of C-reactive protein complexed with phosphocholine, calcium ions are yellow and phosphocholine is green **(Thompson et al., 1999).**

Although CRP can initiate cell-mediated pathways by activating complement as well as to binding to Fc receptors of IgG It is binds to Fc receptors with the resulting interaction leading to the release of pro-inflammatory cytokines **(Pradhan et al., 2001)**.

On the contrary, the degradation of CRP yields small soluble bioactive peptides that inhibit many of the pro-inflammatory and tissue destructive potential of neutrophils. These peptides are possibly involved in signal transduction pathways leading to neutrophil activation **(Baltz and Pepys, 1983).**

C-reactive protein (CRP), therefore is an important molecule in the host's innate immune system and in the protection against autoimmunity **(Sérvine et al., 2004).** It is well established that CRP is an acute marker of inflammation and that its concentration increases in circulation during inflammatory events where could deposited at sites of inflammation and tissue damage in both naturally occurring and experimental conditions **(Ashworth and Sproston, 2018).**

III.6. C- reactive protein and cardiovascular disease

Over a dozen major studies demonstrate that baseline levels of CRP in apparently healthy men and women are highly predictive of future risk of heart attack, stroke, sudden cardiac death, and the development of peripheral arterial disease. Doctors also know that CRP levels predict recurrent coronary events among patients who already suffer from heart disease and that the prognosis of patients in the acute phase of a heart attack is tightly linked to CRP levels **(Paul and Ridker, 2003).**

Individuals with elevated levels of CRP have a risk about 2 to 3 times higher than the risk of those with low levels. It is important that your physician request a "high-sensitivity" test for CRP if he or she is using CRP for the purpose of cardiovascular risk assessment **(Libby et al., 2002).**

This is because older tests for CRP, which are adequate for monitoring severe inflammatory conditions, do not have the ability to measure levels accurately within the range needed for cardiac risk detection **(Libby et al., 2002).** The hs-CRP is the most widely evaluated biomarker in the quest for an ideal biomarker for global cardiovascular disease (CVD) risk prediction **(Ridker, 2003) (Table 1).**

Table 1: The relationship between hs-CRP plasma concentrations and the risk factor **(Ridker, 2003)**

Risk degree	**hs-CRP concentration (mg/L)**
Low risk	< 1
Intermediate risk	1-3
High risk	> 3

Several studies confirm that hs-CRP predicts cardiovascular events in healthy women and men **(Ridker et al., 2000)**, in individuals with traditional risk factors **(Kuller, 1996)** or with CVD **(Haverkate et al., 1997).** The capacity of hs-CRP to predict CVD risk is independent from traditional risk factors **(Ridker et al., 2000)**. The protein (hs-CRP) is an additional risk factor for coronary artery disease when associated with high plasma levels of cholesterol **(Jialal and Devaraj, 2001).**

For many years, CRP was used as a complementary method for diagnosis of inflammatory processes of any nature. Meanwhile, with the discovery of inflammatory components involved in cardiovascular events, mainly atherosclerosis, CRP was assigned as a risk indicator for coronary disease and cerebral vascular accidents, being an inflammatory marker considered strong predictor that is independent of the risk for cardiovascular event or death **(Bezerra et al., 2008).**

III. 7. Sugar and inflammation

One of the reasons inflammation occurs is from a rapid rise in blood sugar, which causes biochemical changes in the cell **(Pacholyk, 2006).**

According to observational data reports, it has been consistently reported that dietary sugar intake (more specifically, sugar-sweetened beverages) may be one stimulus of subclinical inflammation, as measured by the inflammatory marker C-reactive protein (CRP) **(De Koning et al., 2012).**
Pacholyk, 2006 reported that, people with elevated CRP levels were four and one half times more likely to have a heart attack. Central to the potentially relevant mechanisms is the fact that dietary sugar promotes de novo synthesis of free fatty acids (FFA) in the liver **(Softic et al., 2016).** On the other hand **(Houston and Minich, 2015) (Malik and Hu, 2015)** reported that fructose it does not stimulate insulin secretion, provides a rapid substrate for lipid synthesis, and may increase uric acid concentrations and stimulate endogenous inflammatory glycated products.

It has been postulated that dietary sugar consumption contributes to increase inflammatory processes in humans **(Chung et al., 2014).**

Chapter 2: sugar and cardiovascular diseases

IV.Cardiovascular system

IV.1. Anatomy of the heart

The human heart has a weight of approximately 250-300 g and a size similar to a closed fist The heart is positioned in the thorax surrounded by a fibrous sac, the pericardium. The external layer of the heart tissue is called the epicardium and the innermost layer in connection to the ventricles the endocardium. The tissue between the two aforementioned layers, the myocardium, is responsible for ventricular contraction and consists of muscular tissue **(Tortora and Grabowski, 2003)**.

IV.1.1. The chambers of the heart

The heart is made up of four chambers. The superior chamber consists of the right atrium and the left atrium, which lie primarily on the posterior side of the heart **(Bernet al., 1997).**

Blood drains into the atria from the pulmonary and systemic circulatory system. Composing the lower chambers are the right ventricle and left ventricle, which are much larger than the atria. The right ventricle pumps blood through the pulmonary circulatory system and the thicker walled left ventricle pumps blood through the longer systemic circulatory system. Internally, the two ventricles are separated by a thick myocardial wall called the interventricular septum **(Christoffels et al., 2000).**

On the anterior surface of the heart, the interventricular septum is marked by a shallow diagonal groove known as the anterior interventricular sulcus, which is occupied the anterior interventricular artery, great cardiac vein and adipose tissue. On the posterior surface of the heart, the ventricles are separated by the posterior interventricular sulcus, which contains the posterior interior artery, middle cardiac vein and adipose tissue **(Kalaria et al., 2002).**

IV. 1.2. The heart valve anatomy

Four valves maintain the unidirectional flow of blood through the heart. The valves are located between each atrium and ventricle and in the two arteries that empty blood from the ventricle **(Charitos and Sievers, 2013).**

A. The tricuspid valve

The Tricuspid valve (right atrioventricular) is composed of three caps or flaps and controls blood flow from the right atrium to the right ventricle **(Greenspan et al., 1980).**

B. The bicuspid valve

The bicuspid valve is made up of two cusps or flaps and controls blood flow from the left atrium to the left ventricle **(Padala et al., 2010).**

C. Semilunar valves

The semilunar valves (pulmonary valve and aortic valve) are one-way valves that separate the ventricles from major arteries. The aortic valve separates the left ventricle from the aorta, while the pulmonary valve separates the right ventricle from the pulmonary artery. As the ventricles contract, ventricular pressure exceeds arterial pressure, the semilunar valves open and blood is pumped into the major arteries. However, when the ventricles relax, arterial pressure exceeds ventricular pressure and the semilunar valves snap shut. This is due to the elevated pressures in the aorta and the pulmonary artery pushing the blood back toward the ventricles to close the semilunar valves **(EL-houry et al., 2014).**

The four heart valves open and close in response to pressure changes that occur in the ventricles during each cardiac cycle **(Lachman et al., 2002) (Figure10).**

IV.1.3. Pericardic membrane

The pericardium is a fibrous serosal conical sac enclosing the roots of the aorta and the pulmonary artery **(Chinchoy, 2005).**

In humans, pericardium is located inside the middle mediastinum posteriorly to the sternum and the cartilages of the third to seventh left rib. Pericardium isolates the heart from the adjacent tissues, allowing it's free movement within the boundaries of the pericardial cavity and is filled with a small amount of fluid which is called pericardial fluid **(Chinchoy, 2005).**

IV. 1.3.1. Anatomy and histology of pericardium

The pericardium consists of two layers: external sac of fibrous connective tissue, called fibrous pericardium and an internal called serous pericardium. The latter coats the internal surface of the fibrous pericardium and the heart **(Randall and Ardell, 1985)**.

Arterial branches from thoracic aorta, right and left pericardiophrenic artery (internal mammary artery branches), are responsible for the blood supply of the whole pericardium while the venous drainage is accomplished through the venae pericardiales which drain to the azygos vein, to the superior vena cava or to the brachiocephalic **(Chinchoy, 2005).**

The pericardium is innervated by the two phrenic nerves, each one giving an afferent branch (pericardial branch) **(Randall and Ardell, 1985), (Ardell and Randall, 1986) and (Chiou et al., 1997).**

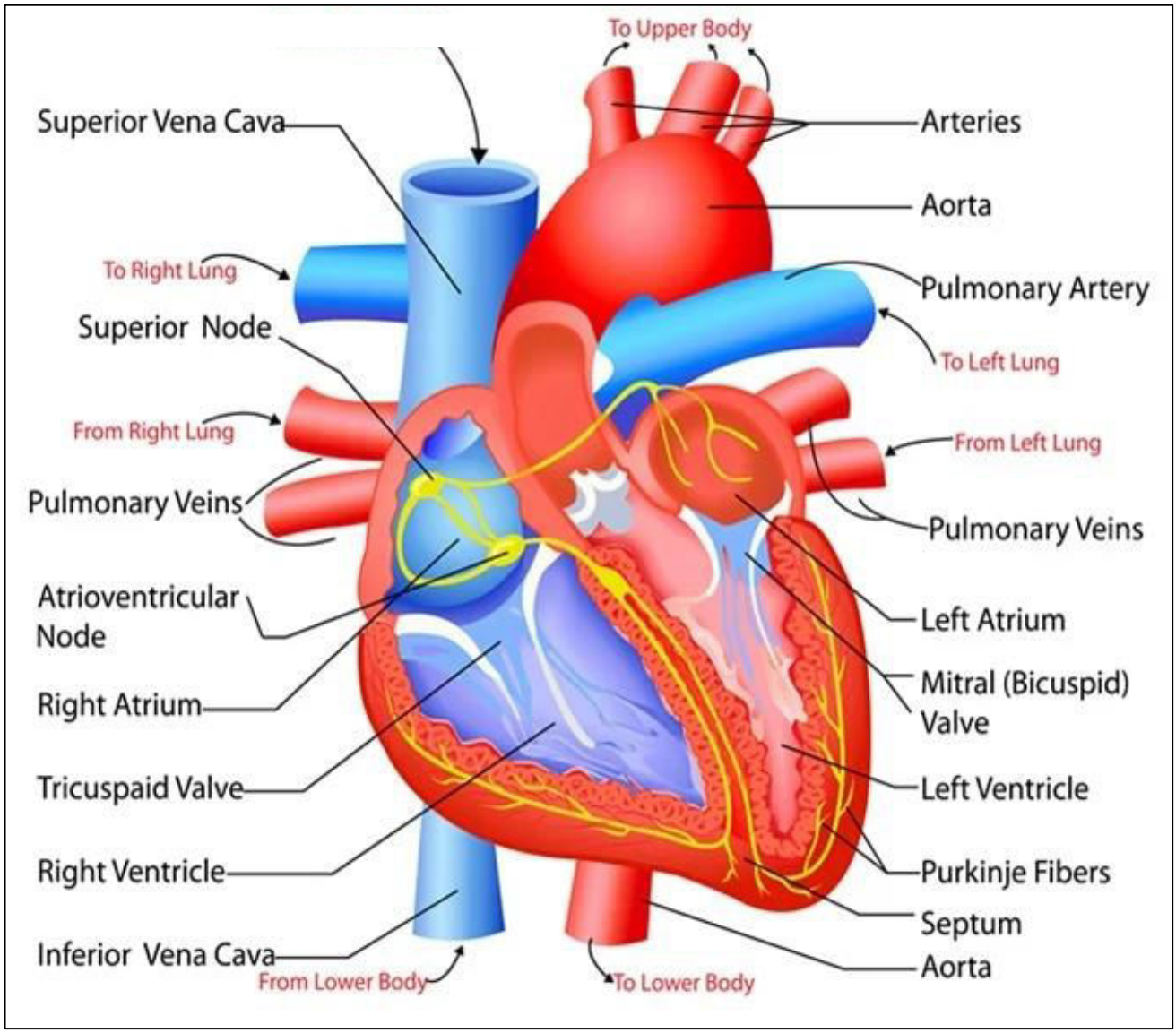


Figure 10: The structure of the heart **(Marieb,2015).**

The thickness of the pericardium increases proportionally to the size of the heart and the pericardial cavity, with the exception of humans who have considerably thicker pericardium compared to the mammals with the same heart size (human 1–3.5 mm, sheep 0.32 ± 0.01 mm, pig 0.20 ± 0.01 mm) **(D'Avila, 2003)**.

The parietal lamina of the serous pericardium is composed of a monolayer of flattened, squamous like, mesothelial cells. Mesothelial cells rest on a thin basement membrane supported by connective tissue stroma in a narrow submesothelial space **(Ishihara et al., 1980) (Mutsaers, 2002).**

The connective tissue stroma contains variously oriented layers of collagen fibrils and small elastic fibers **(Mutsaers, 2002)**. The luminal surface of the mesothelial cells has well developed microvillous border with occasional cilia. The latter bear friction and increase the surface area for fluid transport. There are junctional complexes between adjacent mesothelial cells that consist of desmosomes, which reinforce intercellular adhesion and zonulae occludents **(Ishihara et al., 1980).**

Between the mesothelial cells of the parietal pericardium, not the epicardium, there are milky spots, bulging toward the pericardial cavity. These structures are enclosed with cuboidal mesothelial cells **(Takada et al., 1991) (Mutsaers, 2002)** and **(Michailova and Usunoff, 2006).** These openings provide direct access to the underlying submesothelial lymphatic system allowing rapid removal of fluid and cells from the pericardial cavity **(Takada et al., 1991).**

Inside the pericardial cavity and submesothelial layers of the pericardium, there are resident macrophages, readily available in case of immunological response **(Ishihara et al., 1980) (Mutsaers, 2002)** and **(Michailova and Usunoff, 2006).**

IV.1.4 Layers of the heart walls

The heart wall consists of three layers enclosed in the pericardium:

- Epicardium: the outer layer of the wall of the heart and is formed by the visceral layer of the serous pericardium.
- Myocardium: the muscular middle layer of the wall of the heart and has excitable tissue and the conducting system.
- Endocardium: the inner layer of the heart wall, composed of endothelial cells that provide a smooth, elastic surface for blood collection and pumping **(Marieb,2015) (Figure11).**

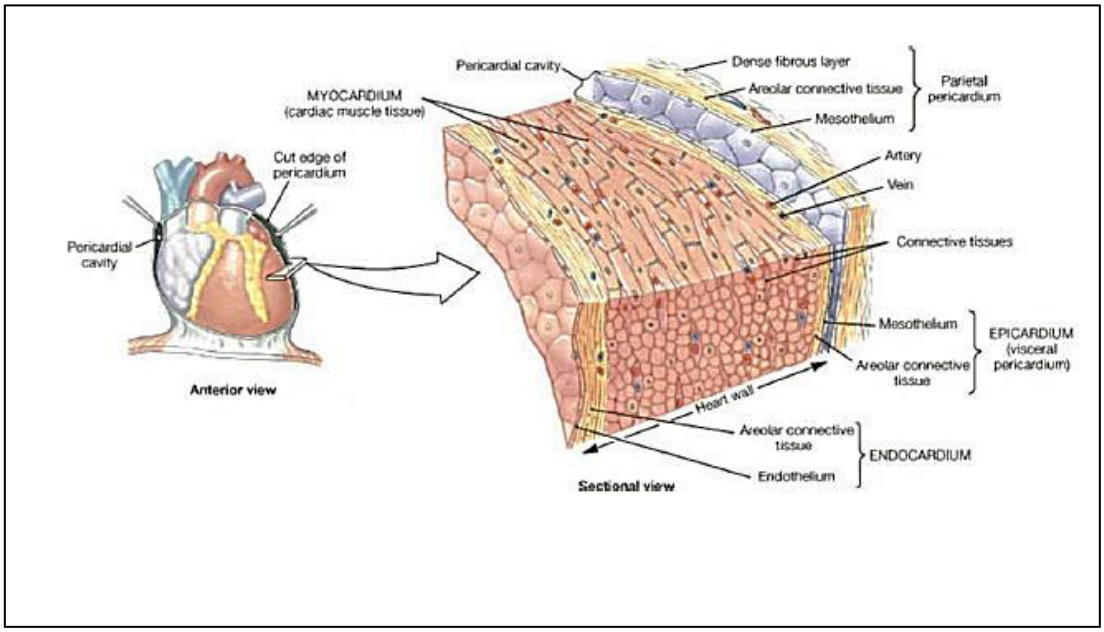


Figure 11: Different layers of heart wall and their composition **(Frederic et al., 2003)**

IV.1. 5. Coronary vascular

Coronary arteries supply oxygenated blood to the heart, and cardiac veins drain away the blood once it has been deoxygenated **(Betts, 2013).**

A-The coronary arteries

The heart muscle, like every other part of the body, needs its own oxygen-rich blood supply. Arteries branch off the aorta and spread over the outside surface of the heart. The right coronary artery (RCA) supplies the bottom part of the heart. The short left main (LM) artery branches into the left anterior descending (LAD) artery that supplies the front of the heart and the circumflex (Cx) artery that supplies the back of the heart **(Kalaria et al ., 2002).**

B-The coronary venous

Coronary venous flow occurs during diastole and systole, and the coronary venous system drains the myocardium of oxygen-depleted blood. The coronary venous system dominates the arterial system; there are at least twice as many veins as arteries in human myocardial tissue **(Hutchins et al., 1986).**

In general, veins are considered to be "low-resistance conduits" to the heart and can alter their capacity to maintain venous pressure **(Spencer et al., 2013).**

The coronary veins can be organized into 2 subgroups:

1- The greater cardiac venous system is comprised of the coronary sinus and its tributaries, as well as the anterior cardiac veins, atrial veins, and the veins of the ventricular septum (**Ho et al ., 2004).**

2-The smaller cardiac venous system, is comprised of the arterioluminal vessels and venoluminal vessels, which are small vessels that drain directly into their respective heart chambers **(Loukas et al., 2009) (Figure12).**

IV.2. The anatomy of aorta

The term aorta is derived from the greek word aeiro, which means to raise. It is the first arterial segment of the systemic blood circulation, directly connected to the heart.

The aorta is the largest artery in the human body with a diameter of 3 cm at its origin (ascending aorta), 2.5 cm in the descending portion (thoracic aorta), and 1.82 cm in the abdomen (abdominal aorta). In addition to the conduit function, the aorta also accomplishes a buffering function, its visco-elastic compliance plays a pivotal role in regulating left ventricular performance, myocardial perfusion and arterial function in the entire cardiovascular system **(Nichols et al., 2011) (Figure 13).**

IV.2.1. Histology and morphology of the aorta

Similar to other vessels, extracellular matrix (ECM) components (elastin, collagen, proteoglycans (PGs), fibronectin, fibrilin, etc.) ensure the aortic wall's structural integrity, whereas cells (endothelial cells, smooth muscle cells (SMC), fibroblasts, myofibroblasts, etc.) maintain its metabolism. Specifically, the proteins elastin and collagen almost entirely define the aorta's passive mechanical properties, while SMCs are responsible for its active properties, and, together with fibroblasts, also for the production of ECM components **(Nichols et al., 2011).**

The aorta should always be regarded as dynamic structure which, within certain physiologic ranges, is able to adapt to functional needs. The aorta's geometrical, histological and mechanical properties change from the ascending aorta towards the abdominal aorta **(Figure 15)**, likely to maintain conditions for optimal mechanical operation **(Rachev et al., 2013).**

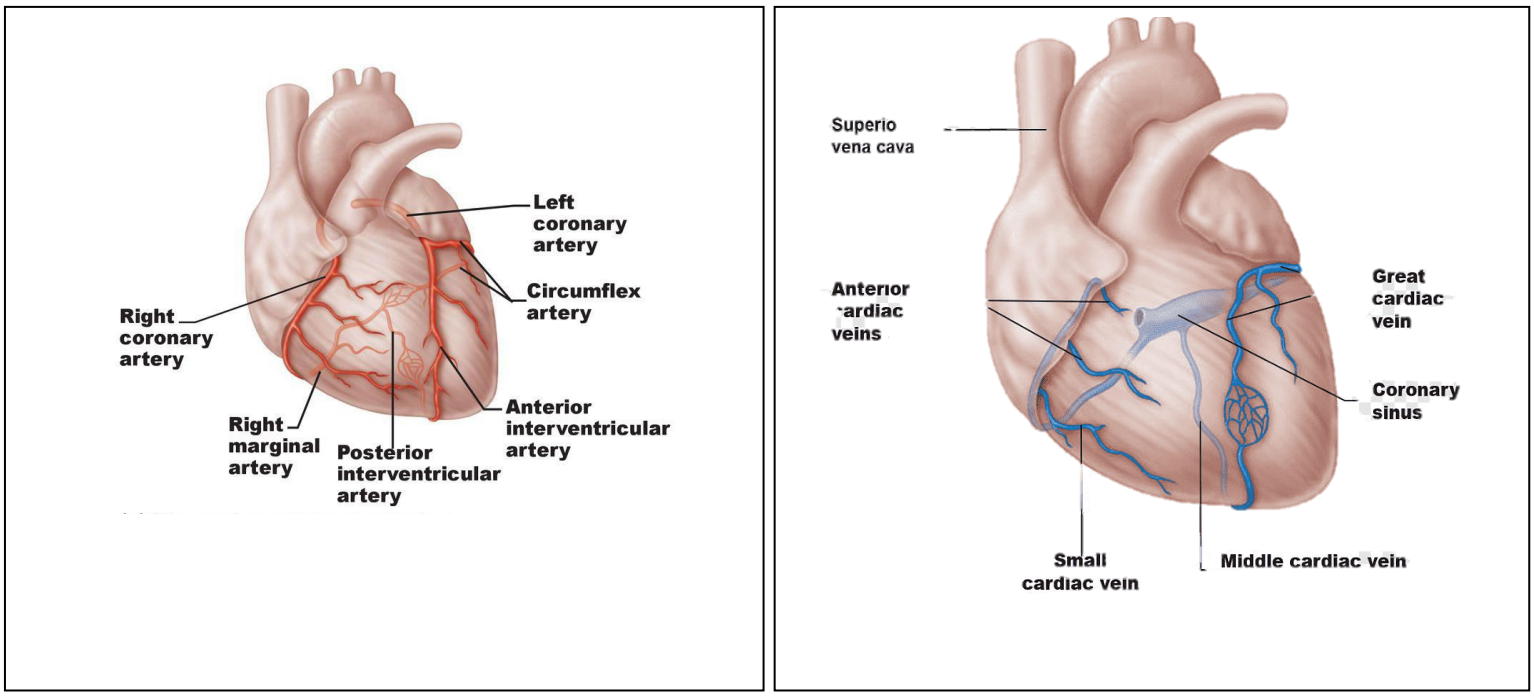


Figure12: coronary vascular **(web site3)**

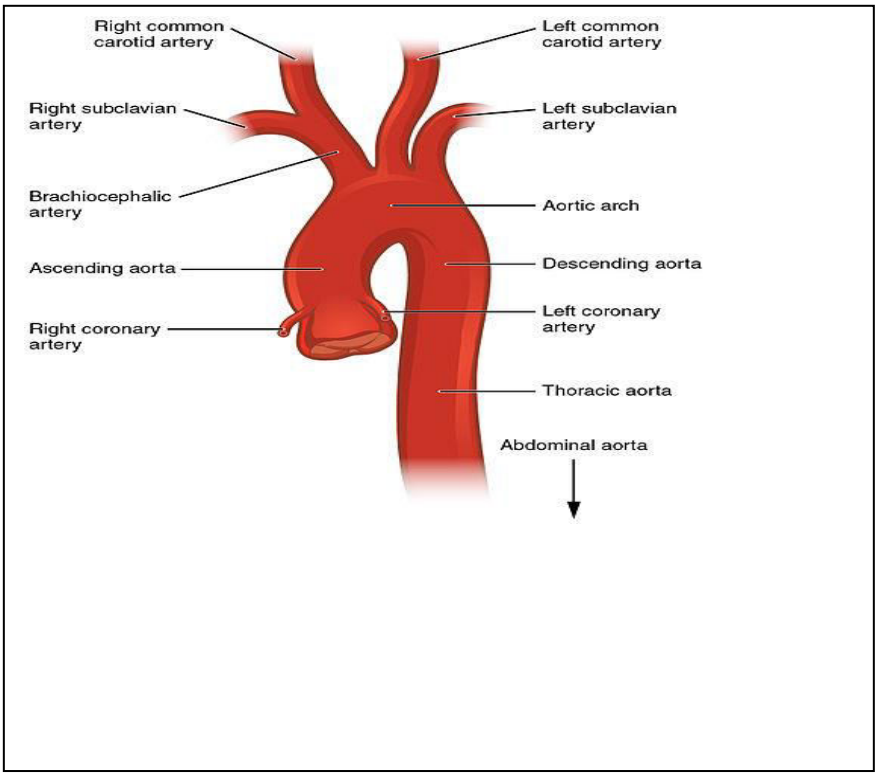


Figure13: Anatomy of aorta artery **(web site4).**

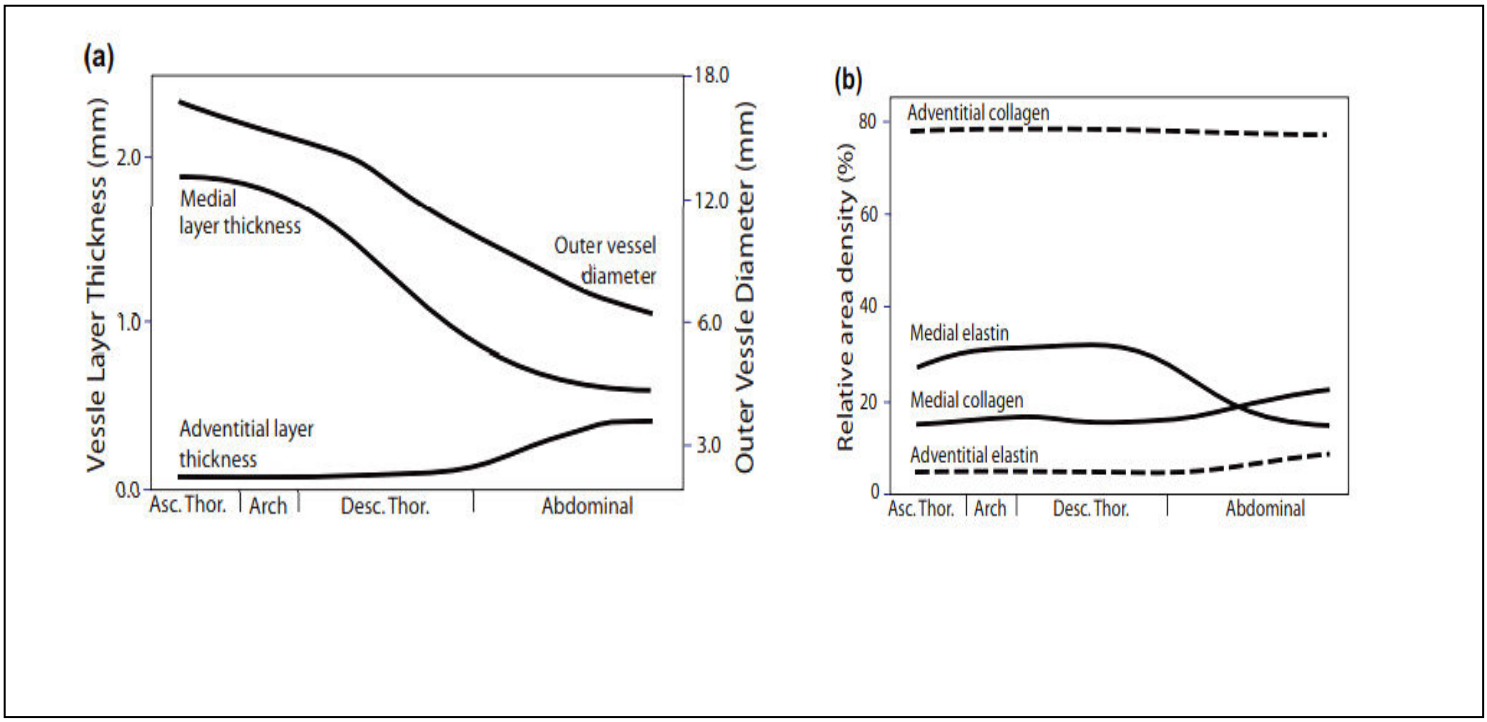


Figure14: Variation of geometrical properties and histological composition of the porcine aorta **(Sokolis, 2007).**

(a) Change of outer aortic diameter and thickness of medial and adventitial layers. Intimal layer thickness covers less than 1% of the total wall thickness.

(b) Relative area density of elastin and collagen in medial and adventitial layers. The relative area density represents the area covered by a constituent in histological stains. Asc.Thor. - Ascending thoracic aorta; Arch. - Aortic arch; Desc.Thor. - Descending thoracic aorta; Abdominal .

A. Tunica intima

- Tunica intima delimits the vessel wall towards the lumen of the vessel and comprises its endothelial lining called endothelium which is composed of squamous epithelium cells organised longitudinally, joined by tight and gap junctions **(Hengel, 2008).**

B. Tunica media

- Layer of smooth muscle and variable amounts of connective tissue.
- A second layer of elastic fibers, the external elastic lamina, is located beneath the smooth muscle.
- **Components**
  - Elastin - fenestrated sheets or lamellae between muscle layers.
  - Smooth muscle cells arranged in layers.
  - Collagen fibre and ground substance **(Hengel, 2008)**.

C. Tunica adventitia

The tunica adventitia is a connective tissue rich in fibers; thin collagen fibers, elastic fibers, fibroblasts, macrophages and with network of small blood vessels called vasa vasorum **(Hengel, 2008) (Figure 15).**

V. Atherosclerosis

V.1. Definition of atherosclerosis

Atherosclerosis has been derived from a greek word, athero meaning gruel **(Virmani et al., 2006)**, Felix Marchand in 1904 introduced the term "atherosclerosis" describing the assosciation of fatty degeneration and vessel stiffening. The earliest lesion is the fatty streak, which evolve to fibrous plaque and unstable plaque are responsible for clinical events **(Aschoff, 1933).**

Atherosclerosis (also known as arteriosclerotic vascular disease or ASVD) is the condition in which an artery wall thickens as the result of a build-up of fatty materials such as cholesterol **(George and Johnson, 2010)**.

It is a syndrome affecting arterial blood vessels, a chronic inflammatory response in the walls of arteries, in large part due to the accumulation of macrophage white blood cells and promoted by low density (especially small particle) lipoproteins (plasma proteins that carry cholesterol and triglycerides) without adequate removal of fats and cholesterol from the macrophages by functional high density lipoproteins (HDL) **(Maton et al., 1993).**

V. 2. Atherosclorosis development

There are six types lesion of atherosclerosis as cited below:

1. The initial or type 1 lesion: consisting of lipids deposits in the intima.
2. Fatty streak or type II lesion: are visible as yellow colored streak, patches, or spots on the intimal surface of arteries. Microscopically these lesions are characterized by intracellular accumulation of lipids (foam cell).
3. The fatty streak progress to type III or intermediate lesion: this growth characterized by extracellular pools of lipids.
4. Type IV lesion or atheroma: the pools coalesce to create a core of extracellular lipids.
5. Type V lesion or fibro atheroma: the blood vessel architecture is destroyed, smooth cells proliferation and collagen deposition.
6. Type VI lesion hemorrage or thrombus: thus resulting in vessel occlusion (**Leon, 2004).**

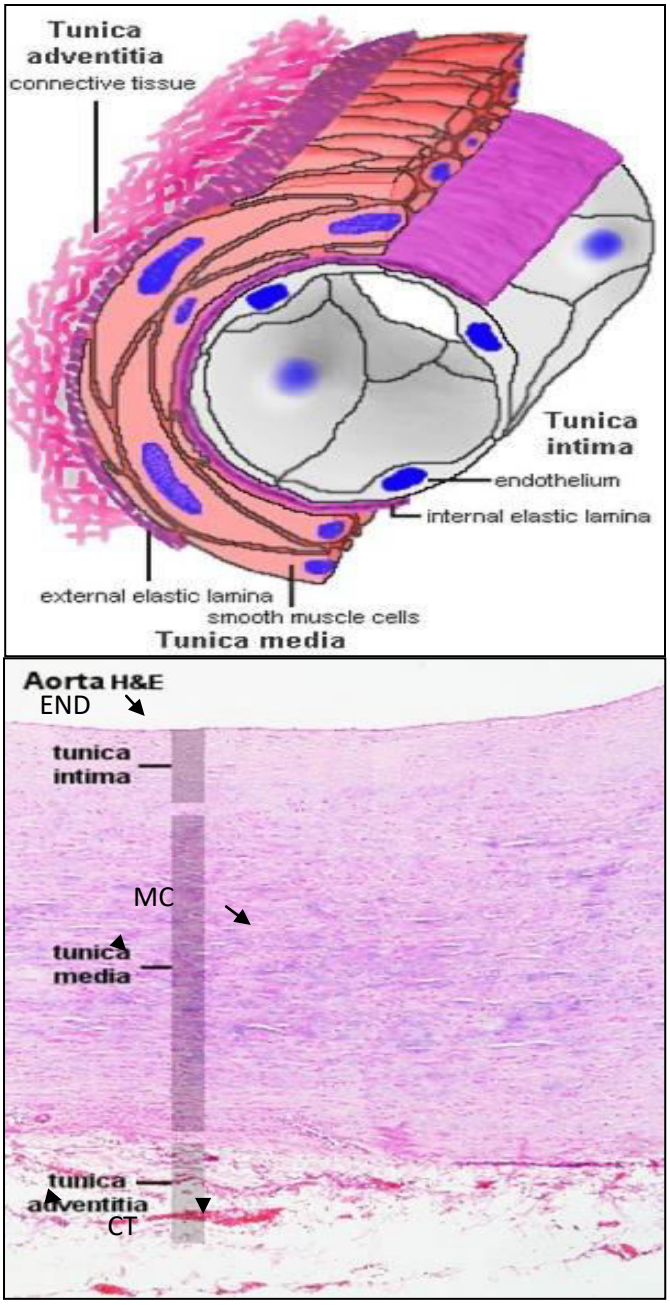


Figure 15: Histology of aorta **(Hengel, 2008).**

END: Endothelium , MC: Muscular cells, CT: Connective tissue

V.3. Atherosclerosic plaque

The atherosclerotic plaque is cholesterol and fatty acid **(Gerald and Daphne, 2012).** In addition to lipids, atheromata also contain leukocytes **(Oliver and Filipe, 2013).**

The formation of plaques constituted by a cholesterol rich core (atheroma) **(Caroline et al., 2017).** The theroma , which is the nodular accumulation of a soft flaky, yellowish material at the center of large plaques, composed of macrophages nearest the lumen of the artery surrounded by a fibrous cap (sclerosis) **(Jagdish, 2009)**. The histological classification describes the progression of lesions: types I and II are early lesions (intimal thickening and fatty streaks), where as types II to VI lesions correspond to advanced lesions (fibro-lipidic, calcified and complicated plaques) **(Caroline et al., 2017).**

V. 4. Atherosclerosis in cardiovascular disease

As the underlying cause of heart attack, stroke, and peripheral vascular disease, atherosclerosis is the major cause of death and morbidity in the United States and the industrial world (**Mozaffarian et al., 2015**). atherosclerosis is an inflammatory disease has led to tremendous progress in our understanding of the pathogenesis of atherosclerosis **(Ross, 1999).**

V. 5. Inflammation in atherosclerosis

Over years an understanding of the importance of inflammation during all stages of atherosclerosis, from its inception through its progression and its final complication of thrombosis, has greatly increased **(Libby, 2002)**.

Under normal conditions, the endothelial cells of the arterial wall resist adhesion and aggregation of leukocytes and promote fibrinolysis. When activated by stimuli such as hypertension, smoking, an unhealthy diet, obesity, insulin resistance or inflammation, the endothelial cells express a series of adhesion molecules that selectively recruit various classes of leukocytes, blood monocytes, the most numerous of the inflammatory cells that populate plaques, adhere to the dysfunctional endothelial surface by binding to leukocyte adhesion molecules not expressed by normal endothelial cells, but induced by mediators associated with risk factors such as pro-inflammatory cytokines, angiotensin II, and oxidized lipoproteins **(Figure 16).** Once the monocytes adhere to the activated endothelium, pro-inflammatory proteins known as chemokines

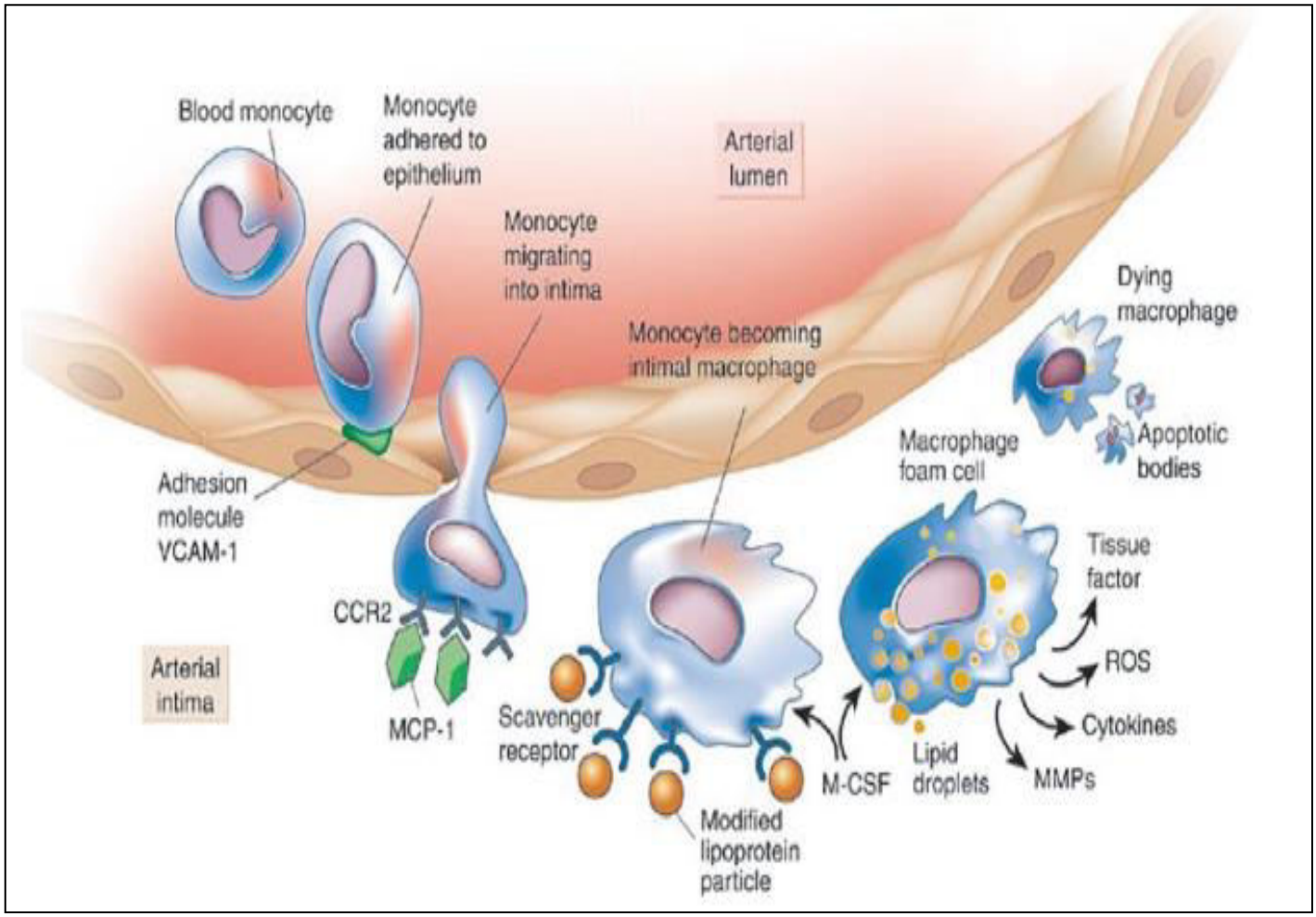


Figure 16: Mononuclear phagocytes in atherogenesis **(Libby et al., 2002).**

provide a chemotactic stimulus that induces them to enter the intima. Within the intima, the monocytes mature into macrophages, which express scavenger receptors that allow them to engulf modified lipoprotein particles. The cytoplasm becomes engorged with lipid particles, giving the macrophages the typical microscopic frothy appearance of the foam cells found in atherosclerotic lesions. The macrophages proliferate within the intima, sustaining and amplifying the inflammatory process by releasing several growth factors, cytokines, and enzymes that can destroy the arterial extracellular matrix, such as metalloproteinases (MMPs) and the procoagulant tissue factor (TF) **(Libby, 2002) (Rader and Daugherty, 2008).**

Examples of specific mediators involved in initiation of atherosclerotic plaques include vascular cell adhesion molecule-1 (VCAM-1) **(Cybulsky and Gimbrone, 1991) (Li et al., 1993).**

The chemoattractant cytokine, monocyte chemoattractant protein-1 (MCP-1) interacts with the monocyte chemokine receptor CCR2, recruiting the monocytes to the arterial endothelium and facilitating their entry between endothelial cells by diapedesis **(Gu et al., 1998).**

One key mediator of monocyte maturation into macrophages within the intima, macrophage colony-stimulating factor, increases in experimental and human atherosclerotic lesions and can induce scavenger receptor expression **(Clinton et al., 1992).**

VI. Association between sugar consumption on cardiovascular diseases and hypertension

VI .1. Sugar and cardiovascular diseases

Convincing evidences show that altered plasma glucose levels are associated with cardiovascular (CV) morbidity and mortality in the general population and in diabetic individuals **(Booth et al., 2006).** The overall risk of CV disease for people with diabetes is two to three fold higher in men, and three to five fold higher in women as compared to non-diabetic **(Juutilainen et al., 2008).**

Hyperglycemia increases the CV risk, this can already be apparent at the time of the diagnosis of diabetes. Based on epidemiologic data, CV risk is already increased 15 years prior to the development of overt hyperglycemia **(Fukuo et al, 1988)**, so that a continuous relationship between blood glucose and CV risk has been suggested **(Coutinho et al., 1999).**

To further increase the risk, altered glucose levels are often associated with other CV risk factors as indicated by the high prevalence of the metabolic syndrome among individuals with pre and manifest diabetes **(Isomaa et al 2001).**

Chronic ingestion of high dose sugar has been linked to obesity, metabolic syndrome, type 2 diabetes, cardiovascular disease, some cancers, Alzheimer's disease, and cellular aging. There

has been much discussion regarding the relative contribution of various dietary factors to the development of coronary heart disease (CHD). Since the 1960s, much of the focus has been on dietary and metabolic fats **(White, 2018).**

Yudkin and colleagues in the 1960s and 1970s found that a higher intake of sugar was associated with increased cardiovascular diseases (CVD) **(Howard and Wylie-Rosett, 2002),** the other study was defined by Ancel Keys' hypothesis that dietary fat was the primary causative agent. Medicine embraced fat as the primary causative agent and discounted or essentially ignored the possibility that refined sugar might be a salient contributor to this problem **(White, 2018).**

Historical documents from the Sugar Research Foundation, a pro-sugar trade organization, found that industry sponsored research in the 1960s and '70s was successful in casting doubt on the possibility that refined sugar was partially responsible for the observed increase in coronary heart disease (CHD), while promoting dietary fat as the offender **(Kearns et al., 2016).** Recently, in the Nurses Health Study, a positive association between sugar sweetened beverage (SSB) intake and risk of coronary heart disease (CHD) **(Fung et al., 2009).**

Sugar sweetened beverage (SSB) may lead to weight gain as a result of incomplete compensation for liquid calories at subsequent meals, resulting in positive energy balance. Independently of weight gain, SSBs may increase the risk of metabolic syndrome (MetSyn), type 2 diabetes (T2DM), and cardiovascular disease because of their large contribution to a high dietary glycemic load (GL) and large fructose fraction, leading to the development of insulin resistance, beta cell dysfunction, inflammation, hypertension, visceral adiposity, and atherogenic dyslipidemia **(Malik and Hu., 2015) (Figure17).**

Gerald and Daphne, 2012 reported that**,** atherosclerosis is associated with diet and tobacco. In "Westernized" societies the disease begins in childhood and progresses inexorably unless lifestyle is changed (**Hsu et al., 1995**).

Also **Ridker et al., 2009** reported that, a number of factors such as diet, tobacco, and inactivity could inactivate the nitric oxide and cause endothelial dysfunction.

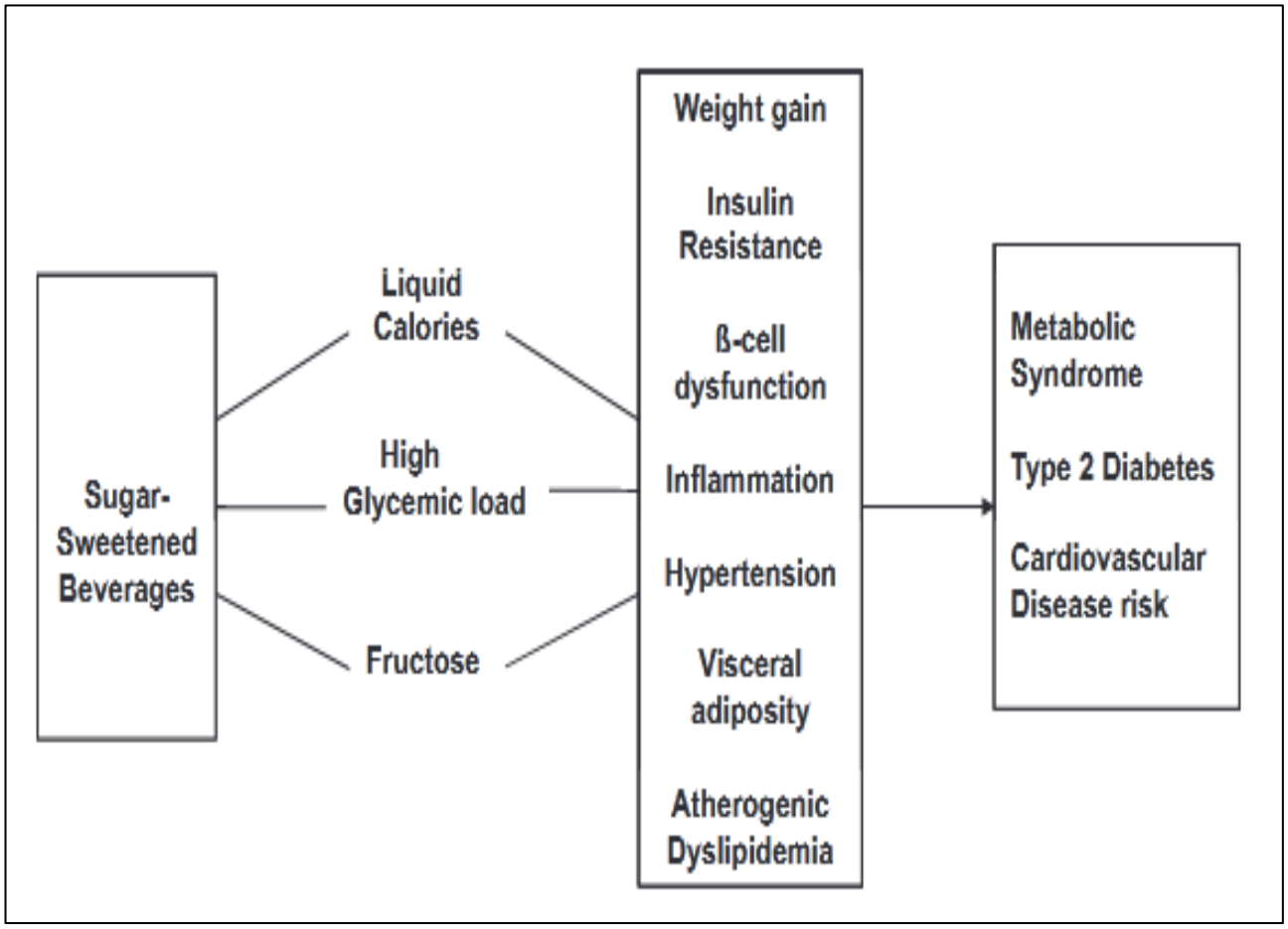


Figure17: Sugar sweetened beverage (SSB) consumption and Cardiovascular Risk **(Malik and Hu., 2015)**

VI .2. Sugar and hypertension

Hypertension is generally defined as a blood pressure greater than 140/90mmHg. Blood pressure should be brought closer to what's considered optimal: 120/80. An elevated blood pressure raises the risk for heart attack and stroke **(Seriki, 2017).**

VI .2.1 Types of hypertension

There are two primary hypertension types. For 95% percent of people with high blood pressure, the cause of their hypertension is unknown; this is called essential or primary hypertension. When a cause can be found, the condition is called secondary hypertension **(Stanley et al., 2009).**

A-Essential hypertension

Essential of hypertension is diagnosed after blood pressure remains high after about three or more measurements and all other causes of hypertension are eliminated. Usually people with essential hypertension have no symptoms, but may experience frequent headaches, tiredness, dizziness, or nosebleeds. Researchers have observed that obesity, smoking, alcohol, diet and heredity all play a role in essential hypertension **(Seriki, 2017).**

Animal studies in which rats were fed high doses of fructose and acute ingestion studies in which humans were fed high doses of different sugars, and more recently, epidemiological studies, such as the Framingham Heart Study, in which consumption of ≥1 soft drink per day significantly increased the odds of developing high blood pressure **(Nguyen et al., 2016).**

Nonetheless, results from studies in humans are inconsistent, **(Vander et al., 1999)** and the chronic effects of a high intake of simple sugars on blood pressure remain uncertain **(Hallfrischet et al., 1983).**

The fact is that an underlying cause of high blood pressure is often related to production of too much insulin and leptin in response to a high-carbohydrate and processed food diet. As insulin and leptin levels rise, it causes blood pressure to increase. Eventually, there may become insulin and/or leptin resistant **(Seriki, 2017).**

The physiology behind it is that insulin stores magnesium, but if its receptors are blunted and the cells grow resistant to insulin, the body can't store magnesium, so it passes out of the body through urination.

Magnesium stored in the cells relaxes muscles. If magnesium level is too low, the smooth muscle of the blood vessels will be unable to fully relax, and this constriction raises blood pressure **(Marianne et al., 2010).**

Fructose also elevates uric acid, which drives up blood pressure by inhibiting the nitric oxide in the blood vessels; in fact, fructose typically generates uric acid within minutes of ingestion **(Pôrto et al., 2011).**

Nitric oxide helps blood vessels maintain their elasticity, so nitric oxide suppression leads to increases in blood pressure. So any program adapted to address high blood pressure needs to help normalize both insulin/leptin sensitivity and uric acid level. Eliminating excess sugar/fructose from diet has incidentally been found to address all these three issues (insulin, leptin, and uric acid) in one fell swoop **(Seriki, 2017).**

B-Secondary hypertension

Secondary hypertension is an abnormality in the arteries supplying blood to the kidneys. Other causes include airway obstruction during sleep, diseases and tumors of the adrenal glands, hormone abnormalities, thyroid disease, and too much salt or alcohol in the diet. Drugs can cause secondary hypertension, including over-the-counter medications such as ibuprofen (Motrin, Advil, and others) and pseudoephedrine (Afrin, Sudafed, and others). If the cause is found, hypertension can often be controlled **(Siyad, 2011).**

Conclusion and future work

In this thesis we have researched the association of sugar consumption on cardiovascular diseases.

Some researchers demonstrated that high consumption of sugar has been implicated in the development of hypertension, hyperlipidemia and obesity, all of which are involved in the pathogenesis of cardiovascular disease (CVD). This thesis provides an important mechanistic understanding of how does sugar affect heart disease.

As with most other dietary constituents, long-term trial data relating sugar consumption to the development of CVD events are unavailable.

Shorter-term studies show consistent adverse effects of sugar consumption on HDL and triglyceride levels, which could accelerate atherosclerosis.

Based on the present thesis, this subject can evaluate many topics in the future:

1- Treatment of animals (mice, rats or rabbits) with diet rich in sugar (glucose or fructose) during 21 days.
2- Treatment of animals with fructose during 21 days.
3- Evaluation of lipids status, and hs-CRP.
4- Evaluation of antioxidant enzymes and proteins.
5- Histological study on some organs (Liver, aorta, liver and pancreas).

References

References

- **Aeberli I., Gerber P.A., Hochuli M., Kohler S., Haile S.R., Gouni-Berthold I., Berthold H.K., Spinas G.A., Berneis K**. (2011). Low to moderate sugar-sweetened beverage consumption impairs glucose and lipid metabolism and promotes inflammation in healthy young men: arandomized controlled trial. *Am J Clin Nutr,* 94 (2): 479-485.
- **Altameemi A., Mohammed Z**. (2019). Inflammation. https:// www. researchgate.net/ publication /331651547_inflammation
- **Ardell J. L., Randall W. C**. (1986). Selective vagal innervation of sinoatrial and atrioventricular nodes in canine heart. *Am. J. Physiol*, 251 : 764–773.
- **Aschoff L.** (1933). Introduction. in: arteriosclerosis: a survey of the problem. new york. cowdry ev (ed): 1-18.
- **Ashworth J., Sproston N. R**. (2018). Role of C-reactive protein at sites of inflammation and infection. *Front immunol*, (10): 7-8.
- **Asif H.M., Muhammad Akram., Tariq Saeed., Ibrahim Khan M., Naveed Akhtar., Riaz ur Rehman., Ali Shah S.M., Khalil Ahmed., Ghazala Shaheen.** (2011). Carbohydrates. *International research journal of biochemistry and bioinformatics*, 1(1): 1-5.
- **Baltz M., Pepys M.** (1983). Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein. *AdvImmuno*, 34: 141-212.
- **Baumeister D., Akhtar R., Ciufolini S., Pariante C.M., and Mondelli V.** (2016). Childhood trauma and adulthood inflammation: a meta-analysis of peripheral C-reactive protein, inetleukin-6 and tumour necrosis factor-α. *Mol Psychiatry*, 21: 642– 1038.
- **Berg J.M., Tymoczko J.L., Stryer L.** (2002). Biochemistry. 5th edition. new york: 303.
- **Bernet., Robert M., and Matthew N.** (1997). Cardiovascular physiology. 7th ed. levy mosby-year book. U.S.A: 310-311.
- **Betts J. G.** (2013). Anatomy & physiology. 1st ed. eddie johnson. floride : 787–846.
- **Bezerra C.F., Amaral B.A., Camelo F.P., Ana R.L., and Eduardo G.S.** (2008). O papel da proteína C-reativa na relação entre as doenças periodontais e cardiovasculares. *R Periodontia*, 18: 7-13.
- **Black S., Kushner I., and Samolos D.** (2004). C-reactive protein. *Biological Chemistry*: 48487- 48488.

References

- **Booth G.L., Kapral M.K., Fung K., and Tu J.V**. (2006). Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. *Lancet,* 368: 29–36.
- **Caroline C., Mélanie P., Anne N. S., and Robert S.** (2017). Angiogenesis in the atherosclerotic plaque. *Redox Biology*, 12: 18–34.
- **Charitos E.I., and Sievers HH**. (2013). Anatomy of the aortic root: Implications for valve-sparing surgery. *Ann Cardiothorac Surg journal*, 2 (1): 425- 433.
- **Chinchoy E.** (2005). Handbook of cardiac anatomy, physiology and devices. totowa. *NJ: Humana Press Inc*: 101–110.
- **Chiou C. W., Eble J. N., and Zipes D. P**. (1997). Efferent vagal innervation of the canine atria and sinus and atrioventricular nodes. The third fat pad. *Circulation*, 95 : 2573–2584.
- **Christian N.** (2015). Inflammation: causes, symptoms and treatment. *Medical news today* : 1-13.
- **Christoffels V.M., Habets P.E., Franco D., Campione M., de Jong F., Lamers W.H., Bao Z., Palmer S., Biben C., Harvey R.P., Moorman A.F.** (2000). Chamber formation and morphogenesis in the developing mammalian heart. *Dev Biol,* 225 (1): 266.
- **Chung M., Ma J., Patel K., Berger S., Lau J., and Lichtenstein A.H**. (2014). Fructose, high-fructose corn syrup, sucrose, and non alcoholic fattyliver disease or indexes of liver health: A systematic review and meta-analysis. *Am J Clin Nutr*, 100 : 833–849.
- **Clinton S., Underwood R., Sherman M., Kufe D., and Libby P**. (1992). Macrophage-colony stimulating factor gene expression in vascular cells and in experimental and human atherosclerosis. *Am J Pathol*, 140: 301–316.
- **Coutinho M., Gerstein H.C., Wang Y., and Yusuf S.** (1999). The relationship between glucose and incident cardiovascular events. a metaregression analysis of published data from 20 studies of 95-783 individuals followed for 12.4 years. *Diabetes Car,*22: 233–40.
- **Cybulsky M.I., Gimbrone M.A.** (1991). Endothelial expression of a mononuclear leukocyte adhesion molecule during atherogenesis. *Science*, 251: 788–791.
- **D'Avila A.** (2003). Pericardial anatomy for the interventional. Electrophysiologists. *Cardiovasc. Electrophysiol Journal*, 14 :422–430.

- **De Koning L., Malik V.S., Kellogg M.D., Rimm E.B., Willett W.C., and Hu F.B.** (2012). Sweetened beverage consumption, incident coronary heart disease, and biomarkers of risk in men. *Circulation*, 125:1735–1741.
- **EL-houry M.E., EL-segaien M., Monemah T., and Galal M.O.** (2014). Combined semilunar valve stenosis in neonated: management approaches and literature. *Pediar Cardiol*, 35: 1469-1473.
- **Fantone J.C., Ward P.A.** (1999). Inflammation. 3rd ed. Philadelphia, PA. Lippincott-Raven Publishers: 36-75.
- **Frederic H., Martini M. J., and Robert B. (2003).** Human Anatomy. 4 th ed. U.S.A: 553.
- **Fukuo Y., Nakatani T., Shinohara H., and Matsuda T**. (1988). The mouse pericardium: it allows passage of particulate matter from the pleural to the pericardial cavity. *Anat. Rec*, 222 : 1–5.
- **Fung T.T., Malik V., Rexrode K.M., Manson J.E., Willett W.C., and Hu F.B.** (2009). Sweetened beverage consumption and risk of coronary heart disease in women. *Am J Clin Nutr*, 89:1037–1042.
- **George S.J and Johnson J**. (2010). Atherosclerosis: molecular and cellular mechanism.1st ed. U.S.A: 43-62.
- **-Gerald H T., Daphne O.** (2012). LDL as a cause of atherosclerosis. *The Open Atherosclerosis and Thrombosis Journal,* 5:13-21.
- **Gould J.M ., Weiser J.N.** (2001). Expression of C-reactive protein in the human respiratory tract. *Infect Immun*, 69 (3): 1747-1754.
- **Greenspan M., Iskandrin A. S., Catherwood E., Kimbiris D., Bemis C.E., and Segal B.L.** (1980). Myocardial bridging of the left anterior descending artery valuation using exercise thallium-201 myocardial scintigraphy. *Catheter Cardiovasc Diagn Journal*, 6: 173-180.
- **Gu L., Okada Y., Clinton S., Gerard C., Sukhova G., and Libby P**. (1998). Absence of monocyte chemoattractant protein-1 reduces atherosclerosis in low-density lipoprotein-deficient mice. *Mol Cell*, 2: 275–281.
- **Hallfrisch J., Reiser S., and Prather E.S**. (1983). Blood lipid distribution of hyperinsulinemic men consumingthreelevels of fructose. *Am J Clin Nutr*, 37 (5): 740-748.
- **Haverkate F., Thompson S.G., Pyke S .D., Gallimore J.R., and Pepys M.B.** (1997). Production of C-reactive protein and risk of coronary events in stable and unstable angina.

European concerted action on thrombosis and disabilities angina pectoris study group. *Lancet,* 349: 462-466.

- **Hengel Karel van** . (2008). Abdominal aortic wall thickness and compliance master medical engineering university. University of technology eindhoven company university medical centre maastricht, 33: 6.
- **Herrington S**. (2014). Muir's textbook of pathology.15th ed. CRC Press : 59.
- **Hirschfield G.M., Pepys M.** (2003). C-reactive protein: a critical update. *J Clin Invest*, 111(12): 1805- 1810.
- **Ho S., Sanchez-Quintana D., and Becker A**. (2004). A review of the coronary venous system. *Clinical Anatomy Journal*, (1): 107-112.
- **Houston M., Minich D.M.** (2015). Fructose-containing sugars do not raise blood pressure or uricacid at normal levels of human consumption. *J Clin Hypertens*, 17: 5–7.
- **Howard Barbara V., Wylie-Rosett Judith.** (2002). Sugar and cardiovascular disease. *AHA scientific statement*, 106: 523-527.
- **Hsu H.Y., Nicholson A.C., Pomerantz K.B., Kaner R.J., and Hajjar D.P**. (1995). Altered cholesterol trafficking in herpesvirus-infected arterial cells. Evidence for viral protein kinas mediated cholesterol accumulation. *J Biol Chem*, 270 (33): 19630–7.
- **Hutchins G., Moore G., and Hatton E.** (1986). Arterial-venous relationships in the human left ventricular myocardium, Anatomic basis for countercurrent regulation of blood flow. *Circulation Journal*, 74:1195-1202.
- **Ishihara T., Ferrans V. J., Jones M., Boyce S. W., Kawanami O., and Roberts W. C.** (1980). Histologic and ultrastructure features of normal human parietal pericardium. *Am. J. Cardiol*, 46: 744–753.
- **Isomaa B., Almgren P., Tuomi T., Forsén B., Lahti K., Nissén M., Taskinen M. R., Groop L**. (2001). Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*, 24: 683–9.
- **Jagdish K.** (2009). Causes, Symptoms, Pathophysiology and diagnosis of atherosclerosis. *Pharmacology online*, (3): 420-442.
- **Jana O., Ladislava M., Jarmila VA., Kobert V., Jiri M**. (2015). Fatty acids composition of vegetebale oils and it contribution to dietry energy intake and dependence of cardiovascular mortality ondietry intake of fatty acids. *Int Mol Sci*,16: 12871-12890.
- **Jéquier E. (**1994). Carbohydrates as a source of energy. *Am J Clin Nutr*, 59 (3): 682-685.

- **Jialal I., Devaraj S**. (2001). Inflammation and atherosclerosis: the value of the high-sensitivity C-reactive protein assay as a risk marker. *Am J Clin Pathol*, 116: 108-115.
- **Jialal I., Devaraj S., and Venugopal S.K.** (2004). C-reactive protein: risk marker or mediator in atherothrombosis?. *Hypertension*, 44 (1): 6-11.
- **Juutilainen A., Lehto S., Ronnemaa T., Pyörälä K., and Laakso M**. (2008). Similarity of the impact of type 1 and type 2 diabetes on cardiovascular mortality in middle-aged subjects. *Diabetes Care*, 31:714–9.
- **Kalaria V.G., Koradia N., and Breall J.A.** (2002). Myocardial bridge: a clinical review. *Catheter Cardiovasc lnterv Journal*, 57: 552-556.
- **Kamal Mohammad A., Klein Peter.** (2011). Determination of sugars in honey by liquid chromatography. *Saudi Journal of Biological Sciences*, 18 (1):17-21.
- **Kearns C, Schmidt L, Glantz S.** (2016). Sugar industry and coronary heart disease research: a historical analysis of internal industry documents. *JAMA Intern Med*, 176:1680–1685.
- **Khowala Suman ., Deepak Verma .,and Samudra P.** (2008). Banik drug developement and biotechnology. *Indian Institute of Chemical Biology* : 4.
- **Kuller L.H., Tracy R.P., Shaten J., and Meilahn E.N.** (1996). Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study. Multiple risk factor intervention trial. *American Journal of Epidemiology*, 144: 537-547.
- **Kumar V., Abbas A.k., Fausto N., Robbins., and Cotran.** (2009). Bases patológicas das doenças. 8ª edição. rio de janeiro: elsevier : 1592.
- **Kuta A.E., Baum L.L**. (1986). C-reactive protein is produced by a small number of normal human peripheral blood lymphocytes. *J ExpMed*, (164): 321-326.
- **Lachman N., Satyapal K.S., and Vanker E.A.** (2002). Angiographic manifestation and anatomical presence of the intramural LAD: surgical significance. *Clin Anat Journal*, 15: 426.
- **Lawrence T., Gilroy D. W.** (2007). Chronic inflammation: a failure of resolution?. *International journal of experimental pathology*, 88 (2), 85–94.
- **Lawrence W.T.** (1998). Physiology of the acute wound. *Clin Plast Surg*, 25:321.
- **Lei Yu.** (2003). Inflammation and oxidative stress. Free and radicals biology program. The University of lowa. lowa city: 52246-1187.
- **Leon V., Clark N**. (2004). Trends in atherosclerosis research. Nova biomedical books. NewYork: 1- 330.

- **Li H, Cybulsky M.I., Gimbrone M.A Jr., and Libby P**. (1993). Inducible expression of vascular cell adhesion molecule-1 (VCAM-1) by vascular smooth muscle cells *in vitro* and within rabbit atheroma. *Am J Pathol*, 143: 1551–1559.
- **Libby P**. (2002a). Atherosclerosis: The new view. *Sci Am*, 286: 46– 55.
- **Libby P**. (2002b). Inflammation in atherosclerosis. *Nature*, 420: 868 – 874.
- **Libby P., Ridker P .M., and Maseri A**. (2002). Inflammation and atherosclerosis. *Circulation*, 105: 1135–1143.
- **Lima J.C., Correia L.C., and Silva A.M.** (2000). Proteína C reativa de alta sensibilidade como biomarcador de risco na doença coronária. Newslab, 41: 164-166.
- **Loukas M ., Bilinsky S., Bilinsky E., el-Sedfy A., and Anderson R.** (2009) .Cardiac veins. *a review of the literature Clinical Anatomy*, 22 (1):129-145.
- **Maiorana A ., O'Driscoll G., Taylor R., and Green D**. (2003). Exercise and the nitric oxide vasodilator system. *Sports Med*, 33 (14):1013-35.
- **Malik V.S., Hu F.B.** (2015). Fructose and cardiometabolic health: what the evidence from sugar-sweetened beverages tells us. *J Am Coll Cardiol*, 66: 1615–24.
- **Manolescu A. R., Witkowska K., Kinnaird A., Cessford T., and Cheese-man C**. (2007). Physiology. *American physiological society,* 22 :234–240.
- **Marianne U.J., Claus D., Albert M.J., Jakob S., and Anne T**. (2010). Intake of carbohydrates compared with intake of saturated fatty acids and risk of myocardial infarction: importance of the glycemic index. *Am J Clin Nutr*, 91 (6): 1764-1768.
- **Marieb E. N.** (2015). Anatomie et physiologie humaines. 9th ed . Québec: 1194.
- **Masaaki M., Toshio H**. (2012). The molecular mechanisms of chronic inflammation development. *Frontiersin Immunology*, 3(323): 1-2.
- **Maton, A., Roshan L., Jean H.C., William M., Susan J., Maryanna Q. W., David L., and Jill D**. (1993). Human biology and health. englewood cliffs, new jersey, USA: prentice hall: 587-588.
- **Michailova K. N., and Usunoff K. G.** (2006). Serosal membranes (Pleura, Pericardium, Peritoneum): normal structure, development and experimental pathology. *Adv. Anat. Embryol. Cell Biol*, 183: 1–144.
- **Mitchell R .N., Cotran R.S**. (2003). Acute and chronic inflammation. in kumar v, cotran rs, robbins sl ed. robbins basic pathology 7th. philadelphia, pa. saunders press : 33-59.
- **Mondal S.** (2017). Chemistry of carbohydrates. *Pharm V sem_applied biochemistry*: 1-20.

- **Mozaffarian D., Benjamin E.J, Go A.S., Arnett D.K., Blaha M.J., Cushman M., de Ferranti S., Despres J.P., Fullerton H.J., Howard V.J., Huffman M.D., Judd S.E., Kissela B.M., Lackland D.T., Lichtman J.H., Lisabeth L.D., Liu S., Mackey R.H., Matchar D.B., McGuire D.K., Mohler E.R., Moy C.S., Muntner P., Mussolino M.E., Nasir K., Neumar R.W., Nichol G., Palaniappan L., Pandey D.K., Reeves M.J., Rodriguez C.J., Sorlie P.D., Stein J., Towfighi A., Turan T.N., Virani S.S., Willey J.Z., Woo D., Yeh RW., and Turner M.B**. (2015). Heart disease and stroke statistics- update: a report from the American Heart Association. *Circulation*, 131:229–322.
- **Mutsaers S. E.** (2002). Mesothelial cells: their structure, function and role in serosal repair. *Respirology,* 7 : 171–191.
- **Neuman R.** (2013). Organic chemistry : carbohydrates. University of california. Riverside: 20-32.
- **Nguyen K., Kerrihard A.L., Beggio M., Craft B.D., and Pegg R.B**. (2016). Modeling the impact of residual fat-soluble vitamin (FSV) contents on the oxidative stability of commercially refined vegetable oils. *Food Res*, 84 : 26–32.
- **Nichols W., O'Rourke M. F., and Vlachopoulos C.** (2011). McDonald's blood flow in arteries, 6 th ed. Theoretical, experimental and clinical principles. Arnold. London: 195-225.
- **Noah T. A., Zachary M. W., and Randy J. N**. (2012). Inflammation: mechanisms, costs, and natural variation. *Rev eco levol Syst*, 43: 385–406.
- **Oliver S., Filipe K. S.** (2013). Trends hypercholesterolemia links hematopoiesis with atherosclerosis in endocrinology and metabolism. *Physiological reviews*, 24 (3): 129-136.
- **Pacholyk A.** (2006). Sugar and inflammation. https://balancewomenshealth.com/wp-content/uploads/2020/03/Sugar-and-Inflammation.pdf.
- **Padala M., Sacks M.S., Liou S.W., Balachandran K., He Z.M., and Yoganathan A.P.** (2010). Mechanics of the mitral valve strut chordae insertion region. *Biomech Journal*, 132: 081004.
- **Paul M., Ridker M.D.** (2003). C-reactive protein a simple test to help predict risk of heart attack and strok. *Circulation*, 108: 81-85.
- **Pôrto-Laura C;J., Savergnini-Sílvia S.Q., de Castro C.H., Mario É.G., and Ferreira Adaliene V.M**. (2011). Carbohydrate-enriched diet impairs cardiac performance by decreasing the utilization of fatty acid and glucose. *Ther Adv Cardiovasc Dis*, *5 (1): 11-22.*

References

- **Pradhan A.D., Manson J.E., Rifai N., Buring J.E., and Ridker P.M**. (2001). C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *J Am Med Assoc*, 286(3): 327.
- **Rachev S., Greenwald E., and Shazly T**. (2013). Are geometrical and structural variations along the length of the aorta governed by a principle of optimal mechanical operation? *J. Biomech*, 135: 081006.
- **Rader D.J., Daugherty A.** (2008). Translating molecular discoveries into new therapies for atherosclerosis. *Nature*, 451: 904–913.
- **Randall W.C., and Ardell J. L.** (1985). Selective parasympathectomy of automatic and conductile tissues of the canine heart. *Am. J. Physiol*, 248 : 61–68.
- **Raven, P. H., Johnson, G. B., Mason, K. A., Losos, J. B., and SingeS. R.** (2014). Sugar isomers have structural differences. in biology .10th ed., AP ed., New York, NY: McGraw-Hill: 38.
- **Ridker P.M**. (2003). Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation*, 107: 363–9.
- **Ridker P.M., Danielson E., Fonseca F.A., Genest J., and Gotto A.M.** (2009). Reduction in C-reactive protein and LDL cholesterol and cardiovascular event rates after initiation of rosuvastatin: a prospective study of the JUPITER trial. *Lancet*, 373: 1175-1182.
- **Ridker P.M., Hennekens C.H, Buring J.E., and Rifai N**. (2000). C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *Engl J Med*, 342: 836-843.
- **Robbins S., Cotran R., Kumar V., Abbas A., and Aster J.** (2020). Pathologic basis of disease. 10th ed . saunders elsevier. philadelphia: 69-99.
- **Ross R**. (1999). Atherosclerosis an inflammatory disease. *New England Journal of medicine*, 340: 115–126.
- **Ruslan M.** (2008). Origin and physiological roles of inflammation. *Nature*, 454 (10): 1038.
- **Scallan J, Huxley VH, Korthuis RJ**. (2010). Capillary fluid exchange: regulation, functions, and pathology. San Rafael (CA): Morgan & Claypool Life Sciences: Chapter 4, Pathophysiology of Edema Formation.
- **Seriki A Samue**. (2017). Salt, Glucose, and hypertension: interactions, benefits and risk. *J Cardiol & Cardiovasc Ther,* 4(2): 1-7.

- **Severine V., Gert V. A., and Paul R**. (2004). C-reactive protein as a marker for inflammatory bowel disease. *Inflamm Bowel Dis*, (10): 661–665.
- **Shrive A. K., Cheetham G. M., Holden D., Myles D. A., Turnell W. G., Volanakis J. E., Pepys M. B., Bloomer A. C., and Greenhough T. J.** (1996). Nat. struct. *Biol*. (3): 346–354.
- **Silva D., Lacerda A.P.** (2012). Proteína C reativa de alta sensibilidade comobiomarcador de risco na doença coronária. *Revista Portuguesa de Cardiologia*, 31: 733-745.
- **Siyad A.R**. (2011). Hypertension. *J.D.Med* .3 (1):1-16.
- **Softic S., Cohen D.E., and Kahn C.R.** (2016). Role of dietary fructose and hepatic de novo lipogenesis in fatty liver disease. *Sci*, 61 :1282–1293.
- **Sokolis P.** (2007). Passive mechanical properties and structure of the aorta: segmental analysis. *Acta Physiol*, 190:277–289.
- **Spencer J., Anderson S., and Iaizzo P.** (2013). Human coronary venous anatomy for interventions. *card trans res*, 6(2):208-217.
- **Srikantiah C**. (2014). C - reactive protein: an inflammatory marker with specific role in physiolog. *Journal of Rheumatology and Clinical Immunology*, 2 : 1.
- **Stanley W.C., Shah K.B., and Essop M.F**. (2009). Does junk food lead to heart failure? Importance of dietary macronutrient composition in hypertension. *Hypertension*, 54 (6): 1209-1210.
- **Takada K., Otsuki Y., and Magari S**. (1991). Lymphatics and pre-lymphatics of the rabbit pericardium and epicardium with special emphasis on particulate absorption and milky spot-like structures. *Lymphology*, 24: 116–124.
- **Thompson D., Pepys M. B., and Wood S. P.** (1999). The physiological structure of human C-reactive protein and its complex with phosphocholine. *Structure*, 7:169–177.
- **Thornley S., Tayler R., and Sikaris K**. (2012). Sugar restriction: the evidence for a drug-free intervention to reduce cardiovascular disease risk. *Intern Med J*, 42: 46-58.
- **Tortora G. J., and Grabowski S. R**. (2003). The cardiovascular system: the heart, in principles of anatomy and physiology. Division of Medical Engineering. School of Technology and Health. Royal Institute of Technology : 659-695.
- **Van der Schaaf M.R., Koomans H.A., and Joles J.A.** (1999). Dietary sucrose does not increase twenty-four-hour ambulatory blood pressure in patients with either essential hypertension or polycystic kidney disease. *J Hypertens* , 17(3): 453-454.

References

- **Venugopal S.K., Devaraj S., and Jialal I.** (2005). Macrophage conditioned medium induces the expression of C-reactive protein in human aortic endothelial cells. Potential for paracrine/autocrine effects. *Am J Pathol*, 166 (4):1265-1271.
- **Vijay K.** (2018). Toll-like receptors in immunity and inflammatory diseases: Past, present, and future. *International immunopharmacology*, 59 : 391–412.
- **Virmani R., Burke AP., Farb A., and Kolodgie F.D.** (2006). Pathology of the vulnerable plaque. *J Am CollCardiol*, 47: 13-18.
- **Wakim S., Grewal, M.** (2021). Carbohydrates. https://bio .libretexts. org /Bookshelves /Human_Biology/Book%3A_Human_Biology_(Wakim_and_Grewal)/03%3A_Chemistry_of_Life/3.05%3A_Carbohydrates.
- **White John R.** (2018). Sugar. *Clin Diabetes*, 36 (1): 74–76.
- **Zhang, Y.; Wang, F**. (2015). Carbohydrate drugs: current status and development prospect. *Drug Discov*, 9 : 79–87.

References

Reference web:

1- Monosaccharides are classified based on the position of the carbonyl group and the number of carbons in the backbone : https://courses.lumenlearning.com/bio1/chapter/reading-types-of-carbohydrates/

2- Acute inflammation : https://teachmesurgery.com/skills/wounds/acute-inflammation/

3- Coronary vascular: https://www.pngwing.com/en/free-png-tifwp

4- Anatomy of aorta artery: https: //www. Lecturio .com/ magazine /subclavian-arteries/

Summary :

Cardiovascular disease (CVD) is the single largest cause of mortality in world. Numerous risk factors have been identified for CVD, including a number of nutritional factors. Recently, attention has been focused on fructose-containing sugars and their putative link to risk factors for CVD.

In this thesis, we focus on studies related to sugar consumption and cardiovascular risk factors.

Most studies have shown that sugar consumption leads to a lack of insulin secretion or a lack of use of it. Since the cells cannot enter glucose, it accumulates in the blood and damages heart arteries

It was also found that eating sugar leads to raising the level of cholesterol in the blood and increases the accumulation of fat in the vessels and arteries of the heart, which leads to atherosclerosis and causes insufficient blood supply to the heart, which causes the heart to be unable to carry out its normal functions.

Key word: Sugar, carbohydrates, cardiovascular disease, inflammation, atherosclerosis.

Résumé

Les maladies cardiovasculaires sont l'une des principales causes de mortalité dans le monde. Il a été déterminé que ces maladies sont causées par de nombreux facteurs de risque dont certains sont d'origine nutritionnelle.

Ces derniers temps l'attention s'est portée sur les sucres comme le fructose et leurs effets sur les maladies cardiovasculaires (les maladies vasculaires périphériques, les maladies coronariennes, les maladies cardiovasculaires athérosclérotiques, et les maladies vasculaires ischémiques).

Dans cette thèse, les recherches sont axées sur les études liées à la consommation des sucres et aux facteurs de risque des maladies cardiovasculaires.

La plupart des études ont révélé que la consommation des sucres entraîne un manque de sécrétion d'insuline ou un manque de son utilisation, ce qui engendre l'accumulation du glucose dans le sang et endommage les artères du cœur .

Il a également été constaté que la consommation des sucres provoque une augmentation du taux de cholestérol dans le sang et de l'accumulation de graisses dans les vaisseaux engendrant ainsi la formation de l'athérosclérose ce qui diminue le flux sanguin donc avec un apport de sang insuffisant au cœur ce qui entraîne par exemple un infarctus du myocarde (IDM) ou une crise cardiaque.

Mots clés : sucres, fructose, hydrates de carbone, maladies cardiovasculaires, inflammation, athérosclérose.

ملخص:

تعتبر أمراض القلب و الأوعية الدموية من المسببات الأولى للوفاة في العالم حيث تم تحديد العديد من عوامل الخطر المسببة في هذه الأمراض القلبية من بينها العوامل الغذائية ، حيث في الآونة الأخيرة تم تركيز الأبحاث على السكريات خاصة التي تحتوي على الفركتوز ومدى تأثيرها على الإصابة بأمراض القلب و الأوعية الدموية.

في هذه المذكرة تناولنا دراسة تأثير استهلاك السكر على القلب و عوامل الخطر المسببة لأمراض القلب و الأوعية الدموية، حيث أظهرت معظم الدراسات أن استهلاك السكر يؤدي إلى نقص إفراز الأنسولين أو قلة استخدامه وهذا ما يؤدي إلى تراكم الغلوكوز في الدم وهذا راجع أن الخلايا لا تستطيع إدخاله مما يؤدي إلى تلف شرايين القلب، كما وجد أن تناول السكر يؤدي إلى رفع نسبة الكولسترول في الدم مما يؤدي إلى تراكم الدهون في الأوعية الدموية و شرايين القلب و هذا ما ينتج عنه تصلب هذه الشرايين مسببا نقص في تروية القلب وبهذا يكون غير قادر على أداء وظيفته.

الكلمات المفتاحية: الكربوهيدرات، السكر، أمراض القلب، الإلتهاب، تصلب الشرايين.

Academic year: 2020-2021 **Presented by:** BOUZID Bouchra
HAMRI Djihane

Title: The effect of consumption sugar on cardiovascular disease

Thesis submitted for the degree of Master Immunology molecular and cellular

Cardiovascular disease (CVD) is the single largest cause of mortality in world. Numerous risk factors have been identified for CVD, including a number of nutritional factors. Recently, attention has been focused on fructose-containing sugars and their putative link to risk factors for CVD.

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Key word: sugar, carbohydrates, cardiovascular disease, inflammation, atherosclerosis.

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