

الآية

(وَلِيَبْتَلِيَ اللَّهُ مَا فِي صُدُورِكُمْ وَلِيُمَحَّصَ مَا فِي قُلُوبِكُمْ وَاللَّهُ عَلِيمٌ بِذَاتِ الصُّدُورِ)

سورة آل عمران (154)

Dedication

To my parent

If I didn't have you

How I will be here

If I didn't know you

How I can be there

Somehow somewhere

Aim a pace of your, soul, hope, love and patience
with all Passion.

To my sister, brothers I will be stronger to live my life
for family.

Whatever where aim or how far away you are.
Still my family give me a good faith after my God to
live my life.

For the future in the distance, and the good that I can
do.

Acknowledgment

Thanks to my family for their love and support.
It is a great pleasure to acknowledgment my deepest thanks
and gratitude to
Dr. Mohammed Mohammed Omer. As he my supervisor. It is
a great honor to work under his supervision. I would like
express my deepest thanks and sincere appreciation to
Dr. Mohamed Elfadil at Faculty of Nuclear Medicine
collage - Sudan University of science and technology for
his comprehensive advice and supporting during the
study until this work came to existence.
I would like to offer my special thanks to the administrative
staff and specially the echocardiography at the Sudan
Cardiac Hospital, and Aljazeera Medical Group Center
(Department of Nuclear Medicine ELISA and Immunoassay
Section)

Abstract

This study was conducted to study whether there is a relationship between the variation of the serum thyroid hormone levels (TSH, FT3 and FT4) and the presence heart disease.

The study was done at Sudan cardiac Center and Radioimmunoassay laboratory of Khartoum (RICK) at the nuclear medicine department and medical laboratory (January 2016 to August 2016).

A total of 50 patients their average age was 55.9 selected from Echocardiography patients and then followed persons prospectively to assess measured thyroid function

Data collected included information of Echocardiography report and results of TFT and Lipid profile, reviewers independently abstracted and assessed studies.

The results of this study revealed that when thyroid hormones (T3) increase the heart beating increase, relation between the two variable (EF, T3),with the maximum hormone level between 1&3 T3 ml/dl , and 40% EF starting point and 75% ending point. When thyroid hormones (TSH) decrease the heart beating decrease, (EF ,TSH),with the maximum hormone level between 0.78 & 1 T3 ml/dl ,and 78% EF starting point and 60% ending point , when thyroid hormones (TSH) decrease the heart beating decrease, (T3, TSH),with the maximum hormone level between 0.4 &1 TSH ml/dl and 2 T3 ml/dl starting point and 1.80 T3 ml/dl ending point, when thyroid hormones (TSH) decrease the heart beating decrease, (T4, TSH),with the maximum hormone level between 0.3 & 3 TSH ml/dl and 150 T4 ml/dl starting point and 3 T4 ml/dl ending point.

It concluded that thyroid hormones exerts multiple effects on the heart and vascular system.

الخلاصة

وقد أجريت هذه الدراسة لدراسة ما إذا كانت هناك علاقة بين التغير في مستويات هرمون

الغدة الدرقية

في الدم (TSH، T3، T4) وأمراض القلب.

وقد أجريت الدراسة في مركز السودان للقلب، والمقاييس المناعية الشعاعية في مختبر

مستشفى

الخرطوم قسم الطب النووي والمختبرات الطبية الموافق من (يناير 2016 إلى أغسطس 2016).

تكونت من مجموعه 50 مريضا متوسط أعمارهم 55.9 تم اختيارهم من مرضى ضربات القلب

ثم يتبع

لنفس المرضى تقييم وظيفة الغدة الدرقية.

وتضمنت البيانات التي تم جمعها من المعلومات من تقرير ضربات القلب ونتائج TFT

المستخرجة بشكل

مستقل ودراسات التقييم.

كشفت نتائج هذه الدراسة أنه عندما يزيد هرمون الغدة الدرقية (T3) تزيد نبضات القلب،

العلاقة بين

متغيرين (EF، T3) مع الحد الأقصى للمستوى من الهرمون بين 1 و 3 T3 مل / دل ، و 40%

في EF

نقطة البداية و 75 ٪ في نقطة النهاية. بينما هرمون الغدة الدرقية (TSH) ٲ يقل من معدل

الضربات

القلبية، (EF، TSH) مع الحد الأقصى للمستوى من الهرمون بين 0.78 و 1 T3 مل / دل، و

78 ٪ EF في نقطة البداية و 60 ٪ في نقطة النهاية، بينما هرمون الغدة الدرقية ((TSH ٲ يقل

من معدل الضربات القلبية ، (T3، TSH) مع الحد الأقصى للمستوى هرمون بين 0.4 و 1 تش

مل / دل و 2 T3 مل / دل نقطة البداية و 1.80 T3 مل / دل في نقطة النهاية، بينما هرمون

الغدة الدرقية (TSH) ٲ يقل من معدل

الضربات القلبية ، (T4، TSH) مع الحد الأقصى للمستوى هرمون بين 0.3 و 3 تش مل / دل

و 150 T

نقطة انطلاق مل / دل و 3 T4 في نقطة النهاية مل / ديسيلتر.

وهذا ما يخلص إلى أن هرمونات الغدة الدرقية تمارس تأثيرات متعددة على نظام القلب

والأوعية الدموية.

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LIST OF ABBREVIATIONS

ABBREVIATIONS	WORDS STAND FOR
T3	Triiodothyronine
T4	Thyroxine
TSH	Thyroid-stimulating hormone
EF%	Ejection Fraction
LV	Left Ventricle
BP	Blood Pressure

TFT	Thyroid Function Test
TG	Triglyceride
TC	Cholesterol
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
LVDs	left ventricular end-systolic diameter
LVDD	left ventricular end-dystolic diameter
HR	Heart Rate
RIA	Radioimmunoassay

Chapter one

1.1 Introduction

The cardiovascular system is one of the most important targets on which thyroid hormones act.(1,2) More than 80% of the biologically active hormone Triiodothyronine (T3) derives form peripheral convection of thyroxine (T4) secreted by the thyroid gland.(3) Clinical and experimental evidence has shown that T3 plays a major role in modulating heart rate and cardiac contractility as well as arterial peripheral resistance.(1,2) T3 actions are carried out by binding with specific nuclear receptor

that regular responsive genes encoding for structural and functional cardiac proteins: direct, extra-nuclear, non-transcriptional effects have also been described. (1,2) Atypical pattern of altered thyroid hormone metabolism characterized by low T3 circulating levels been described in patients with acute myocardial infarction (4,3) and heart failure 6 and in adults and children after cardiopulmonary bypass.(7,9) The principal pathophysiology mechanism underlying low circulating T3 is the reduced enzyme activity of five monodeiodinase responsible for converting T4 into T3 in peripheral tissue.(10,11) this low-T3 syndrome has commonly been interpreted by the medical community as an euthyroid sick syndrome, an adaptive compensatory and thus beneficial response that decreases energy consumption in diseased status. This interpretation however, has recently been questioned. Although clinical data documented the benefit gained from treating patients with synthetic thyroid hormones, (12,20) no studies have focused on documenting a direct link between low-T3 state and poor prognosis in cardiac patients . As prospectively evaluate the impact of low circulating T3 on the prognosis of large population of patients with heart disease, in January 1999 we systematically assessed thyroid hormone profile in patients admitted to cardiology department.

The cardiovascular sign and symptoms of thyroid disease are some of the most profound and clinically relevant findings that

Accompany both hyperthyroidism. Based on the understanding of the cellular mechanisms of thyroid hormone action on the heart and cardiovascular system, it is possible to explain the changes in cardiac output, cardiac contractility, blood pressure, vascular resistance, and rhythm disturbance the result from thyroid dysfunction. The importance of the recognition of the effects of the thyroid disease on the heart also derives from the observation that restoration of normal thyroid function most often reverses the abnormal cardiovascular hemodynamic. In the present review we discuss the appropriate thyroid function test to establish a suspected diagnosis as well as the treatment modalities necessary to restore patients to a euthyroid state. We also review the alternations in thyroid hormone metabolism that accompany chronic congestive heart failure and approach to the management of patients with induced alterations in thyroid function test. Mechanism underlying the effect of thyroid hormone on the cardiovascular system beside its metabolic and thermoregulatory tissue effects, thyroid hormone regulates cardiac performance by acting on the heart and vascular system, the

relationship between thyroid hormone and cardiovascular system. This association has recently confirmed by significant changes in cardiac structure and function in patients with persistent thyroid dysfunction. Triiodothyronine (T3) is biological active thyroid hormone: and generated by 5` monodeiodination of T4 in peripheral tissue.

The availability of T3, the active form of thyroid hormone in the heart, has controlled by the deiodinases, which regulate cardiac levels of T3. The heart is particularly vulnerable to the local Triiodothyronine levels because T3 is essential to preserve both cardiac morphology and performance in adult life. In fact, thyroid hormone influence cardiac performance by genomic and non-genomic effects and increases cardiac output by affecting stroke volume and heart rate many of the physiological effects of thyroid hormone mediated by its genomic nuclear effects. These effects result from the binding of T3 to specific nuclear thyroid hormone receptors (TRs). Several important cardiac structural and functional proteins where transcriptionally by T3, namely, sarcoplasmic reticulum calcium adenosine triphosphates (ATP-ase).

Cardiovascular Function in hyperthyroidism Short-term hypothyroidism are shown by high cardiac output state with a remarkable increase in heart rate and cardiac preload, and is reduction in peripheral vascular resistance, resulting in a hyperactive dynamic circulation. Cardiac preload (left ventricular end diastolic volume) is increase in blood volume and the improvement in diastolic function. The improvement in diastolic relaxation in the presence of T3 promotes relaxation of the peripheral vasculature. It decreases systemic vascular.

1.2 Problem of the Study:

There is highly correlation between heart disease and dysfunction of thyroid, which many studies tried to find out this relation. In this study, we try to enter the heart disease, which can be caused, by thyroid hormones secretion which can effect the heartbeat or dysfunction of the cardiac output using the relation of thyroid hormone assays and echocardiography and see how it will put out the results.

1.3.1 Objectives of the study:

The objective of this study is to rollout the relation of the heart disease related to the thyroid function

To study thyroid function in relation to heart disease the general objective of this study is also find association between the thyroid function and heart disease under facility objective treatment, to established high predicted correlation between hyperthyroidism induces and cardiovascular state (high cardiac output with low systemic vascular resistance), which enhanced left ventricular (LV) systolic and diastolic function.

1.3.2 Specific objective

- To evaluate the thyroid function test(TSH, T4, and, T3)
- To measure the BP (Systolic, Diastolic) and heart beat rate.
- To investigate to interface between thyroid dysfunction and cardiac disorder.
- To compare between the cardiac disease history, age, and gender of the patient with the TFT result.

1.4 Significant of the study:

To explain the important of thyroid function test and heart disease patients, which are essential for the clinical to

optimal manage the patient? The suggestions for subsequent research arise from the findings that to focus on the effect of heart medication on thyroid gland, and the result of the proposed research can give suggest used as a marker for survival in patient with heart disease.

1.5 Overview of the study:

This study will be consisted of five chapters, with chapter, one is an introduction, which, includes: objectives, problem of the study and importance of the study. While chapter two will includes a comprehensive literature review, and chapter three will describe the material and method. Chapter four will include result presentation; finally, chapter five include the discussion and conclusion.

Chapter Two

2.1 Anatomy of Heart:

The heart weighs between 7 and 15 ounces (200 to 425 grams) and is a little larger than the size of your fist. By the end of a long life, a person's heart may have beat (expanded and contracted) more than 3.5 billion times. In fact, each day, the average heart beats 100,000 times, pumping about 2,000 gallons (7,571 liters) of blood.

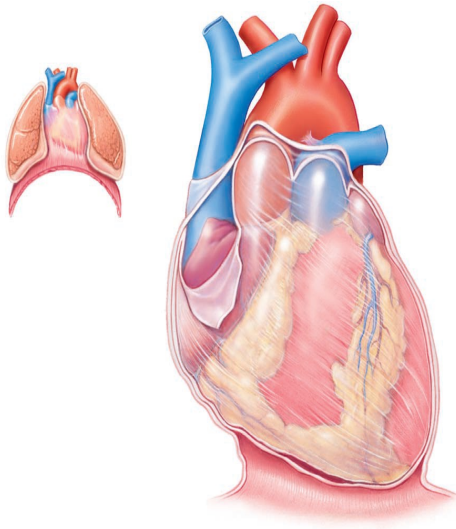


Figure 2.1 Location and membranes of the heart.(22)

Structures of the Heart

The heart is a cone-shaped organ about the size of a loose fist. It is located within the mediastinum and extends

from the level of the second rib to about the level of the sixth rib. Although many people think that the heart is found in the left side of the chest, the heart is located only slightly left of the midline of the body. The heart is bordered laterally by the lungs, posteriorly by the vertebral column, and anteriorly by the sternum. Inferiorly, the heart rests on the diaphragm.

Cardiac Membranes. A membrane called the Pericardium covers the heart and the large blood vessels attached to it (Figure 1-1). The pericardium consists of an outer fibrous layer that covers two inner layers. The innermost layer is called the visceral pericardium, and it lies directly on top of the heart. The layer on top of the visceral pericardium is called the parietal pericardium. The fibrous pericardium and the parietal pericardium form the pericardial sac. The space between the parietal pericardium and visceral pericardium is called the pericardial cavity. The pericardial cavity contains a slippery fluid called serous fluid. Serous fluid reduces friction between the membranes when the heart contracts.

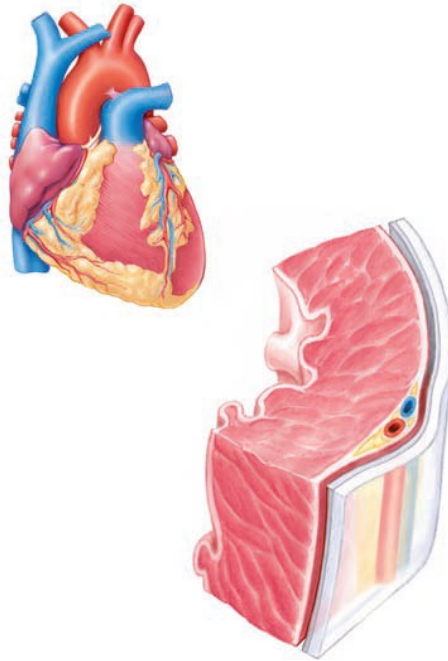


Figure 2.2 Layers of the wall of the heart. (22)

The Heart Wall. The wall of the heart (Figure 1-2) is made of the following three layers: Epicardium. This outermost layer is also known as the visceral pericardium and contains fat, which helps to cushion the heart.

Myocardium. This middle layer is the thickest layer of the wall and is made primarily of cardiac muscle.

Endocardium. This innermost layer is thin and very smooth and stretches as the heart pumps blood. This layer also contains Purkinje fibers.

Normal Heart

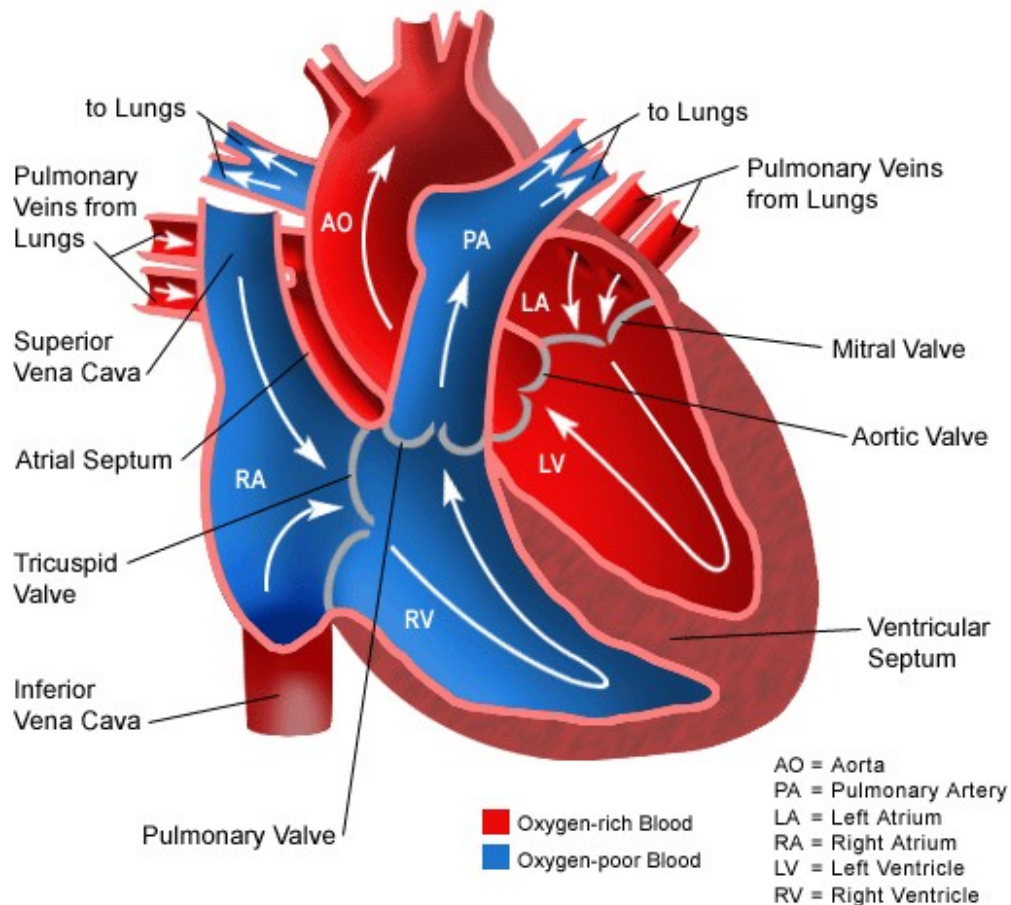


Figure 2.3 Coronal section of the heart, pathways of the blood circulation inside the heart. (24)

Heart Chambers and Valves. The heart contains four hollow chambers, two on the left and two on the right (Figure 1-3). The upper chambers of the heart are called atria. They have thin walls and function to receive blood returning to the heart from the lungs and the body. The bottom chambers of the heart are called ventricles.

They function to pump blood into the arteries. The four valves of the heart keep blood flowing in one direction and include the tricuspid, bicuspid, pulmonary, and aortic valves.

Tricuspid Valve. The tricuspid valve has three cusps and is situated between the right atrium and the right ventricle. It prevents blood from flowing back into the right atrium when the right ventricle contracts. This valve is also called the right AV (atrioventricular) valve. The cusps of this valve are anchored by cordlike structures called chordae tendineae to bumps of cardiac muscle called papillary muscles. These muscles contract when the ventricles contract to close the valve.

Bicuspid Valve. The bicuspid valve has two cusps and is located between the left atrium and the left ventricle. It prevents blood from flowing back into the left atrium when the left ventricle contracts. This valve is known as the mitral valve and the left AV valve. Like the tricuspid valve, the bicuspid valve also has chordae tendineae attached to papillary muscles.

Pulmonary Valve. The pulmonary valve is situated between the right ventricle and the pulmonary trunk. It prevents blood from flowing back into the right ventricle. Because its cusps are shaped like a half moon, this valve is called a semilunar valve. **Aortic Valve.** The aortic valve is situated between the left ventricle and the aorta. It

prevents blood from flowing back into the left ventricle and is also known as a semilunar valve. (24)

The Conduction System

Electrical impulses from the heart muscle (the myocardium) cause the heart to contract. This electrical signal begins in the sinoatrial (SA) node, located at the top of the right atrium. The SA node is sometimes called the heart's "natural pacemaker." An electrical impulse from this natural pacemaker travels through the muscle fibers of the atria and ventricles, causing them to contract. Although the SA node sends electrical impulses at a certain rate, the heart rate may still change depending on physical demands, stress, or hormonal factors.

This pathway is made up of 5 elements:

1. 1-The sino-atrial (SA) node
2. The atrio-ventricular (AV) node
3. The bundle of His
4. The left and right bundle branches
5. The Purkinje fibres.(25)

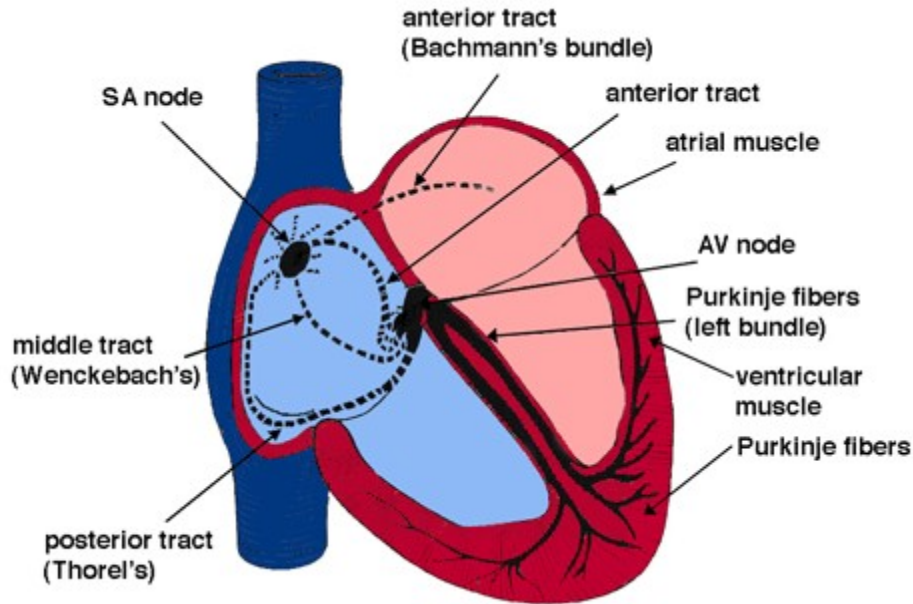


Figure 2.4 the conduction system of the heart. Normal excitation originates in the sinoatrial (SA) node then propagates through both atria (internodal tracts shown as dashed lines). The atrial depolarization spreads to the atrioventricular (AV) node, passes through the bundle of His (not labeled), and then to the Purkinje fibers which make up the left and right bundle branches; subsequently all ventricular muscle becomes activated.

2.1.1 Physiology of heart:

The heart lies in the center of the thoracic cavity and is suspended by its attachment to the great vessels within a fibrous sac known as the pericardium; note that humans have relatively thick walled pericardium's compared to those of the commonly studied large mammalian cardiovascular models (i.e., dog, pig or sheep). A small amount of fluid is

present within the sac (pericardial fluid) which lubricates the surface of the heart and allows it to move freely during function (contraction and relaxation). The pericardial sac extends upwards enclosing the great.

The pathway of blood flow through the chambers of the heart is indicated in Recall that venous blood returns from the systemic organs to the right atrium via the superior and inferior venae cavae. It next passes through the tricuspid valve into the right ventricle, and from there is pumped through the pulmonary valve into the pulmonary artery. After passing through the pulmonary capillary beds, the oxygenated pulmonary venous blood returns to the left atrium through the pulmonary veins. The flow of blood then passes through the mitral valve into the left ventricle, and is pumped through the aortic valve into the aorta.(25)

In general, the gross anatomy of the right heart pump is considerably different from that of the left heart pump, yet the pumping principles of each are primarily the same. The ventricles are closed chambers surrounded by muscular walls, and the valves are structurally designed to allow flow in only one direction. The cardiac valves passively open and close in response to the direction of the pressure gradient across them... The myocytes of the ventricles are organized primarily in a circumferential orientation; hence when they contract,

the tension generated within the ventricular walls causes the pressure within the chamber to increase. As soon as the ventricular pressure exceeds the pressure in the pulmonary artery (right) and/or aorta (left), blood is forced out of the given ventricular chamber. This active contractile phase of the cardiac cycle is known as systole. The pressures are higher in the ventricles than the atrium during systole; hence the tricuspid and mitral (atrioventricular) valves are closed. When the ventricular myocytes relax, the pressure in the ventricles falls below that in the atria, and the atrioventricular valves open; the ventricles refill and this phase is known as diastole. The aortic and pulmonary (semilunar or outlet) valves are closed during diastole because the arterial pressures (in the aorta and pulmonary artery) are greater than the intraventricular pressures. The effective pumping action of the heart requires that there be a precise coordination of the myocardial contractions (millions of cells), and this is accomplished via the conduction system of the heart (see Fig. 5). Contractions of each cell are normally initiated when electrical excitatory impulses (action potentials) propagate along their surface membranes. The myocardium can be viewed as a functional syncytium; action potentials from one cell conduct to the next cell via the gap junctions. In the healthy heart, the

normal site for initiation of a heartbeat is within the sinoatrial node, located in the right atrium.

The heart normally functions in a very efficient fashion and the following properties are needed to maintain this effectiveness:

1. the contractions of the individual myocytes must occur at regular intervals and be synchronized (not arrhythmic);
2. the valves must fully open (not stenotic);
3. the valves must not leak (not insufficient nor regurgitant);
4. the ventricular contractions must be forceful (not failing nor lost due to an ischemic event);
5. The ventricles must fill adequately during diastole (no arrhythmias or delayed relaxation).(28)

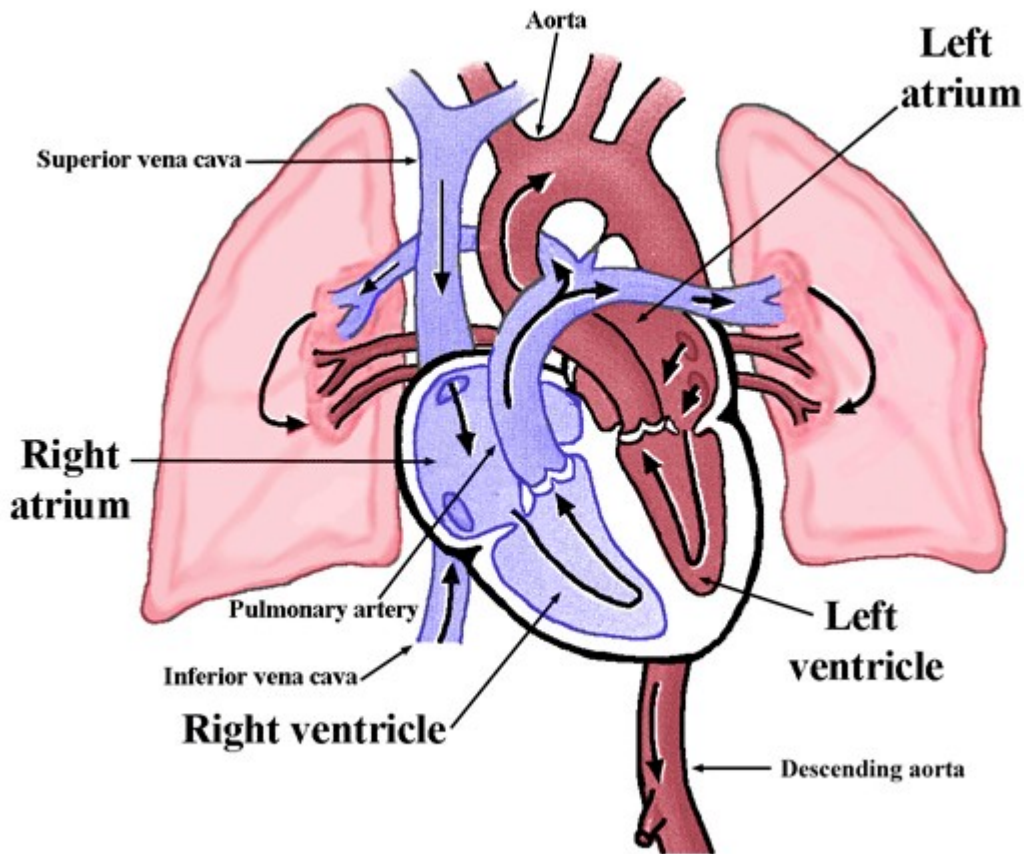


Figure 2.5 Pathway of blood flow through the heart and lungs. Note that the pulmonary artery (trunk) branches into left and right pulmonary arteries. There are commonly four main pulmonary veins that return blood from the lungs to the left atrium.(29)

The Circulatory System

The heart and circulatory system make up to cardiovascular system.

The heart works as a pump that pushes blood to the organs, tissues, and cells of your body. Blood delivers oxygen and nutrients to every cell and removes the carbon dioxide and waste products made by those cells. Blood is

carried from the heart to the rest of the body through a complex network of arteries, arterioles, and capillaries. Blood is returned to your heart through venules and veins. If all the vessels of this network in to the body were laid end-to-end, they would extend for about 60,000 miles (more than 96,500 kilometers), which is far enough to circle the earth more than twice!

The circulatory system consists of the heart and blood vessels. It is responsible for sending blood to the lungs to pick up oxygen and to the digestive system to pick up nutrients in order to deliver oxygen and nutrients to all the organ.

This systems in the body. This system also circulates waste products to certain organ systems so that these wastes can be removed from the blood. This chapter discusses the lymphatic system because it also circulates fluids throughout the body.(23)

The cardiac cycle describes the complete movement of the heart or heartbeat and includes the period from the beginning of one heartbeat to the beginning of the next one. The cycle consists of diastole (ventricular relaxation and filling) and systole (ventricular contraction and emptying). The right heart (blue side) is the pump for the pulmonary circuit; the left heart (red side) is the pump for the systemic circuit.

Disorders involving the valves of the heart disturb the pumping efficiency of the heart. Valvular heart disease produces either stenosis (narrowing) or insufficiency. Valvular stenosis is the failure of a valve to open fully, slowing blood flow from a chamber. Valvular insufficiency, or regurgitation, on the other hand, is failure of the valve to close completely, usually owing to nodule formation on (or scarring and contraction of) the cusps so that the edges do not meet or align. This allows a variable amount of blood (depending on the severity) to flow back into the chamber it was just ejected from. Both stenosis and

insufficiency result in an increased workload for the heart. Because valvular diseases are mechanical problems, damaged or defective cardiac valves are often replaced surgically in a procedure called valvuloplasty. Most commonly, artificial valve prostheses made of synthetic materials are used in these valve replacement procedures, but xenografted valves (valves transplanted from other species, such as pigs) are also used.(30)

2.1.2 Pathology of heart:

Any disorder of the [heart](#). Examples include [disease](#), [congenital](#), and [pulmonary heart disease](#), as well as [rheumatic heart disease \(rheumatic fever\)](#), [hypertension](#), [inflammation](#) of the heart muscle (myocarditis) or of its inner or outer

membrane ([endocarditis](#), [pericarditis](#)), and [heart valve](#) disease. Abnormalities of the heart's natural [pacemaker](#) or of the nerves that conduct its impulses cause [arrhythmias](#). Some [connective tissue](#) diseases (notably systemic [lupus erythematosus](#), [rheumatoid arthritis](#), and [scleroderma](#)) can affect the heart. [Heart failure](#) may result from many of these disorders. The circulatory system acts as the transport system for the body. It brings oxygen to tissues and carries carbon dioxide away. Nutrients are picked up from the digestive system and delivered throughout the body, while waste products are carried away so that certain organs may remove them. The circulatory system consists of the heart and blood vessels and includes arteries, veins, and capillaries. Blood is the transport medium that is pumped throughout the body. It is a liquid tissue that consists of plasma and formed elements (red blood cells, white blood cells, and platelets). It is important for the medical assistant to have an understanding of this system in order to effectively perform electrocardiograms, phlebotomy, and blood tests.

Clinical and Pathological Aspects of Heart Disease:

The vast majority of myocardial infarcts result from complications of coronary [atherosclerosis](#). Atherosclerotic plaques can develop surface erosions or rupture their

fibrous caps, exposing arterial blood to factors that promote blood **thrombosis** (clotting). Occlusion of the coronary artery results in myocardial ischemia (deficiency of blood flow to the heart muscle). Myocardium has very high metabolic demands, and once blood flow ceases, irreversible injury to the tissue begins within 20 minutes. Cell death proceeds in a surprisingly orderly fashion over time, beginning in the innermost layers of the ventricular wall (sub endocardium) and moving as a **wave front** toward the outer layers (sub epicardium). If the heart is reperfused (has blood flow restored) by 3 hours, the infarct will be approximately 80% of its final size. If reperfusion is delayed until 6 hours, infarcts are no smaller than those caused by permanent coronary occlusion.

Although there is considerable proliferation of connective tissue and vascular cells **after infarction**, the heart's muscle cells, unfortunately, have very little intrinsic regenerative ability. As a result, cardiac muscle that dies from infarction is essentially never replaced. Instead, a wound healing process ensues, where the dead muscle tissue is digested by white blood cells (macrophages), and a provisional repair tissue, termed **granulation tissue**, and grows in to replace the damaged muscle. Granulation tissue (perhaps the only new tissue that adult males can grow), is highly proliferative and rich in

blood vessels and connective tissue cells. Granulation tissue remodels over time to form [scar tissue](#). Scar tissue is a tough, fibrous tissue that has good tensile strength, but it is unable to contract. As a result, many patients are left with significant deficits in contractile function after infarction that result in progressive heart failure.

When infarct repair proceeds “well”, the patient is left with a scar, typically smaller than the muscle it replaced, which follows the outline of the original ventricular wall. Often times, however, the infarct wall thins considerably and the ventricular chamber dilates. According to the Law of Laplace, the combination of ventricular chamber dilation and wall thinning greatly increases wall stress, which in turn may contribute to progressive ventricular failure. The constellation of infarct thinning, chamber dilation, muscle cell hypertrophy and ventricular fibrosis are referred to as [left ventricular remodeling](#).

Heart Diseases and Disorders

Millions of people experience irregular heartbeats, called arrhythmias, at some point in their lives. Most of the time, they are harmless and happen in healthy people free of heart disease. However, some abnormal heart rhythms can be serious or even deadly. Having other types of heart disease can also increase the risk of arrhythmias.(31)

Disease Categories

Electrical: Abnormal heart rhythms (arrhythmias) are caused by problems with the electrical system that regulates the steady heartbeat. The heart rate may be too slow or too fast; it may stay steady or become chaotic (irregular and disorganized). Some arrhythmias are very dangerous and cause sudden cardiac death, while others may be bothersome but not life threatening.

Circulatory: High Blood Pressure and coronary artery disease (blockage in the pipes of the heart) are the main causes of blood vessel disorders. The results, such as stroke or heart attack, can be devastating. Fortunately, there are many treatment options.

Structural: Heart muscle disease (cardiomyopathy) and congenital abnormalities (problems present from birth) are two problems that can damage the heart muscle or valves.

Electrical Disorders

Arrhythmias that start in the heart's upper chambers, the atria, include:

- [Atrial Fibrillation \(AF or AFib\)](#)

More than 2 million people in the U.S. have atrial fibrillation. In AFib, the heartbeat is irregular and rapid due to disorganized signals from the heart's electrical system. The upper chamber of the heart may beat as often as 300 times a minute, about four times faster than normal. Though AFib isn't life threatening, it can lead to other rhythm problems, feeling tired all the time, and heart failure (with symptoms such as filling up with fluid, swelling in hands, legs and feet, shortness of breath). People with AFib are five times more likely to have a stroke compared to people without the condition. Doctors often prescribe blood thinners (anticoagulants) to patients with AFib to reduce this higher risk of stroke.
- [Atrial Flutter \(AFL\)](#)

Atrial flutter is similar to AFib because it also causes a fast beat in the atrium. However, AFL is caused by a single electrical wave that circulates very rapidly in the atrium, about 300 times a minute. This leads to a very fast, but steady, heartbeat.
- [Sick Sinus Syndrome \(SSS\)](#)

Sick sinus syndrome is not a disease, but a group of signs or symptoms that show the heart's natural electrical pacemaker, the sinus node, is not working properly. In SSS,

the heart rate can alternate between slow (bradycardia) and fast (tachycardia). Treatment for SSS is usually an artificial pacemaker, along with medication.

- Sinus Tachycardia

A harmless faster rhythm, sinus tachycardia is a normal increase in heart rate that happens with fever, excitement, and exercise. There is no need for treatment, except in rare cases when it is caused by an underlying problem, such as anemia (low blood count) or hyperthyroidism (overactive thyroid gland).

Arrhythmias that originate in the heart's lower chambers, the ventricles, include:

- Ventricular Tachycardia (VT)

a life-threatening arrhythmia, ventricular tachycardia is usually seen along with other serious heart disease but sometimes happens in people with normal hearts. Because VT can lead to ventricular fibrillation (a dangerously fast and disorganized heartbeat), it is a serious condition that needs aggressive treatment and follow up.

Treatment options are surgery, radiofrequency ablation (scarring or burning the area of heart tissue that triggers the abnormal rhythm), and/or medication. People with VT are often protected by a defibrillator (a device that can shock the heart out of the dangerous heartbeat) that is implanted in the body.

- Ventricular Fibrillation (VF)
Sudden cardiac arrest caused by ventricular fibrillation is the cause of half of all cardiac deaths. In VF, the heartbeat is fast and chaotic, causing the lower heart chambers, or ventricles, to spasm. Sometimes, a heart attack (blockage of the heart pipes/arteries) can lead to VF. VF is sudden, happens without warning, and stops the heart from working. The lack of oxygen to the body, especially to the brain, is deadly. Sudden cardiac arrest is caused by an electrical problem.
- It is not the same as a heart attack (myocardial infarction), which is a circulatory (plumbing) problem caused by clogged blood vessels that cut off the supply of blood to the heart. Though CPR may help, the only truly effective VF treatment is defibrillation, which uses paddles or electrodes to “shock” the heart back to normal rhythm. Without treatment, the person with VF will pass out suddenly and die. Other arrhythmias include:
 - Premature Contractions
Extra, early, or “skipped” beats are the most common cause of irregular heart rhythms. These can start in the upper or lower chambers of the heart.
 - Long QT Syndrome (LQTS)
Long QT Syndrome is a disorder of the electrical system. It can be inherited, brought on by taking certain medications, or caused by a combination of both. People with LQTS are at

risk for VF, the most dangerous heart rhythm that causes sudden death.

- **Heart Block**

When electrical signals from the upper chambers of the heart (atria) cannot travel to the lower chambers (ventricles), heart block happens. The heart then beats too slowly, decreasing the amount of oxygen that gets to the body and brain.

- **Syncope (Fainting)**

Fainting, or feeling as if one might pass out, can be caused by serious heart rhythm disorders and needs to be evaluated carefully. Sometimes the cause is not heart related, as in cases of low blood sugar, but it can still be dangerous due to the risk of injuries from falling.

Circulatory Disorders

- **Heart Attack (Myocardial Infarction)**

when arteries become so clogged that the flow of blood to the heart is reduced or stopped, the lack of oxygen can damage or kill the heart muscle, causing a heart attack. Knowing the symptoms of a heart attack and getting immediate emergency treatment can limit or prevent heart muscle damage.

- **Stroke**

Strokes (brain attacks), although not true heart disorders, are caused by blockage or reduced blood flow to the brain.

While some strokes occur when a blood vessel bursts, most happen due to clogged or blocked vessels to the brain, in the same way clogged vessels in the heart can cause a heart attack. Abnormal heart rhythms such as atrial fibrillation and atrial flutter can lead to the formation of blood clots in the heart. When dislodged, a blood clot can travel to the brain, block a vessel and cause a stroke. All strokes pose serious health threats.

Structural Disorders

- [Heart Failure](#)
when the heart muscle is too weak to effectively pump blood through the body, heart failure, or cardiomyopathy, sets in. Early diagnosis and treatment can stop or slow down the worsening of heart failure.
 - [Heart Valve Problems](#)
Heart valve problems can be inherited or develop on their own, affecting the heart's ability to push blood from chamber to chamber. Medication and surgery are treatment options.
- (32)

2.2.1 Anatomy of thyroid:

As it is known the endocrine system together with the nervous system enables other systems in the body to work in coordination with each other and protect

homeostasis using hormones. Hormones secreted by the endocrine system are carried to target organs and cause affect through receptors.

The thyroid gland is a highly vascularized organ located anteriorly in the neck, deep to the platysma, sternothyroid and sternohyoid muscles, and extending from the 5th cervical (C5) to the 1st thoracic (T1) vertebrae. The gland consists of two lobes (left and right) connected by a thin, median isthmus overlying the 2nd to 4th tracheal rings, typically forming an "H" or "U" shape. Occasionally the isthmus is absent and the thyroid exists as two distinct lobes. Embryologically, the thyroid gland develops as a thickening in the pharyngeal floor that elongates inferiorly as the thyroglossal duct, dividing into two lobes as it descends through the neck

Beneath the visceral layer of the pretracheal, deep cervical fascia, the thyroid gland is surrounded by a true inner capsule, which is thin and adheres closely to the gland. The capsule sends projections into the thyroid forming septae and dividing it into lobes and lobules. Dense connective tissue attachments secure the capsule of the thyroid to both the cricoid cartilage and the superior tracheal rings.

The lobules of the gland are composed of follicles, the structural unit of the thyroid. Each follicle is lined by a simple layer of epithelium surrounding a colloid-filled

core. This colloid contains iodothyroglobulin, the precursor to thyroid hormones.

Supply and Nerves

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Because the thyroid gland is a hormone secreting organ, it is highly vascularized. It receives its blood supply from the superior and inferior thyroid arteries. These arteries lie between the fibrous capsule and the pretracheal layer of deep cervical fascia.

The superior thyroid artery is the first branch of the external carotid artery and supplies the top half of the thyroid gland. It divides into anterior and posterior branches supplying respective sides of the thyroid. On the anterior side, the right and left branches anastomose with each other. On the posterior side, the right and left branches anastomose with their respective inferior thyroid arteries.

The inferior thyroid artery supplies the lower half of the thyroid and is the major branch of the thyrocervical trunk, which comes off the subclavian artery. It too divides into several branches, supplying the inferior portion of the thyroid and anastomosing posteriorly with the superior thyroid branches.

There are three main veins that drain the venous plexus on the anterior surface of the thyroid. They include the superior, middle, and inferior thyroid veins, and each drains its respective portion of the thyroid. The superior and middle thyroid veins drain into the internal jugular veins, whereas the inferior thyroid vein drains into the brachiocephalic veins, behind the manubrium of the sternum.

Lymphatic drainage of the thyroid gland is quite extensive and flows multidirectional. Immediate drainage flows first to the periglandular nodes, then to the prelaryngeal (Delphian), pretracheal, and paratracheal nodes along the recurrent laryngeal nerve, and then to mediastinal lymph nodes.

The principal innervation of the thyroid gland is derived from the superior, middle, and inferior cervical sympathetic ganglia of the autonomic nervous system and parasympathetic fibers from the vagus nerves. These nerves reach the thyroid gland by coursing with the blood vessels (superior and inferior thyroid periarterial plexuses).(33)

2.2.2 Physiology of thyroid:

Synthesis and Release of Thyroid Hormones

Hormones are produced in the colloid when atoms of the mineral iodine attach to a glycoprotein, called thyroglobulin that is secreted into the colloid by the follicle cells. The following steps outline the hormones' assembly:

Binding of TSH to its receptors in the follicle cells of the thyroid gland causes the cells to actively transport iodide ions (I^-) across their cell membrane, from the bloodstream into the cytosol. As a result, the concentration of iodide ions "trapped" in the follicular cells is many times higher than the concentration in the bloodstream.

Iodide ions then move to the lumen of the follicle cells that border the colloid. There, the ions undergo oxidation (their negatively charged electrons are removed). The oxidation of two iodide ions ($2 I^-$) results in iodine (I_2), which passes through the follicle cell membrane into the colloid.

In the colloid, peroxidase enzymes link the iodine to the tyrosine amino acids in thyroglobulin to produce two intermediaries: a tyrosine attached to one iodine and a tyrosine attached to two iodines. When one of each of these intermediaries is linked by covalent bonds, the resulting compound is triiodothyronine (T_3), a thyroid hormone with three iodines. Much more commonly, two copies of the

second intermediary bond, forming tetraiodothyronine, also known as thyroxine (T_4), a thyroid hormone with four iodines. The thyroid hormones, triiodothyronine (T_3) and its prohormone, thyroxine (T_4), are tyrosine-based hormones produced by the thyroid gland that are primarily responsible for regulation of metabolism. T_3 and T_4 are partially composed of iodine (see molecular model). A deficiency of iodine leads to decreased production of T_3 and T_4 , enlarges the thyroid tissue and will cause the disease known as simple goitre. The major form of thyroid hormone in the blood is thyroxine (T_4), which has a longer half-life than T_3 .^[11] In humans, the ratio of T_4 to T_3 released into the blood is between 14:1 and 20:1. T_4 is converted to the active T_3 (three to four times more potent than T_4) within cells by deiodinases (5'-iodinase). These are further processed by decarboxylation and deiodination to produce iodothyronamine (T_{1a}) and thyronamine (T_{0a}). All three isoforms of the deiodinases are selenium-containing enzymes, thus dietary selenium is essential for T_3 production.(34).

These hormones remain in the colloid center of the thyroid follicles until TSH stimulates endocytosis of colloid back into the follicle cells. There, lysosomal enzymes break apart the thyroglobulin colloid, releasing free T_3 and T_4 , which diffuse across the follicle cell membrane and enter the bloodstream.

In the bloodstream, less than one percent of the circulating T_3 and T_4 remains unbound. This free T_3 and T_4 can cross the lipid bilayer of cell membranes and be taken up by cells. The remaining 99 percent of circulating T_3 and T_4 is bound to specialized transport proteins called thyroxine-binding globulins (TBGs), to albumin, or to other plasma proteins. This “packaging” prevents their free diffusion into body cells. When blood levels of T_3 and T_4 begin to decline, bound T_3 and T_4 are released from these plasma proteins and readily cross the membrane of target cells. T_3 is more potent than T_4 , and many cells convert T_4 to T_3 through the removal of an iodine atom.

Regulation of TH Synthesis

The release of T_3 and T_4 from the thyroid gland is regulated by thyroid-stimulating hormone (TSH). As shown in, low blood levels of T_3 and T_4 stimulate the release of thyrotropin-releasing hormone (TRH) from the hypothalamus, which triggers secretion of TSH from the anterior pituitary. In turn, TSH stimulates the thyroid gland to secrete T_3 and T_4 . The levels of TRH, TSH, T_3 , and T_4 are regulated by a negative feedback system in which increasing levels of T_3 and T_4 decrease the production and secretion of TSH.

Functions of Thyroid Hormones

The thyroid hormones, T_3 and T_4 , are often referred to as metabolic hormones because their levels influence the body's basal metabolic rate, the amount of energy used by the body at rest. When T_3 and T_4 bind to intracellular receptors located on the mitochondria, they cause an increase in nutrient breakdown and the use of oxygen to produce ATP. In addition, T_3 and T_4 initiate the transcription of genes involved in glucose oxidation. Although these mechanisms prompt cells to produce more ATP, the process is inefficient, and an abnormally increased level of heat is released as a byproduct of these reactions. This so-called calorogenic effect (calor- = "heat") raises body temperature.

Adequate levels of thyroid hormones are also required for protein synthesis and for fetal and childhood tissue development and growth. They are especially critical for normal development of the nervous system both in utero and in early childhood, and they continue to support neurological function in adults. As noted earlier, these thyroid hormones have a complex interrelationship with reproductive hormones, and deficiencies can influence libido, fertility, and other aspects of reproductive function. Finally, thyroid hormones increase the body's sensitivity to catecholamines (epinephrine and norepinephrine) from the adrenal medulla by upregulation of receptors in the blood vessels. When

levels of T_3 and T_4 hormones are excessive, this effect accelerates the heart rate, strengthens the heartbeat, and increases blood pressure. Because thyroid hormones regulate metabolism, heat production, protein synthesis, and many other body functions, thyroid disorders can have severe and widespread consequences.

Disorders of the Endocrine System: Iodine Deficiency, Hypothyroidism, and Hyperthyroidism As discussed above, dietary iodine is required for the synthesis of T_3 and T_4 . But for much of the world's population, foods do not provide adequate levels of this mineral, because the amount varies according to the level in the soil in which the food was grown, as well as the irrigation and fertilizers used. Marine fish and shrimp tend to have high levels because they concentrate iodine from seawater, but many people in landlocked regions lack access to seafood. Thus, the primary source of dietary iodine in many countries is iodized salt. Fortification of salt with iodine began in the United States in 1924, and international efforts to iodize salt in the world's poorest nations continue today.

Dietary iodine deficiency can result in the impaired ability to synthesize T_3 and T_4 , leading to a variety of severe disorders. When T_3 and T_4 cannot be produced, TSH is secreted in increasing amounts. As a result of this hyper stimulation, thyroglobulin accumulates in the thyroid

gland follicles, increasing their deposits of colloid. The accumulation of colloid increases the overall size of the thyroid gland, a condition called a goiter. A goiter is only a visible indication of the deficiency. Other iodine deficiency disorders include impaired growth and development, decreased fertility, and prenatal and infant death. Moreover, iodine deficiency is the primary cause of preventable mental retardation worldwide. Neonatal hypothyroidism (cretinism) is characterized by cognitive deficits, short stature, and sometimes deafness and muteness in children and adults born to mothers who were iodine-deficient during pregnancy.

In areas of the world with access to iodized salt, dietary deficiency is rare. Instead, inflammation of the thyroid gland is the more common cause of low blood levels of thyroid hormones. Called hypothyroidism, the condition is characterized by a low metabolic rate, weight gain, cold extremities, constipation, reduced libido, menstrual irregularities, and reduced mental activity. In contrast, hyperthyroidism—an abnormally elevated blood level of thyroid hormones—is often caused by a pituitary or thyroid tumor. In Graves' disease, the hyperthyroid state results from an autoimmune reaction in which antibodies overstimulate the follicle cells of the thyroid gland. Hyperthyroidism can lead to an increased metabolic rate, excessive body heat and sweating, diarrhea, weight

loss, tremors, and increased heart rate. The person's eyes may bulge (called exophthalmos) as antibodies produce inflammation in the soft tissues of the orbits. The person may also develop a goiter.

Calcitonin: The thyroid gland also secretes a hormone called calcitonin that is produced by the parafollicular cells (also called C cells) that stud the tissue between distinct follicles. Calcitonin is released in response to a rise in blood calcium levels. It appears to have a function in decreasing blood calcium concentrations by:

- Inhibiting the activity of osteoclasts, bone cells that release calcium into the circulation by degrading bone matrix
- Increasing osteoblastic activity
- Decreasing calcium absorption in the intestines
- Increasing calcium loss in the urine

However, these functions are usually not significant in maintaining calcium homeostasis, so the importance of calcitonin is not entirely understood. Pharmaceutical preparations of calcitonin are sometimes prescribed to reduce osteoclast activity in people with osteoporosis and to reduce the degradation of cartilage in people with osteoarthritis. The hormones secreted by thyroid are summarized in.

Thyroid Hormones Associated hormones	Chemical class	Effect
Thyroxine (T ₄), triiodothyronine (T ₃)	Amine	Stimulate basal metabolic rate
Calcitonin	Peptide	Reduces blood Ca ²⁺ levels

Of course, calcium is critical for many other biological processes. It is a second messenger in many signaling pathways, and is essential for muscle contraction, nerve impulse transmission, and blood clotting. Given these roles, it is not surprising that blood calcium levels are tightly regulated by the endocrine system. The organs involved in the regulation are the parathyroid glands.

The thyroid gland is a butterfly-shaped organ located in the neck anterior to the trachea. Its hormones regulate basal metabolism, oxygen use, nutrient metabolism, the production of ATP, and calcium homeostasis. They also contribute to protein synthesis and the normal growth and development of body tissues, including maturation

of the nervous system, and they increase the body's sensitivity to catecholamines. The thyroid hormones triiodothyronine (T_3) and thyroxine (T_4) are produced and secreted by the thyroid gland in response to thyroid-stimulating hormone (TSH) from the anterior pituitary. Synthesis of the amino acid-derived T_3 and T_4 hormones requires iodine. Insufficient amounts of iodine in the diet can lead to goiter, cretinism, and many other disorders. (35)

Thyroid Hormone Synthesis

The first step in the synthesis of thyroid hormones is the organification of iodine. Iodide is taken up, converted to iodine, and then condensed onto tyrosine residues which reside along the polypeptide backbone of a protein molecule called thyroglobulin. This reaction results in either a mono-iodinated tyrosine (MIT) or di-iodinated tyrosine (DIT) being incorporated into thyroglobulin. This newly formed iodothyroglobulin forms one of the most important constituents of the colloid material, present in the follicle of the thyroid unit.

The other synthetic reaction that is closely linked to organification is a coupling reaction, where iodotyrosine molecules are coupled together. If two di-iodotyrosine molecules couple together, the result is the formation of thyroxin (T_4). If a di-iodotyrosine and a mono-

iodotyrosine are coupled together, the result is the formation of tri-iodothyronine (T3).

From the perspective of the formation of thyroid hormone, the major coupling reaction is the di-iodotyrosine coupling to produce T4. Although T3 is more biologically active than T4, the major production of T3 actually occurs outside of the thyroid gland. The majority of T3 is produced by peripheral conversion from T4 in a deiodination reaction involving a specific enzyme which removes one iodine from the outer ring of T4.

The T3 and T4 released from the thyroid by proteolysis reach the bloodstream where they are bound to thyroid hormone binding proteins. The major thyroid hormone binding protein is thyroxin binding globulin (TBG) which accounts for about 75% of the bound hormone.

In order to attain normal levels of thyroid hormone synthesis, an adequate supply of iodine is essential. The recommended minimum intake of iodine is 150 micrograms a day. Intake of less than 50 micrograms a day is associated with goiter.

High iodine levels inhibit iodide oxidation and organification. Additionally, iodine excess inhibits thyroglobulin proteolysis (this is the principal mechanism for the antithyroid effect of inorganic iodine in patients with thyrotoxicosis).

2.2.3 Pathology of thyroid:

Pathophysiology and Diagnosis of Thyroid Disease

The thyroid is a butterfly-shaped gland located in the front of the neck just above the trachea. It weighs approximately 15 to 20 grams in the adult human. The thyroid produces and releases into the circulation at least two potent hormones, thyroxine (T_4) and triiodothyronine (T_3), which influence basal metabolic processes and/or enhance oxygen consumption in nearly all body tissues. Thyroid hormones also influence linear growth, brain function including intelligence and memory, neural development, dentition, and bone development.(26)

The thyroid gland produces T_4 and T_3 utilizing iodide obtained either from dietary sources or from the metabolism of thyroid hormones and other iodinated compounds. About 100 μg of iodide is required on a daily basis to generate sufficient quantities of thyroid hormone. Dietary ingestion of iodide in the United States ranges between 200 and 500 $\mu\text{g}/\text{day}$ and varies geographically; ingestion is higher in the western part of the United States than in the eastern states. The specialized thyroid epithelial cells of the thyroid gland are equipped with a Na/I symporter that helps concentrate iodide 30 to 40 times the level in plasma to ensure adequate amounts for the synthesis of thyroid hormone. The iodide trapped by the thyroid gland is

subsequently oxidized to iodine by the enzyme thyroid peroxidase. The iodine then undergoes a series of organic reactions within the thyroid gland to produce tetraiodothyronine or thyroxine (T_4) and triiodothyronine (T_3). T_3 is also produced in other tissues such as the pituitary, liver, and kidney by the removal of an iodine molecule from T_4 . T_4 is considered to be more of a pro-hormone, while T_3 is the most potent thyroid hormone produced. T_4 and T_3 are both stored in the thyroglobulin protein of the thyroid gland and released into the circulation through the action of pituitary derived thyrotropin (thyroid stimulating hormone or TSH). A normal individual produces from the thyroid gland approximately 90 to 100 μg of T_4 and 30 to 35 μg of T_3 on a daily basis. An estimated 80 percent of the T_3 produced daily in humans is derived from peripheral metabolism (5'-monodeiodination) of T_4 , with only about 20 percent secreted directly from the thyroid gland itself. On a weight basis, T_3 is about 3 to 5 times more potent as a thyroid hormone than T_4 and is believed to be the biologically active form of the hormone.(36)

TSH, secreted by thyrotroph cells located in the anterior pituitary gland, regulates thyroid gland function and hormone synthesis and release. The pituitary secretion of TSH in turn is influenced by the releasing factor, thyrotropin-releasing hormone (TRH) produced in the

hypothalamus (see Figure 2-1). The secretion of both TSH and TRH is regulated by negative feedback from thyroid hormone, predominantly T_3 , from the circulation and/or T_3 that is produced locally from intracellular conversion of T_4 to T_3 . When circulating thyroid hormone levels are elevated, both the synthesis and secretion of serum TSH are blunted. In contrast, when circulating levels of T_4 and T_3 are low, serum TSH levels are increased in a compensatory fashion. The geometric mean level of serum TSH in normal individuals is approximately 1.5 $\mu\text{U}/\text{ml}$ as recently reported in the NHANES III study (Hollowell et al., 2002). When hypothalamic pituitary function is intact,

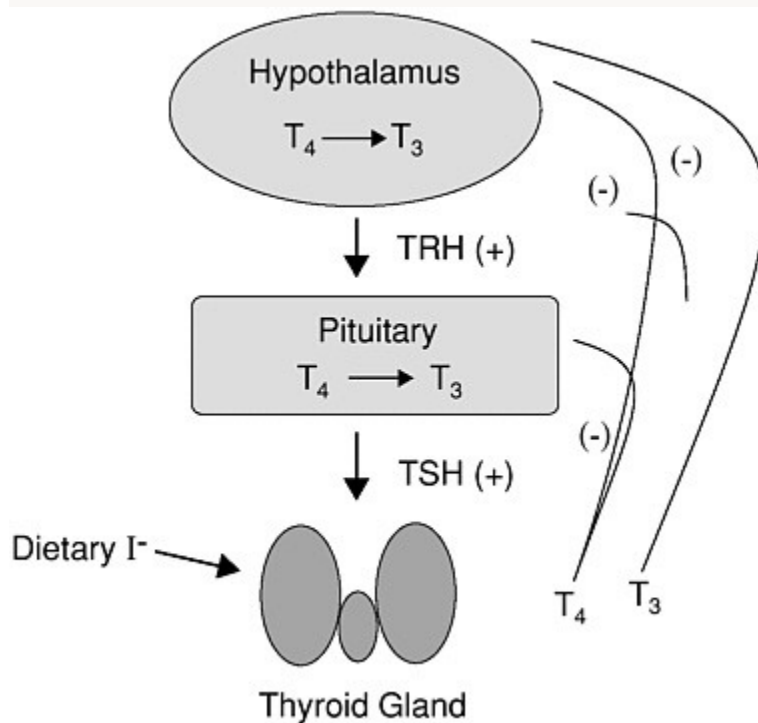


FIGURE 2.6

Serum TSH levels are markedly suppressed (to $<0.05 \mu\text{U/ml}$) in patients with hyperthyroidism and elevated circulatory levels of serum thyroxine, while a marked increase in TSH ($>5 \mu\text{U/ml}$) occurs in patients with hypothyroidism and low blood levels of serum T_4 . The mechanism through which TSH binds to and activates the thyroid gland is well understood. TSH binds to a specific membrane receptor located on the surface of the thyroid epithelial cell and activates the cell signaling mechanisms through the enzyme adenylate cyclase located in the plasma membrane. Activation of adenylate cyclase increases intracellular cyclic adenosine monophosphate (cAMP) levels, which in turn stimulate additional intracellular signaling events that lead to thyroid hormone formation and secretion.

T_4 and T_3 circulate bound primarily to carrier proteins. T_4 binds strongly to thyroxine binding globulin (TBG, ~ 75 percent) and weakly to thyroxine binding prealbumin (TBPA, transthyretin, ~ 20 percent) and albumin (~ 5 percent). T_3 binds tightly to TBG and weakly to albumin, with little binding to TBPA. The geometric mean for serum T_4 in normal individuals is approximately $8 \mu\text{g/dl}$, while the mean serum T_3 level is approximately 130 ng/dl . Under normal protein binding conditions, all but 0.03 percent of serum T_4 and 0.3 percent of serum T_3 is

protein bound. Only a small amount of unbound (or free) T_4 (approximately 2 ng/dl) and T_3 (approximately 0.3 ng/dl) circulates in a free state, and it is this free concentration that is considered responsible for the biological effects of the thyroid hormones. There are physiologic situations associated with a change in the serum concentration of these thyroid-binding proteins—such as pregnancy, non-thyroidal illness, or ingestion of drugs—that affect the level and/or affinity of these binding proteins. Under these circumstances, the serum concentrations of total T_4 and total T_3 change in parallel to the changes that occur in the thyroid hormone binding proteins, but the serum concentrations of free T_4 and free T_3 remain normal and the individual remains euthyroid. In contrast, the serum concentration of free T_4 and free T_3 are raised in hyperthyroidism and decreased in hypothyroidism.(37)

2.2.4 THYROID FUNCTION TESTING

At the present time, serum-based tests available by immunoassay for measuring the concentration of thyroid hormones in the circulation include total (TT_4 and TT_3) and free (FT_4 and FT_3) hormone. In addition, direct measurements of thyroid hormone binding plasma proteins, thyroxine binding globulin (TBG), transthyretin (TTR)/prealbumin (TBPA), and albumin are also available. However, the thyroid test measurement that has the

greatest utility for evaluating patients suspected of thyroid disease is the third-generation thyroid stimulating hormone (TSH, thyrotropin) assay. Most third-generation TSH assays today that can reliably detect differences of 0.02 μ U/ml or better (interassay imprecision <20 percent) can easily distinguish both hyper- and hypothyroidism from euthyroidism (normal thyroid function) and may differentiate the patient suffering from the "euthyroid sick syndrome" from true hyperthyroidism. Other methods in thyroid testing include the measurement of thyroid gland autoantibodies, including antithyroid peroxidase (TPOab), antithyroglobulin (Tgab), and antibodies against the TSH receptor (Trab). All of these thyroid test methods are routinely available on automated immunoassay instruments located in most hospital and reference laboratories with tight (<10 percent) method between run coefficients of variation.

TESTING FOR DIAGNOSIS AND MANAGEMENT OF THYROID DYSFUNCTION

The most sensitive test in an ambulatory population at risk for thyroid dysfunction is the serum TSH (Demers and Spencer, in press). Serum TSH assays today have sufficient sensitivity and specificity to identify individuals with all forms of thyroid dysfunction in the general population. However, among individuals with serious,

acute illness, the serum TSH is less specific for thyroid disease because a serious illness alone can depress TSH secretion (to be discussed). TSH screening of the neonatal population to detect congenital hypothyroidism before it is clinically evident is mandated throughout the United States and in many other countries.

When an abnormal serum TSH value is obtained, the usual next step is to repeat the measurement of TSH and also measure a serum free T₄. The latter can be performed in several ways and among non-hospitalized individuals, most methods give results that are inversely correlated with the serum TSH result. The most common cause of discordance between the TSH and free T₄ result occurs in patients with subclinical thyroid dysfunction with high or low serum TSH values and a normal serum free T₄ result.

Serum TSH measurements may yield misleading results for individuals with changing levels of thyroid hormones. For example, a serum TSH level may remain high for weeks in hypothyroid patients treated with T₄. Similarly, serum TSH levels may remain low for weeks after the serum T₄ level falls to normal in patients treated for hyperthyroidism.(36)

2.2.5 Reference Intervals for Thyroid Function Tests

Typical reference intervals for thyroid function tests in normal adults are shown in [Table 2-1](#). The median serum concentration in U.S. subjects 12 years and older, as

reported from 1988 to 1994 in the NHANES III study, was 1.49 $\mu\text{U/ml}$, a value that is considerably below the upper limit of normal (4.5 $\mu\text{U/ml}$) reported by most laboratories (Hollowell et al., 2002). This finding has led to the suggestion that a serum TSH value above 3 $\mu\text{U/ml}$ may not be normal. In the same study, median serum TSH concentrations in subjects more than 50 years old were higher than in younger individuals: 1.60 $\mu\text{U/ml}$ after age 50, 1.79 $\mu\text{U/ml}$ after age 60, 1.98 $\mu\text{U/ml}$ after age 70, and 2.08 $\mu\text{U/ml}$ after age 80. Serum total and free T_4 levels do not change significantly with age, while serum total and free T_3 do show an age-related decline in concentration.

TABLE 2-1 Serum TSH and Thyroid Hormone Reference Ranges in Adults

Hormone	Reference Range
TSH	0.4 - 4.5 $\mu\text{U/ml}$
Total thyroxine (total T_4)	4.0 - 12.0 $\mu\text{g/dl}$
Free thyroxine (free T_4)	0.7 - 1.8 ng/dl
Total triiodothyronine (total T_3)	100 - 200 ng/dl
Free triiodothyronine (free T_3)	208 - 596 pg/dl

1.98 $\mu\text{U/ml}$ after age 70, and 2.08 $\mu\text{U/ml}$ after age 80. Serum total and free T_4 levels do not change significantly with age, while serum total and free T_3 do show an age-related decline in concentration.

2.2.6 Thyroid Function Testing in the Elderly

The prevalence of both low and high serum TSH levels (with normal serum free T₄ results) is increased in elderly subjects compared with younger people. With respect to high serum TSH values, the increase is thought to represent an increased prevalence of autoimmune thyroiditis, especially in women, as will be discussed. The higher prevalence of low serum TSH values may be due to thyroid nodular disease or unrecognized non-thyroid illness.

2.2.7 Diagnosis of Hypothyroidism

Hypothyroidism is a hypometabolic state that results from a deficiency in T₄ and T₃. Its major clinical manifestations are fatigue, lethargy, cold intolerance, slowed speech and intellectual function, slowed reflexes, hair loss, dry skin, weight gain, and constipation. It is more prevalent in women than men. The most common cause of hypothyroidism is disease of the thyroid itself, primary hypothyroidism.

The most common cause of primary hypothyroidism is chronic autoimmune thyroiditis (Hashimoto's disease), in which the thyroid is destroyed by antibodies or lymphocytes that attack the gland. Other causes are radioactive iodine and surgical therapy for hyperthyroidism or thyroid cancer, thyroid inflammatory disease, iodine deficiency, and several drugs that

interfere with the synthesis or availability of thyroid hormone. Hypothyroidism may also occur rarely (<1 percent of cases) as a result of deficiency of TRH or impaired TSH secretion due to hypothalamic or pituitary disease, respectively. This is known as secondary or central hypothyroidism because of the negative feedback relationship between serum T_4 and T_3 levels and TSH secretion. As noted earlier and shown in [Figure 2-1](#), people with primary hypothyroidism have high serum TSH levels. If an individual has a high serum TSH value, serum free T_4 should be measured. The concomitant finding of a high serum TSH concentration and a low free T_4 level confirms the diagnosis of primary hypothyroidism. People with a high serum TSH concentration and a normal or low-normal serum free T_4 level have, by definition, subclinical hypothyroidism. The diagnosis of secondary hypothyroidism is based on the findings of a low serum free T_4 level and a serum TSH level that is normal or low. People with secondary hypothyroidism are unlikely to be detected by a screening program based on measurements of serum TSH, but the condition is much less common than primary hypothyroidism.

2.2.8 Diagnosis of Hyperthyroidism

Hyperthyroidism is a hypermetabolic state that results from excess production of T_4 and T_3 . Its major clinical

manifestations are nervousness, anxiety, heart palpitations, rapid pulse, fatigability, tremor, muscle weakness, weight loss with increased appetite, heat intolerance, frequent bowel movements, increased perspiration, and often thyroid gland enlargement (goiter). Most individuals with hyperthyroidism are women.

The most common cause of hyperthyroidism is Graves' disease, an autoimmune disease characterized by the production of antibodies that activate the TSH receptor, resulting in stimulation of T_4 and T_3 production and enlargement of the thyroid. Other causes of hyperthyroidism are a multinodular goiter, solitary thyroid adenoma, thyroiditis, iodide- or drug-induced hyperthyroidism, and, very rarely, a TSH secreting pituitary tumor.

The diagnosis of hyperthyroidism is based on the findings of a high serum free T_4 level and a low serum TSH concentration. Occasionally, people with hyperthyroidism have a normal serum free T_4 and high serum free T_3 concentrations. These patients have what is called T_3 -hyperthyroidism. An increase in serum thyroid hormone binding protein will raise the serum total T_4 level but not free T_4 concentrations. In these patients the serum TSH remains normal. Patients with a low serum TSH concentration and normal serum free T_4

and free T_3 levels have, by definition, subclinical hyperthyroidism.

2.2.9 Effect of Medications on Thyroid Test Results

Several medications have in vivo or in vitro effects on thyroid function tests that can create misleading results. Medications, notably estrogens, that raise serum TBG levels result in an increase in serum total T_4 , but no change in serum free T_4 levels and no change in serum TSH concentrations. High doses of glucocorticoids (adrenal hormones) can lower the serum T_3 concentration by inhibiting the peripheral conversion of T_4 to T_3 and lower serum T_4 (and T_3) by inhibiting TSH secretion. Iodide, contained in solutions used to sterilize the skin and in radiopaque contrast media used in coronary angiography and many other radiological.

2.2.10 Thyroid Function Testing and Nonthyroidal Illness

Many people who are seriously ill have abnormal thyroid test results but no other evidence of thyroid dysfunction. These abnormalities occur in people with both acute and chronic illnesses and tend to be greater in those with more serious illnesses. Thus the laboratory diagnosis of thyroid disease can be extremely difficult to make in very sick people, especially those who need to be

hospitalized. The effects of illness include decreased peripheral conversion of T_4 to T_3 , decreases in serum concentrations of thyroid hormone binding proteins, and decreases in TSH secretion. These changes are reversible and do not seem to cause clinical manifestations of thyroid deficiency. Among healthier individuals, a few may have small changes in thyroid test results as a result of unrecognized nonthyroidal illness rather than thyroid dysfunction.

Previous studies

Back Ground and Literature Review

Subclinical hyperthyroidism is common in the community. With the prevalence in iodine replete areas reported to range from 0.5% to 3.9% in adults of all ages (11) and 11.8% in 1 study of the elderly (12)> the prevalence

may be higher in areas of iodine deficiency .it is define as a low-serum TSH concentration in an asymptomatic with normal serum T3 and T4 concentrations (9) the most common cause in the general population in the ingestion of exogenous T4 as replacement or suppressive therapy. Low-serum TSH concentration is generally a sensitive marker of thyroid hormone excess and reported in a large population based study to be associated with a 3-fold higher risk of developing AF in the subsequent decade(9).this study followed up 2007 patients aged 60 yr. or more (from the Framingham Heart Study)for a 10-yr. period. These patients did not have AF at the start of the study and classified according to their serum TSH level. During the 10-yr. follow -up period 192(10 %) developed AF.the cumulative incidence of AF at 10 yr. in subjects with alow TSH concentration(0.1 Mu/liter) was 28%,compared with 11% in those with a normal TSH (P_0.005).the relative risk for developing AF in those with low TSH was 3.1(9% confidence intervals 1.7 to 5.5), compared with those normal TSH (P_0.001).The incidences of AF in those with a slightly low TSH and a high TSH concentration were 16%and 15 %respectively. These incidences were not significantly different when compared with those in the normal TSH group. No long -term follow-up mortality or morbidity data on this cohort yet Thyroid disease

produces characteristic changes in cardiovascular hemodynamic (14, 15) they arise from effects of T3 both on the heart and on the systemic vasculature. Thyrotoxicosis may be associated with as much as a 50% decline in systemic vascular resistance (Fig .2), and T3 is capable of causing rapid relaxation of vascular smooth muscle cells in culture (16, 17).

Because the vascular smooth muscles of resistance arterioles peripheral vascular tone, T3 may directly regulate vascular resistance, which, in turn, causes alterations in blood pressure and cardiac output (18, 21). This postulate supported by another study in which a significant decrease in cardiac output after administration of medicine to hyperthyroid, but not to normal, subjects was noted (19). The ability to block the elevated cardiac output by pharmacologically reversing the changes in vascular resistance of thyrotoxicosis reinforces the possibility that many of the cardiac changes of hyperthyroidism occur in response to changes in ventricle peripheral tissue. Thyrotoxicosis markedly increase oxygen ventricle consumption in the periphery and increase metabolic demands, which require increased blood supply and pump the thyroid function profile was assessed in all patients from 2 to 5 days after the admission. After rapid centrifugation of a venous sample, total T3 (TT3), Ft3, total T4(TT4), ft4,

and TSH are all measured during the same morning by a completely automated AIA 600 system (Tosho Corporation). The reference intervals for our laboratory were as follows: TT3 1.23 to 2.60 nmol/L (80.0 to 170.0 ng/DI), TT4 58.4 to 155.8 nmol/L (4.5 to 12.0 g/DI), fT3 3.1 to 6.5 pmol/L (2.0 to 4.2 pg/mL), fT4 9.2 to 24.0 pmol/L (7.1 to 18.5 pg/DI), and TSH 0.30 to 3.80 IU/MI. The interassay coefficient for all determinations ranged between 8% for TSH and 9.7% for TT4.²¹ On the basis of fT3 value, patients were divided into two subgroups: I, patient with low T3, i.e., with fT3 below the lower limit of the reference interval (fT3 3.1 pmol/L), and group II, patients with normal fT3 (> 3.1 pmol/L). An important finding of the present study was that the hearts of T3-treated animals not only had lowered levels of Cr and Cr_p and ATP/FA DP ratios, but that ATP levels declined significantly at high work levels in the hyperthyroid heart. The decrease in the ATP level at high workload might explain the limitation in the maximal work capacity of the heart in the hyperthyroid state^(5,7,12, and 16). The exact mechanism for this limitation is not entirely clear. However, we speculate that the low levels of free Cr in a micro-compartment adjacent to mitochondrial inner membrane may limit the capacity of mitochondrial Cr kinase to generate ADP near the mitochondrial inner membrane (free ADP⁻; micro-compartmented free ADP⁻), and

may be precisely f ADP that is necessary to maximally stimulate mitochondrial ATP synthesis . Hence, the reduction in free Cr may limit the rise in oxygen consumption and ATP synthesis in the hyperthyroid heart by lowering f ADP -; especially under high work conditions. Further studies are necessary to delineate the maximum level of work that performed by the hyperthyroid heart and to identify the mechanism underlying the limitation in its maximal work capacity.

Chapter Three

Material and Method

In this chapter describe the material used to collect the data and method of the study which include study area, study variable, study design, study sampling, method of data collection and method of data analysis.

3.1 Materials:

In this study there are two procedures the first one is echocardiography and the second is the

Radioimmunoassay was used to measure the values of heart specially Ejection Fraction while administration the patient we take the sample of blood to do the second procedure as mention under Radioimmunoassay technique, as well the data acquired form the patient in the same date of exam with echocardiography with blood sample collected.

3.1.1.1 Exam 1: About Echocardiograph:

Was used the Ultrasound Machine model MyLab 50 ultrasound manufactured by Esaote company

Specification of high end imaging technologies such as stress echo, good at cardiac, vascular, and superficial imaging.

- 2D/3D/4D imaging
- M-Mode
- High Frequency Transducers
- Auto EF Automatic Ejection Fraction calculation
- DICOM
- TVM tissue velocity mapping for LV motion analysis(systolic and diastolic function).

:Principle of operation

We do the echocardiograph through the transthoracic (TTE), or cardiac ultrasound. We use transducer (or prop) which placed on the chest wall of the subject, and images taken through the chest wall. It is a non-invasive, highly accurate and quick assessment of the overall health of

the heart. So that quickly assessment of the patient`s heart values and degree of heart muscles contraction

((Ejection Fraction

EF = End-diastolic volume (LVED) - End-systolic volume

((LVESV

(LVEDV)

Can estimate. The images are displayed on monitor, and are recorded either by videotape (analog) or by digital

.techniques

left parasternal long axis view-1

:left parasternal short axis view-2

Aortic valve level

Mitral valve level

(Mid cavity level (Papillary muscles

Apex

Apical view –3

Four chamber view

Three chamber view

Two chamber view

Five chamber view

Subcostal view –4

;Exam 2: About thyroid hormone test 3.1.1.2

Is to perform radioimmunoassay techniques a known as antigen antibody reaction using a radioactive iodine 125 labeled with known antigen of desired test T4, T3 or TSH.

This isotopes is emits gamma rays of iodine attached to

.tyrosine

This radiolabeled antigen is to run the assays of the patients to sort out the results of the patients using a gamma counter. By Applying known standers, a binding curve can then be generated which allows the amount of antigen in the .patient's serum to be derived

3.2. Methods:

The data of this study was collected from the Sudan cardiac Center and Radioimmunoassay laboratory of Khartoum (RICK) at the nuclear medicine department and medical laboratory in period from January 2014 to august 2014.

3.1.2 Study design:

The design of this study is an analytical method where the result of TFT test will be verified with the echocardiography values result using radioimmunoassay .and U/S ECHO

3.2.3 Sample size of the study:

The sample size of this study included 50 patients (male, 2 female) age range being from 40 to 70 years.

3.2.4 Method of data collection

This study was collected the data from the fifty patients there was did the echocardiography, and in the same day collected the blood samples from them to roll out the result of TFT with Echocardiography values.

3.2.1 Procedure: Echocardiography:

Technical Aspects of 2-D Echocardiography

Transducer type

The main element in transducers is the piezoelectric crystal (titanate ceramic or quartz) that both emits and receives ultrasound waves. The frequency of a transducer is related to the nature and thickness of the piezoelectric crystal.

Transthoracic echocardiogram (TTE), the echocardiography transducer (or probe) is placed on the chest wall (or [thorax](#)) of the subject, and images are taken through the chest wall.

This is a non-invasive, highly accurate and quick assessment of the overall health of the heart. With measuring the values to roll out the result include LVDd, LVDs, EF%, HR.

3.2.2 Procedure: Radioimmunoassay (RIA):

The samples was collected from patients after echocardiography, the method taken under Radioimmunoassay method.

Measured the presence of an antigen with very high sensitivity. Basically any biological substance for which a specific antibody exists can be measured, even in

minute concentrations. RIA has been the first immunoassay technique developed to analyze nanomolar and picomolar concentrations of hormones in biological fluids.

Radioimmunoassay (RIA) method:

The target antigen is labeled radioactively and bound to its specific antibodies (a limited and known amount of the specific antibody has to be added). A sample, for example a blood-serum, is then added in order to initiate a competitive reaction of the labeled antigens from the preparation, and the unlabeled antigens from the serum-sample, with the specific antibodies. The competition for the antibodies will release a certain amount of labeled antigen. This amount is proportional to the ratio of labeled to unlabeled antigen. A binding curve can then be generated which allows the amount of antigen in the patient's serum to be derived.

That means that as the concentration of unlabeled antigen is increased, more of it binds to the antibody, displacing the labeled variant. The bound antigens are then separated from the unbound ones, and the radioactivity of the free antigens remaining in the supernatant is measured. A binding curve can be generated using a known standard, which allows the amount of antigens in the patient's serum to be derived.

Radioimmunoassay is an old assay technique but it is still a widely used assay and continues to offer distinct advantages in terms of simplicity and sensitivity.

Needed substances and equipment:

1. Specific antiserum to the antigen to be measured
2. Availability of a radioactive labeled form of the antigen
3. A method in which the antibody-bound tracer can be separated from the unbound tracer
4. An instrument to count radioactivity

Radioactivity:

¹²⁵I labels are usually applied although other isotopes such as ¹⁴C and ³H have also been used. Usually, high specific activity radio-labeled (¹²⁵I) antigen is prepared by iodination of the pure antigen on its tyrosine residue(s) by chloramine-T or peroxidase methods and then separating the radio-labeled antigen from free-isotope by gel-filtration or HPLC. Other important components of RIA are the specific antibody against the antigen and pure antigen for use as the standard or calibrator.

Separation techniques:

Double antibody, charcoal, cellulose, chromatography or solid phase techniques are applied to separate bound and free radio-labeled antigen. Most frequently used is

the double antibody technique combined with polyethylene. The bound or free fraction is counted in a gamma counter.

Concomitantly, a calibration or standard curve is generated with samples of known concentrations of the unlabeled standards. The amount of antigen in an unknown samples can be calculated from this curve.

Sensitivity:

The sensitivity can be improved by decreasing the amount of radioactively-labeled antigen and/or antibody. The sensitivity can also be improved by the so-called disequilibrium incubation. In this case radioactively labeled antigen is added after initial incubation of antigen and antibody.

Troubleshooting: The antibody must be specific for the antigen under investigation (other antigens must not cross-react with the antibody). If any cross-reactivity is observed, selection of a different antibody is advised or the antibody needs to be purified from the cross-reacting antigen by affinity chromatography.

3.3.1 Study variable:

The data of this study was collected from patient gender, age, TFT (T4, T3, TSH) result(ml/dl),Lipid Profile (TG, TC, HDL ,LDL) result (ml/dl),total echocardiography (LVDd, LVDs, EF%,HR).

3.3.2 Method of Data analysis:

The result of this study analyzed using Exile and SPSS (statistical package for social studies), The result will be shown in a form of the relation of the heart disease related to the thyroid function using Echocardiography values result with TFT values result and the linear association between the EF% with T3 and TSH and TSH with T3 and T4, modified lipid profile.

Chapter Four

4.1 Results

Table: 4.A the mean \pm standard deviation of thyroid hormones values and heart values

	Variable	Mean \pm SD
Variable	test group	control group
age	55.9 \pm 16.3	58.3 \pm 15.0
T4	133.3 \pm 50.4	150.3 \pm 4

		4.7
T3	2±0.9	2.6±0.9
TSH	1.2±1.4	1.1±1.0
TG	185.5±10.8	247.5±11.9
TC	260.5±79.1	235.3±4.7
HDL	71.7±21.3	72.6±22.2
LDL	151.8±68.3	113.2±52.7
LVDd	4.9±0.8	4.9±1.1
LVDs	3.5±1.0	3.6±1.2
EF	53.1±15.6	56.4±16.3
HR	79.3±17.8	83.6±24.1

Table: 4.B the mean ± standard deviation of thyroid hormones values and heart values

	t test for Equality of Means	
	T	Sig. (2-tailed)
age	.431	.668
T4	.990	.326
T3	2.040	.046
TSH	.206	.837
TG	1.620	.111
TC	.969	.337
HDL	.121	.904
LDL	1.684	.098
LVDd	.072	.943
LVDs	.243	.809
EF	.612	.543
HR	.663	.510

Figure 4:1 a scatter plot show direct linear relationship between T3 ml/dl and Ejection Fraction result using blood test and U/S

Figure: 4:2 a scatter plot show an inverse linear relationship between TSH ml/dl and Ejection Fraction result using blood test and U/S

Figure: 4:3 a scatter plot show an inverse linear relationship between TSH ml/dl and Ejection Fraction result using blood test and U/S

Figure: 4:4 a scatter plot show an inverse linear relationship between TSH ml/dl and T4 result using blood test.

Table: 4.A showed result from Radioimmunoassay, Echocardiography, and result for 50 patients, the average patient's age was 55.9 with stander deviation ± 16.3 which is adjusted with the control group 58.3.

Thyroid hormones result (T3, T4, and TSH) was normal and also comparable to the control group.

The lipid profile all result it comparable with the control group except low TG was 185.5 ± 108.8 compare to the 247.5 ± 119.4 in the control group and high LDL was 151.8 ± 68.3 compare to the 113.2 ± 52.7 in the control group.

The Echo result was normal and also comparable to the control group.

Figure 4.1 showed the relation between EF% Ejection Fraction and T3, the heart beating is affected by thyroid function respectively, when thyroid hormones (T3) increase the heart beating increase, the graph approved the direct linear relation between the two variable (EF,T3),with the maximum hormone level between 1&3 T3 ml/dl , and 40% EF starting point and 75% ending point.

Figure 4:2 showed the relation between EF% Ejection Fraction and TSH, the heart beating is affected by thyroid function inverse, when thyroid hormones (TSH) decrease the heart beating decrease, the graph approved the an inverse linear relation between the two variable (EF,TSH),with the maximum hormone level between 0..0 & 1 T3 ml/dl ,and 40% EF starting point and 75% ending point.

Figure 4:3 showed the relation between T3 and TSH, the heart beating is affected by thyroid function inverse, when thyroid hormones (TSH) decrease the heart beating decrease, the graph approved the an inverse linear relation between the two variable (T3,TSH),with the maximum hormone level between 0.0 &1 TSH ml/dl and 1.8 T3 ml/dl starting point and 2.5 T3 ml/dl ending point.

Figure 4:4 showed the relation between T4 and TSH, the heart beating is affected by thyroid function inverse, when thyroid hormones (TSH) decrease the heart beating decrease, the graph approved the an inverse linear relation between the two variable (T4,TSH),with the maximum hormone level between 0.0 & 2.5 TSH ml/dl and 88 T4 ml/dl starting point and 160 T4 ml/dl ending point

Chapter Five

Discussion, Conclusion and Recommendation

5.1 Discussion

The sample of this study included 50 patients with result of using echocardiography values and TFT test by radioimmunoassay, where the main objective was to evaluate this study to find association between the thyroid function and heart disease, to rollout the relation of the heart disease related to the thyroid function

The risk factors for cardiovascular disease and the prevalence of thyroid disorders. Thyroid hormone causes a wide spectrum of cardiovascular changes due to its effects on the cardiac myocytes and vascular smooth muscle (VSM) cells as well as indirect effects mediated by activation of neuroendocrine systems.

Thyroid hormone is an important regulator of cardiac gene expression, and many of the cardiac manifestations of thyroid dysfunction are associated with alterations in T3-mediated gene transcription. So the cardiac output, ejection fraction, and heart rate are all found to be increased while isovolemic relaxation time and peripheral vascular resistance are decreased in the hyperthyroid states. Thyroid hormone increases blood volume and erythropoietin secretion with subsequent increased preload and cardiac output.

The cardiovascular signs and symptoms of thyroid disease are some of the most profound and clinically relevant findings that accompany both hyperthyroidism and hypothyroidism. On the basis of the understanding of the cellular mechanisms of thyroid hormone action on the heart and cardiovascular system, it is possible to explain the changes in cardiac output, cardiac contractility, blood pressure, vascular resistance, and rhythm disturbances that result from thyroid dysfunction. The importance of the recognition of the effects of thyroid disease on the heart also derives from the observation that restoration of normal thyroid function most often reverses the abnormal cardiovascular hemodynamics. In the present review, we discuss the appropriate thyroid function tests to establish a suspected diagnosis as well as the treatment modalities necessary to restore

patients to a euthyroid state. We also review the alterations in thyroid hormone metabolism that accompany chronic congestive heart failure and the approach to the management of patients with amiodarone-induced alterations in thyroid function tests.

Subclinical heart disease may be an independent risk factor for thyroid function, Heart disease have profound effects on thyroid function, but there have been few methods (Radioimmunoassay and Echocardiography) to examining the association between subclinical thyroid dysfunction and cardiovascular disease. Subclinical hyperthyroidism as increase in (T3) is associated with an increased risk of atrial fibrillation and increased cardiovascular diseases , left ventricular dysfunction in person ages 40 up to 70 years or older,

But it is uncertain whether subclinical rest of the TFT (T4,TSH) and lipid profile even low TG/ high LDL, the risk of myocardial infarction was not significantly increased regarding for the result made by Exile and SPSS.

It is important to determine whether it is a risk factor for cardiovascular disease related to thyroid function is associated.

5.2 Conclusion

This study was carried out in order to evaluate cardiac values using Echocardiography and Thyroid Hormones using Radioimmunoassay and hence make it possible to

predict the results using Echocardiography and Radioimmunoassay results.

The data of this study collected from 50 patients their heart function was assessed using Echocardiography and in Sudan cardiac Center and Radioimmunoassay laboratory of Khartoum (RICK) at the nuclear medicine department and medical laboratory in period from January 2014 to august 2014 , where the data were collected prospectively.

The results of this study showed that there is a direct linear relationship between EF% Ejection Fraction and T3, the heart beating is affected by thyroid function respectively, when thyroid hormones (T3) increase the heart beating increase, there is strong correlation between them.

Showed inverse linear association between EF% Ejection Fraction and TSH, between T3 and TSH, and between T4 and TSH.

In summary the results of as associated between heart disease related to thyroid function can be predicted using the correlation between T3 and EF%(ejection fraction) objectively.

5.3 Recommendation

1. This study has an important role in the evaluation of patients with heart disease, it is used in the detection with each patients have left ventricle failure of heart diagnosis, and staging of the disease as well as in assessing the TFT response to monitoring for best evaluation.
2. Emphasizing the appropriate use of computer tomography (CT), magnetic resonance (MR), and positron emission tomography (PET) imaging in patient management.
3. Large sample can be incorporated in similar study to highlight the effect with the all parameter of the study was done before.
4. The main parameter for energy consumption in cells of the body are Triiodothyronine, in spite of that the heart cells need more energy using T3.so we recommended to do more studies for T3 energy turnover and heart muscles.
5. Even we do Lipids parameters for heart diseases we recommended to do further studies for cardiac

parameters to see wide heart disease and related diseases.

6. In this study we do Echocardiography as best-parameter to diagnosis heart disease so we recommended to do more parameters like Doppler Ultrasound for more studies for heart disease.

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Appendix:

Master data sheet

gender	age	T4	T3	TSH	TG	TC	HDL	LDL	LVDd	LVDF%	HR		
1	60	115	0.6	0.77	62.	1191	53.9	124.7	5.5	3.455	65		
2	65	111	1.4	0.34	73.	9139	51.3	57.1	4.1	3.340	62		
2	65	133	1.1	3.01	153	165	78.4	56	6.8	6.120	62		
1	65	105	1.4	0.14	118	202	56.7	121.7	6.6	5.337	82		
2	82	89	2.4	0.26	48.	1184	69.1	105.2	5.6	3.664	70		
1	56	102	0.8	1.91	133	216	69.1	120.	5.6	5.117	75		

								3					
					69.			83.5					
2	49	109	2.4	0.67		4 149	51.6		2	4.6	2.8 70	95	
					68.			104.					
1	21	222		1.24		7 186	67.4		7	4.4	2.9 60	84	
					98.			87.6					
2	61	134	2.3	0.55		9 158	50.6		2	5.7	4.6 35	65	
					75.			84.3					
2	70	136	1.6	0.22		3 150	59		4	4.5	3.1 60	80	
1	29	114	3.2	0.37		344	207	49.5	88.7	3.7	2 75	100	
									206.				
1	55	110	2.2	2.25		170	326	85.4	6	5.5	4.6 25	109	
1	45	99	2.6	1.56		346	411	55.8	286	4.6	2.7 45	69	
									196.				
2	60	145	2.5	3.15		258	304	55.5	9	4.5	3.1 55	67	
									257.				
2	75	97	1.3	0.54		183	386	91.9	5	3.8	2.8 55	77	
					98.			131.					
1	65	158	2.2	0.01		8 197	46.2		0	5.1	3.7 55	85	
								106.	227.				
2	42	182	3.9	0.15		132	360		4	2	5.1	2.8 75	90
									249.				
1	83	130	1.7	2.4		114	331	58.5	7	5.2	4.3 35	85	
									151.				
1	48	208	2.8	0.01		192	258	67.7	9	5.1	2.8 75	101	
									141.				
1	19	77		1.07		312	299	94.9	7	3.9	2.6 65	111	
1	60	98	2.1	1.09		465	201	64.2	43.8	5.9	4.6 42	60	
									113.				
1	32	119	1.5	1.15		199	218	64.8	4	3.6	2.4 60	60	
1	60	336	0.01	0.01		111	262	72.8	167	3.9	2.9 40	55	
1	65	155	1.9	0.23		193	357	89.1	229.	5.2	4.3 35	96	

								3					
								171.					
2	70	63	1.2	3.21	222	292	76.5	1	5.7	4.8	33	65	
1	56	225	2.5	0.29	138	288	78.4	182	5.3	3.8	52	45	
							115.	126.					
2	60	172	2.3	0.01	352	313	7	9	4.7	2.7	74	97	
								333.					
1	30	148		2.82	92	434	82.1	5	4.3	3	56	49	
								244.					
1	66	179	2.8	0.01	201	347	62.3	5	5.1	3	70	124	
								189.					
2	53	83	2.8	2.06	161	258	35.9	9	3.9	2.5	66	80	
1	65	108	1.2	2.87	256	194	76	66.8	7.3	6.1	30	111	
								100.					
1	77	194	2.7	0.6	319	334	3	9	5.4	3.8	56	65	
								272.					
2	40	136	1.7	1.8	167	362	56	6	4.2	3.8	50	88	
								117.					
1	70	101	1.1	4.76	257	237	67.7	9	4.2	2.1	78	60	
								247.					
1	72	100	1.5	1.08	194	388	102	2	5.2	4.3	35	68	
								122.					
1	50	165	2.2	0.03	219	210	43.8	4	5.8	4.5	43	97	
1	60	74	1.6	0.01	506	277	90.5	85.3	4.9	3.9	40	79	
								110.					
					66.			6					
2	63	114	2.3	0.01	7	152	28	6	4.4	2.8	65	66	
								102.					
2	44	201	1.1	1.03	113	307	4	183	5.4	3.5	63	97	
								201.					
2	80	109	1.3	0.86	127	309	81.7	9	4.1	2.6	66	64	
1	30	56	0.9	1.46	106	258	90.5	146.	5.4	4.2	50	95	

								3						
								113.						
1	30	117	5.1			91.		5						
						6	204	72.1	8	4.7	3.4	55	72	
									186.					
1	56	217	2.8	3.7		87	277	73	6	5.3	3.8	50	95	
1	70	130	1.8	1.1		389	228	68.8	81.4	3.9	2.6	62	95	
									159.					
						87.			5					
2	36	134	2.4	0.31		4	250	83	2	4.5	3.3	55	60	
								103.	213.					
1	70	109	1.4	2.03		304	378	4	8	3.4	2	60	70	
									105.					
2	30	122		0.01		134	206	73.5	7	4.3	2.4	75	80	
									108.					
1	70	132	3.7	0.01		220	221	68.8	2	4.3	2.4	75	74	
1	65	104	3.1	0.01		307	123	22.8	38.6	5.1	3.4	61	65	
								118.	174.					
2	50	88	1.9	6.49		139	321	5	7	5.1	4.2	38	97	
						185	260							
									151.					mea
									8	4.9	3.5	53.1	79.3	n
						108								
2	60	188	2.3	0.01		245	217	95.6	72.4	4.7	2.7	74	97	
								109.						
2	30	153	2.2	0.98		301	268	7	98.1	3.3	3	56	49	
2	50	163	1.7	1.03		262	129	48.7	27.9	5.8	4.5	43	97	
2	72	144	3.8	1.97		126	296	58.3	212.	5.2	4.3	35	88	

								5						
								173.						
1	77	238	4.1	0.01	96.	1257	64.6	1	8	5.4	3.856	65		
1	65	93	2.1	0.92	208	189	38.3	109.	1	7.3	6.130	111		
1	40	122	2.5	1.91	403	231	62.3	88.1	4.2	3.856	65			
								146.						
2	70	183	3.6	0.01	145	259	83.7	3	4.2	2.178	60			
2	66	100	1.8	3.15	217	250	89.6	117	5.1	3.70	124			
2	53	119	2.3	1.19	472	257	74.9	87.7	3.9	2.566	80			
					247	235								
					.	.		113.						mea
	58.31	50.32	6	1.1	5	372.6		2	4.9	3.656	483.6			n
					119									
					.47.									
	15.04	4.7	0.9	1.0	4	522.2		52.7	1.1	1.216	324.1			SD

1=Male

2=Female

