CHAPTER I

INTRODUCTION

Thyroid hormone exerts direct cellular effects on almost all tissue of the body including the heart. The cardiovascular abnormalities associated with thyroid dysfunction are varied. The explanation for the altered circulatory hemodynamics of thyroid disease is complex. The reasons for this include

1. the potential direct effects of thyroid hormone on the myocardium;

2. the interplay of the adrenergic nervous system with thyroid hormone on cardiac function;

3. the indirect effects of altered thyroid hormone levels on cardiac function and of adrenergic tone on the peripheral vascular system.

Recent findings have focussed that an energy requiring stereospecific transport step of thyroid hormone and its analogues occur at the level of the plasma and nuclear membrane. Once thyroid hormone enter cardiac cell, they mediate their effects through either a nuclear mechanism and stimulate protein synthesis or by extranuclear effects resulting in rapid stimulation of amino acid and sugar transport.

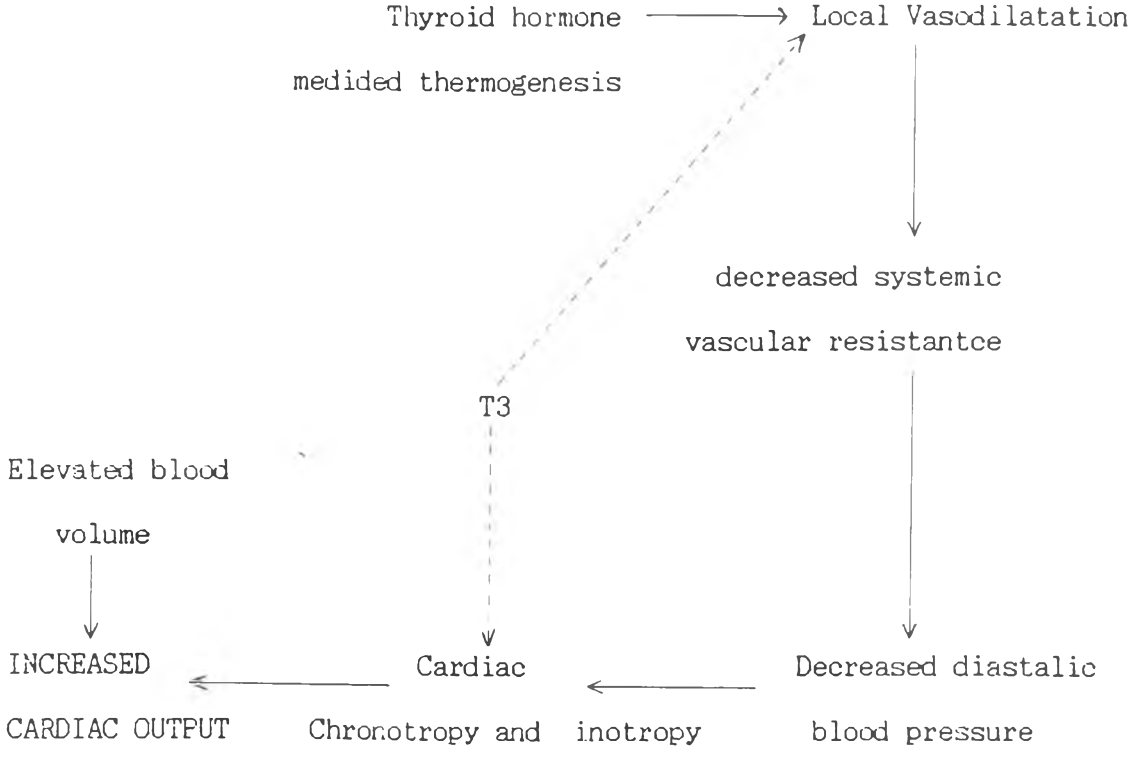
The increase in the synthesis rate of the specific proteins involves the alterations at several steps inside the myocyte. There is selective increase in the production of myosin V1 which has markedly higher myosin ATPase activity than myosin that of V3. This can explain the increases in the velocity and force of systolic contraction in hyper thyroid state

Thyroid hormone also induces changes in calcium ATPase activity by increasing the number of SR calcium ATPase pump units through the increase in the transcription of the gene. The calcium ATPase of the SR is and ion pump responsible for removing calcium form the cytosol thereby affecting diastolic relaxation.

These two mechanisms together are the major direct effects of thyroid hormone on the myocardium. Other minor effects include the thyroid hormone induced increases in sodium-potassium ATPase, atrial natriuretic factor and an increase in the number of calcium channels.

The physiologic effects of thyroid hormone arise from both T4 and T3. The biologic hallmark of abnormal thyroid function is a change in the basal metabolic rate by primarily stimulating cellular oxygen consumption and substrate utilization. This imposes an increased need for oxygen and fuel delivery to peripheral tissue as well as for the efficient removal of waste products. This requires an increase in resting cardiac output. This process will ultimately determine the changes in vascular resistance, blood pressure, and cardiac work.

These changes are summarized in the following diagram



These changes represent the indirect effects resulting from alterations in circulatory hemodynamics imposed upon the heart.

There are numerous indices of left ventricular function, obtained both by invasive and non-invasive methods. The commonly

employed non-invasive techniques include the use of external pulse tracing, phonocardiogram, electrocardiogram, echocardiogram or doppler technique to measure the various intervals of systolic events. Indeed the term "noninvasive" was first used in connection with the systolic time intervals (STI). The STI were one of the first quantitative noninvasive tests of cardiac function and remain one of the simplest and most reliable to perform. The first record of the arterial and venous pulse in normal individuals and patients with various cardiac afflictions were obtained by Marey in 1860. Like all noninvasive techniques, the STI have the advantage that multiple observations can be performed without any discomfort to the patient. The physiologic significance is that the STI respresent time which is a dimension of cardiac performance that is distinct from other functional measures of the extent and force of ventricular wall contraction.

Despite their early introduction, clinical application of the STI has received relatively less attention than have other noninvasive methods for assesssing ventricular performance such as echocardiography and radioisotopic imaging, partly due to the different nature of the STI, which denotes the timing of events of the cardiac cycle rather than the extent of wall and chamber motion. With better understanding that the temporal events of the cardiac cycle can be delineated accurately and that their measurement and interpretation can uncover the presence of significant alterations in left ventricular performance, the STI have gained wider clinical application in recent

years.

Many investigatiors have tried to better quantify the STI and have assessed the left ventricular function by a variety of noninvasive techniques as the advent of newer tools go by. These include echocardiographic and doppler ultrasound which delineate these values to a greater degree of accuraccy by observing the opening and closure of the aortic valve directly rather than obtaining the external pulse tracing to obviate the error due to the change in pulse contour as it reaches the more peripheral sites where the peak becomes smoother and the incisura less sharply defined.

More over, the use of echocardiographic recording, apart from allowing for more accurate measurement of STI, permits the assessment of other parameters of left ventricular function such as the ejection fraction (EF) and velocity of contraction of left ventricular wall etc.

This study utilized the method of simultaneous fast speed recording of M-mode echocardiography and electrocardiography to determine the left ventricular systolic indices and attempted to correlate these values with the level of thyroid hormone in patients with hyperthyroidism who attended the thyroid clinic in Chulalongkorn hospital.