Congestive heart failure: with particular emphasis upon the physiological mechanisms responsible for the production of the cardinal signs

Thomas T. Davidson  
University of Nebraska Medical Center

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CONGESTIVE HEART FAILURE
WITH
PARTICULAR EMPHASIS UPON THE
PHYSIOLOGICAL MECHANISMS RESPONSIBLE
FOR THE
PRODUCTION OF THE CARDINAL SIGNS

Thomas Davidson

Senior Thesis

THE COLLEGE OF MEDICINE
UNIVERSITY OF NEBRASKA

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INTRODUCTION

Men of higher education have long ago ordained the 'dictum', wherein he who aspires to become an accepted associate, must prove his worthiness by contributing something to knowledge for the benefit and welfare of mankind.

The successful aspirant, was he, who arrived at certain conclusions through research, and satisfactorily presented to those previously accepted, a thesis summarizing these conclusions.

The completion of my senior year in the study of medicine is nearing, at which time I am particularly desirous of becoming an accepted associate by the Doctors of Medicine. I therefore, present my thesis, for your consideration. I must confess, however, that the very nature of the subject presented herein, is such, that experimental research on my part is impractical and prohibitive, other than a survey of the literature concerning the subject. I do not propose to advance new theories or in any manner alter the present conceptions of Congestive Heart Failure. Rather it is the purpose of this thesis to present the modern conceptions of Congestive Heart Failure, with a brief historical review of the subject.

It will be noted, by the reader, that I have placed the greater emphasis in this discussion upon the
physiological mechanisms responsible for the production of symptoms. The reason for this approach is two fold and apparently advantageous in regard to cardiac disease. The traditional practice of classifying diseases, whenever possible upon an anatomical basis, does not seem to be suitable in this instance. Sir Thomas Lewis substantiates this point when he says, "Models of heart disease cannot be cast in anatomical moulds, and the persevering efforts so to fashion them have provided images of disease so grotesque in their representation that they largely fail in their purpose of forming guides to the management of disease. It is with the symptoms of disease that the patient and the doctor mainly contends. And the symptoms of heart disease may be said to derive almost exclusively from faults in function. Therefore in managing our patients, our thoughts must be carefully set in terms of function and not of structure."

The second reason for emphasizing the physiological mechanisms is somewhat general, because there are as yet relatively few methods of treating successfully the etiologic causes of cardiac disease. Instead, what is treated, and this can be done with more than a fair degree of success, is their results, which are certain disturbances of function. Therefore until the causes of cardiac disease can be successfully treated. It seems to me, more plausible to secure a better understanding of the major syndromes of
congestive failure, for it is toward these syndromes that
treatment is today directed.

I believe I have made evident the topic of my thesis
and the manner, in which I intend to approach that topic.
Before progressing, it is necessary for me to give my
reasons for choosing as my subject, congestive heart fail-
ure. These reasons are manifold and varied, however, I
feel them to be sufficient in explanation.

I first asked myself, "Should I choose some subject,
about which little has been written, in order that I might
hurriedly read the references, and hand in an obvious
necessity, with the expenditure of as little time as
possible? I decided against this view, for these subjects
about which little has been written, usually are so minor
in importance and so seldom encountered in clinical pract-
ice, that even such a hurried effort would be a waste of
time. Instead I should choose some topic, whereby I would
be able to learn, something which would be of benefit in
practice later on. Therefore, if it were my purpose to
learn, then what subject, did I feel I knew comparatively
the least about? At this point, I recalled very vividly,
a Physiology mark being substantially lowered due to the
writing of a poor examination concerning the heart and its
function. I also recalled how often I was baffled, in both
the dispensary and in the clinical clerkship, with the
interpretation of changes in the pulse, the significance of
altered heart sounds, and just what was the relationship between these alterations and the patient's life? Taken collectively, what I had learned concerning cardiac disease, was nothing more than a jumble of isolated facts, presenting no true picture of any disease process.

Rypin states, (109), that failure of the heart and circulation is the first cause of death in the United States today. With that in mind, I decided to write about some phase of cardiac disease, for to attempt to practice clinical medicine, knowing comparatively the least about the disease which each year claims the most lives, was absurd.

The choosing of cardiac disease is further justified, when one recalls that the patient and his friends are usually indifferent to the most learned diagnosis, but that they are deeply interested in the question of danger or no danger. Therefore, it seems evident that the most essential question in the examination of patients, is the prognosis.

In all serious complaints, whether medical or surgical, acute or chronic, the doctor methodically examines the heart before making a prognosis as to life or eventual death. Mackenzie holds (84), that "death is only considered to take place when the heart ceases to beat." The reason for this is that the vitality of all those organs which maintain life is dependent on an efficient supply of blood. The heart is the organ which does this service, its integrity is ever a matter of essential moment." Therefore, it seems untenable,
for a doctor to predict danger, without a knowledge of the principles governing the functional stage of the heart.

Having decided, that this thesis should be concerned with heart disease, I then realized it would be necessary, because of the immensity and volume of the material written concerning this organ, that I would be forced to limit myself to some phase of cardiac disease. It was Mackenzie who said, "in my endeavor to find out the significance of heart signs, it gradually dawned on me that the essential matter in every case was a question of heart failure...and it became more and more evident that the object of all inquiries into the heart in clinical medicine had for its objective the question of the heart's ability to maintain an efficient circulation, and that without a knowledge of heart failure all such inquiries would be rendered futile." (84-5). Bearing profit from the experience of Mackenzie, I narrowed my subject from Cardiac disease in general to Heart failure. And since there is more than one kind of heart failure, my advisor suggested, that I would derive the greatest benefit should I survey the literature, which had been written concerning heart failure of the congestive type.
BRIEF HISTORICAL REVIEW

The historical growth of knowledge concerning cardiac disease, commenced with the observations of Hippocrates. From his time until the modern era, with the exception of the classical investigative experiments by William Harvey, Stephen Hales, and others, knowledge of cardiac disease progressed mainly by speculative observations. The modern period may be said to have begun with Corvisart, the physician of Napoleon. From his time until today, knowledge of cardiac disease has progressed, not by speculation, but by experimental investigations. (53).

Hippocrates, may have been an astute observer of the pulse, but evidently knew very little concerning the heart. Plato taught that the blood moved through the vessels, but that the motion was oscillatory. Aristotle evolved a theory of cardiac function, whereby the heart was the "seat of the soul" the "source of spiritual heat." (53).

The anatomist Galen, pioneered in the study of circulatory physiology, when he showed that it was possible for the heart to be removed from the body and continue beating. Galen also demonstrated that the arterial pulsations were dependent on the heart. Galen also was the first to have believed that some of the blood passed from the right to the left side of the heart through the lungs, and he was supported in his views later on by Ibn An-Nafis, Colombo, Servetus, Arantio, and Cesalpino. It was Cesalpino, who introduced the term "circulation" and he seemed to have had
a clear and correct idea of the route taken by the blood. (108).

Leonardo da Vinci made excellent drawings of the cardiac valves, vessels and musculature, described the auriculo-ventricular bundle and studied hemodynamics. (53). However, it remained for William Harvey in 1628 to demonstrate that the blood passes from the right to the left ventricle, through the lungs and returns through the tissues to the veins. And according to Roesler, Harvey's work constitutes the firm foundation on which later concepts of circulatory disorders are built. (108).

One century later, Hales measured the blood pressure, by using a water manometer, and in 1828 Poiseulle adopted the mercury manometer for this purpose. It remained for Korotow in 1905 to apply auscultatory methods to the taking of blood pressure. (5-1).

As far back as 1794, Scarpa described the cardiac nerves, and Weber in 1845 demonstrated the inhibitory effect of the vagus. Grehant, Quinquad, Zuntz and Hagemann measured the cardiac output. And Purkinje (1839) described the auriculo-ventricular bundle. (53). Twara, as late as 1906, first described the auriculo-ventricular node, while one year later Keith and Flack discovered the sino-auricular node. In 1881, Gaskell demonstrated that muscular tissue in different regions of the heart possessed rhythmical powers of varying degrees. While the conclusions that the contact of the blood with the
cardiac tissue at successive points was the direct stimulus for the muscular contraction, was made by Haller in the eighteenth century. (5-2). Also a significant discovery pertaining to treatment was made by William Withering, who in 1776 introduced digitalis, to medicine. (24-1).

The modern period, or period of clinical cardiology, has progressed principally by investigative means. This period is said to have begun with Corvisart, who without the aid of auscultation, was able to recognize and differentiate many of the more important types of cardiac disease. He appreciated the frequency of cardiac disease, saying, "I do not hesitate to advance that the most frequent organic diseases, phtisis pulmonalis excepted, are those of the heart." (53). He believed that a knowledge of pathology must be coupled with a knowledge of physiology, and especially with careful clinical observation to become a firm and decisive practitioner, particularly in the treatment of the organic lesions. (53). Corvisart viewed cardiac dyspnea, as being "solely due to the accumulation of the blood in the lungs, from the embarrassment which it suffers on returning into the cavities of the heart, deranged wholly or in part in their natural organization." (53). From this statement it is obvious that Corvisart realized that the manifestations of cardiac failure are in someway related to obstruction of venous blood flow. However, this relationship, seems to have been previously indicated by Raymond Vieussens, in a book published in 1715, in which he described mitral stenosis,
auricular fibrillation and pulmonary congestion as a cause of cardiac dyspnea. ( 87 ).

Though Corvisart realized that cardiac failure is in someway related to venous obstruction, it remained for James Hope, in 1832, to develop this conception more in detail. Hope clearly described the effect on the lungs of left ventricular failure, which Welch was to prove experimentally in 1878. ( 53 ). Harrison states, "Hope probably deserves the credit for the first clear exposition of the "back-pressure" idea. And possibly his contributions to the subject of cardiac disease were greater than those of any other man, for in addition to his view on heart failure, he first demonstrated by experiment the mechanism of the heart sounds, and having learned to correlate the various murmurs with pathological conditions of the valves. He went a step farther and was able to produce the characteristic murmurs by experimental injury of the valves. His work could not have been done without the use of auscultation, which was introduced by Laennec." ( 53 ).

William Stokes, in 1854, was the first to advance the conception that cardiac failure, and its clinical manifestations were to be ascribed to an inadequate blood supply to the tissues. Stokes believed that the tendency of the time was to stress too much the importance of valvular lesions, and emphasized that the most important factor was the state of the cardiac muscle. Stokes called attention to observations made previously by Laennec "that valvular lesions
had but little influence on health when the muscular condition of the heart remained sound, and everyday's experience confirms this observation." (53).

Julius Cohnheim was the first to produce experimental cardiac failure, by introducing fluid into the pericardium of animals and observing an immediate fall in arterial pressure with a simultaneous rise in venous pressure. Cohnheim concluded that the clinical manifestations of cardiac failure were to be ascribed, not only, to a diminished output by the heart, but also, to the retrograde idea, wherein the cavity situated immediately behind an obstruction to the circulation is the first to suffer. (53).

Sir James Mackenzie, discarded the retrograde hypothesis entirely, and developed more in detail the views of Stokes, when he said, "The signs of heart failure are shown by the organs whose blood supply is insufficient, and are not to be found by the examination of the heart." (84-1).

Of recent years, Starling and his collaborators showed that dilatation is the natural response of the heart to overwork and fatigue, and that the rate of the metabolic processes in the heart is determined by the length of the fibers rather than by the work accomplished. Starling likewise demonstrated that the venous pressure is the most important factor controlling the amount of blood pumped by the heart. (116-a).

In this review I have, for the purpose of brevity neglected to mention many individuals, who in the past made
important contributions to the subject of circulatory diseases. Likewise the names of many now living have been omitted, for their contributions will be cited later on. The object has been to survey the general development of present conceptions of cardiac failure. In the final analysis, it will be evident in this thesis, that the clinical manifestations of congestive heart failure are dependent on fatigue of the cardiac muscle. However, it will be seen that there are two different conceptions as to the means whereby fatigue of the muscle brings about these phenomena. According to one idea, hinted by Wiggers, Corvisart, and made clear by Hope, the phenomena of heart failure are brought about by dilatation of one or more of the chambers of the heart with a consequent engorgement of those portions of the body on the venous side of the affected chamber. In contrast to this "back-pressure" hypothesis is the theory alluded to by Stokes, and greatly emphasized by Mackenzie, in which these manifestations are due to an inadequate blood supply to the tissues as a result of an inability of the heart to pump a sufficient amount of blood. This is the so-called "forward-failure" theory. The major task in the thesis to follow will be to consider the recent evidence which bears on the validity of these opposing theories. It will be seen, that in the main, the weight of evidence today, tends to support the "back-pressure" hypothesis, and discredit the forward failure theory. (5-3).
DEFINITIONS of CONGESTIVE HEART FAILURE

Congestive heart failure is the term applied to that condition, in which the heart is unable to maintain an efficient circulation during rest or moderate exertion, and, in which the signs of venous engorgement appear in most instances. (5-3).

The term has many synonyms, which will be mentioned here, as they will be frequently used during the discussion to avoid the monotony of constant repetition. Harrison employs the terms, "decompensation," "backward-failure," and "Congestive Heart Failure." (50). Christian denotes the condition as "decompensation." (26-2). White employs the phrase, "Congestive Heart Failure," and "Myocardial Failure." (123). "Cardiosclerosis" is the connotation applied by Pratt. (105). Whereas, Cabot describes the condition as "Hypertensive Heart Disease." (23). And lastly, Eggleston terms the condition, "Myocardial Insufficiency." (25-b).

The phrases "right-sided heart failure," and "left-sided heart failure" are employed to designate systemic and pulmonary engorgement, respectively. While the terms "mechanical heart failure," obstructive heart failure," and "Congestive heart failure of the mechanical type," are synonyms, which indicate that the congestive phenomena are not due to functional alterations of the myocardium, but are the result of a mechanical hindrance to the filling of the cardiac chambers. (50).
INCIDENCE

Rypins states, "thirty-one and three tenths percent of all causes of death are due to failure of the heart and circulation. Seventeen percent of all deaths between the ages of fifty-five and sixty-four; twenty-eight-and two-tenths percent between the ages of seventy-five and eighty-four, with the highest incidence of twenty-nine percent between the ages of sixty-five and seventy-four." Rypins does not differentiate between the different types of failure, however. (109).

Considering congestive failure specifically, Eggleston places three-fourths of all the deaths from this cause between the ages of forty-one and seventy. Whereas, one-third of all cases appear between the ages of fifty-one to sixty years. (26-b). Cabot (23) states, that out of four thousand autopsies at the Massachusetts General Hospital, 1171 suffered from cardiac lesions, and that fifty-eight percent of these succumbed to hypertensive heart disease. At the Peter Brent Brigham Hospital, Christian found that sixty-one and one-tenths percent of all heart cases were of the decompensated type, and that the condition is more common in females than in males, but that the difference between the sexes is not great enough to be significant. (26-1; 26-6). But Eggleston places the ratio at three males to two females. (25-b).
CLINICAL GENERALITIES

Congestive failure is a syndrome, which is characterized by engorgement occurring in those areas which feed blood toward the failing side of the heart and its outstanding manifestation is an abnormal fullness of certain portions of the vascular bed. This condition must be sharply differentiated from conditions such as peripheral circulatory collapse, which is a manifestation of failure of the circulation, and is characterized by an abnormal emptiness of the vascular bed.

It will be seen in the discussion that congestive failure is of two main types. Failure of the left side of the heart producing pulmonary congestion, and failure of the right side producing systemic congestion. Nevertheless the two types of congestion frequently occur together.
ETIOLOGY

A discussion of the underlying causes of congestive heart failure, would require for each a separate thesis. For that reason, aside from simply enumerating them, any further discussion would be outside the scope of this thesis.

Circulatory failure may be precipitated either by the reduction in the myocardial reserve of the heart working against an abnormal resistance, or as a result of an increase in the burden of a heart whose reserve has already been lowered by myocardial disease. (5-3).

Among the more common causes are hypertension and arteriosclerosis, rheumatic fever and syphilis. Hypertension and arteriosclerosis together are responsible for two-thirds to three-fourths of all the cases of cardiac disease. (50).

Among the less common causes are infections, especially of the respiratory tract, Diptheria, (50) and Trichinosis, the latter rarely, (114) where the increased cardiac work resulting from the rise in metabolic rate caused by the fever, direct poisoning of the myocardium, and cough all conspire to reduce the cardiac reserves to the point where failure ensues. (5-5).

Other etiological factors are: Chronic extensive disorders of the lungs. (50). Pregnancy and Hyperthyroidism, and Rapid Heart, auricular fibrillation, paroxysmal tachycardia, etc. (5-5).
Congenital malformations, severe anemia, bacterial endocarditis, beri-beri are responsible in something less than ten percent of the cases of organic cardiac disease. (25-b).

On the other hand, congestive failure may result, because the heart muscle is so weakened by disease—coronary sclerosis, acute infections, severe anemia and anoxia, that failure ensues though no valvular defect or other condition exists to increase the work of the heart. (5-5).
THE STAGES OF CARDIAC DISEASE

Regardless of the initial cause, the majority of patients with cardiac disorders pass progressively through definite stages. And although these merge gradually into each other, they may be considered separately for convenience.

According to Lewis (81-1), cardiac failure may be divided into two main stages. First the stage of symptoms or waning cardiac reserve, and secondly the stage of circulatory embarrassment and breakdown. Harrison (60), modifies this division somewhat by stating, that there are two stages of cardiac disease which are undergone previous to Lewis's stage of waning cardiac reserve. Harrison says that the first of these is the stage of potential cardiac disease, which refers to "those patients who lack subjective or objective phenomena of cardiac disease, but who have had some disorder which may lead to its development." He cites those with hypertension, rheumatic fever, syphilis, and extensive chronic pulmonary fibrosis. The second stage Harrison calls the stage of "Asymptomatic Cardiac Disease," which refers to those individuals who have definite objective signs; such as, cardiac enlargement or diastolic murmurs—but who are able to carry on a normal life without any symptoms referable to the heart.

The stage of diminished cardiac reserve, refers to patients who are free of symptoms as long as they are at rest, but who suffer from dyspnea on the performance of muscular
exertion of a degree which could previously be performed without discomfort. ( 81-1 ).

The onset of the stage of circulatory embarrassment is present, when the patient becomes conscious of respiratory distress when at rest and occurs when the left side of the heart fails. The failure of the right ventricle, which in most instances occurs later on, is told by the appearance of the phenomena of systemic congestion. (Sala).

Harrison terms the final stage in the progression, Cardiac Cachexia, in which the patients who have had congestive heart failure for a long time eventually develop asthenia, anorexia, loss of weight and anemia. ( 60 ).
THE PRECIPITATING CAUSES OF CONGESTIVE HEART FAILURE

The many etiologic processes which constitute the underlying causes of cardiac disease are usually of progressive nature, and regardless of therapy will in time produce cardiac failure. The rate of progression, however, is usually slow and congestive failure does not usually supervene in the majority of patients until some added factor precipitates it. These precipitating factors are of importance because most of them can be avoided or treated with some measure of success. (21).

I- Infections—especially of the respiratory tract, for aside from the direct poisoning of the myocardium, the fever increases the metabolic rate, which with the usual accompanying cough greatly reduces the cardiac reserves. (5-5).

II- Unusual or violent muscular efforts beyond the capacity of the individual. (21).

III- Cough, which exerts its effect mainly through the muscular effort involved. (5-5).

IV- Pregnancy—Mackenzie was greatly impressed with the importance of this factor, and believed that cardiac disease without symptoms was not a contraindication, but that anyone with any sign of heart failure should be warned against it. (85). Stander and Kuder point out that the heart output increases markedly during pregnancy, and that maternal mortality was three times as high for those mothers with cardiac symptoms. (115). Stanley Meares, states that "heart failure
in the puerperium is a complication that often is unforeseen. The patient may collapse during the third stage of labor, on the following day, or even on the second or third day, and failing compensation sets in and nothing can be done to save the patient." (95). Burwell and Strayhorn (22) hold, that not only is labor itself a very severe strain on the heart, but agree with Stander and Kuder in saying that "throughout the entire course of pregnancy the work of this organ is increased.

V- Obesity- Smith and Willius of the Mayo Clinic, believe that obesity in most cases causes cardiac failure by adding a burden to that imposed by some other disease already present, such as, hypertension or coronary sclerosis, and that any cardiac disease is distinctly more serious if obesity is present. In rare instances cardiac adiposity is primarily responsible for cardiac failure, in that it impairs the function of the heart and the nutrition of the myocardium. (113).

According to Harrison (52), a patient who is overweight has a greater oxygen consumption for a given work and a consequent greater demand on the heart. Furthermore, the high diaphragm may lead to a decrease in the vital capacity and thereby predispose the patient to dyspnea.

VI- Anemia--"It is rare for anemia alone to cause congestive failure, but it is a frequent added factor in patients with organic cardiac disease due to other causes." (21).

VII- Tachycardia and Changes in Rhythm-- "One of the most
frequent determining factors of congestion, according to Lewis, is the onset of very rapid heart action, as in paroxysmal tachycardia or in auricular fibrillation." (81-2). Meakins states, "Pronounced tachycardia appears to play an important role in the production of heart failure. Probably a great decrease in the diastolic period leads to local oxygen debt, accumulation of lactic acid, decrease in glycogen stores, and increase in hydrogen ion concentration, resulting in cardiac fatigue and inefficient systolic function." (91). While Lewis states, "The rapid action affects the heart deleteriously in two ways. First it causes the ventricles to expend more energy. At each of its beats the ventricle must raise the pressure within its cavity to arterial pressure before it begins to do effective work... Secondly rapid beating shortens the time between beats for recovery." (81-2).

VIII- Persistent emotional distress- is rarely a cause of congestive failure but in some instances, they seem to be a decided factor. (21).

Very often these precipitating causes do not operate singly but produce their effects by acting in conjunction. "Thus, a person with lobar pneumonia suffers from the combined effects of infection, tachycardia, cough and psychic disturbances, and anyone of these factors might in itself be sufficient to cause congestive failure to develop in a person already suffering from diminution in the cardiac reserve." (54)
THE DYNAMICS OF CONGESTIVE HEART FAILURE

The "forward-failure" hypothesis ascribes the clinical phenomena of congestive heart failure to a deficiency of the blood supply to the tissues as a result of an inadequate cardiac output. (5-5)

Mackenzie, as we have already seen, was one of the first to emphasize this belief. He states: "The symptoms of heart failure from deficient output of blood might be found in almost any organ did we possess the means of observing them. It so happens that one system which suffers early from an impaired blood supply is one which readily gives rise to distress. This is the respiratory system and it is the distress in breathing on response to effort, which is usually the earliest sign of heart failure. As the heart failure proceeds the distress in breathing becomes more easily provoked until a stage is reached when it is present even when the body is at rest." (84-2).

Sir Thomas Lewis wrote: "Breathlessness is to be ascribed to a deficiency in the flow of aerated blood to the head and neck; at first the deficiency is confined to those exercises which normally the cardiac output is much above the resting values; at last there is a deficiency in the physiological quantity of aerated blood expelled by the heart while the body is at rest." (81-1).

"It is when the output at rest declines that blood begins to collect on the venous side and the patient begins to manifest signs of congested veins and, associated with these, enlargement
of the liver, cyanosis, a high-colored and scanty urine, ascites, dropsy of the lower members, and congestion and oedema of the lungs." (81-1).

Meakins and Long were in agreement with this opinion, when they said; "Circulatory failure may be defined as a state in which the volume of blood circulated per unit of time is not adequate for the physical needs of the moment."

Similarly, Meakins and Davies said, "We are pursuing further work on this question but we would suggest that cardiac failure of this character is due to an incomplete ventricular systole as a consequence of which the circulation rate is greatly and progressively diminished until the amount of circulating blood is grossly insufficient to carry on the functions of the heart, kidneys, nervous system and other important organs." (92).

Blumgart and his coworkers wrote; "It became apparent that circulatory insufficiency consists in the failure of the heart to maintain a blood supply adequate to the ordinary needs of the tissues at any given metabolic level." (10). The same view is expressed by Means, when he states; "The fundamental fault responsible for cardiac dyspnoea is obviously to be found not in the nature of the blood but the rate at which it is pumped...The important point is that the heart either because of increased work, fatigue or degeneration is unable to maintain an adequate rate of blood flow. (94)."
Stewart and Cohn add further support in saying; "The volume output of blood per minute from the heart which is in failure diminished and its size larger than when it is in a state of compensation." (119)

Henderson and co-workers, though physiologists, lend support to the theory advanced by the clinicians just mentioned. For according to them; "The efficiency of the heart is nothing else than the volume of blood that it can pump in relation to the oxygen requirement of the body. This applies to the athlete, the man of sedentary habit and to the cardiac patient." (66).

This then, is the forward-failure hypothesis, and is supported by the authors which have been quoted. It has been advanced because it is easy to comprehend and seems to explain the clinical phenomena. For according to it, a diseased heart has a reduced output, thereby reducing the blood supply to the brain resulting in a state of relative oxygen lack and carbon dioxide excess. The resulting stimulation of the respiratory center gives rise to cardiac dyspnea.

Cyanosis is due to the diminished flow through the vessels of the skin and the greater coefficient of oxygen utilization; the edema, due to increased capillary permeability induced by the local asphyxia, (5-5).

This theory holds that in patients with congestive heart failure, the cardiac output is reduced. That the cardiac output increases with clinical improvement, and that conditions which reduce the cardiac output in proportion to the metabolic needs
result in an increase in severity of the manifestations.

It is now necessary to discuss the evidence concerning these assumptions.

A reduction in cardiac output is the principal assumption advanced by the "forward-failure" hypothesis. Therefore a discussion of the validity of this proposition is in order.

In the paragraphs to follow the term cardiac output, will refer to the output per minute, in contrast to the output per beat, which will be termed the stroke volume.

Stewart and Gilchrist (120) studied the circulation of dogs in which they produced rapid auricular fibrillation and tachycardia with regular rhythm. They found there was a diminution in the output of the heart with auricular fibrillation, and also with tachycardia, whenever a pulse deficit occurred.

Healderson and Haggard, using the ethyl iodide method, found a low cardiac output, in a patient with auricular fibrillation and mitral stenosis, as compared to their normal values (65). Smith and his coworkers, studied two patients before and after restoration of the normal rhythm, with cases of auricular fibrillation. In all cases the cardiac output increased with the restoration of normal rhythm (112). Barcroft et al, using the Fick oxygen method, studied a healthy man, during an attack of paroxysmal tachycardia, in which the minute cardiac output was two and eight-tenths liters, and the stroke volume sixteen cubic centimeters. After the attack the minute output was from five to six liters and the stroke volume
seventy five cubic centimeters. (3).

On the other hand Henderson and Haggard (65) observed that extrasystoles were without influence on the cardiac output of a normal man. And Davies and his associates, (31) using the carbon dioxide method, found that the cardiac output was less in a patient, who had thyrotoxicosis when the heart rhythm was normal, than when the same patient had an attack of auricular fibrillation.

The above investigations do not seem to draw any definite conclusions to indicate that the various irregularities, when associated either with marked tachycardia or with pulse deficit or both, cause a reduction in the cardiac output. However, it should be stated, that in none of the observations were subjects suffering from decompensation used.

In investigations with patients with compensated valvular lesions, Henderson and Haggard (65) reported values of five and two-tenths liters and six and two-tenths liters, respectively, for two patients with mitral stenosis and insufficiency, while their normal patients had outputs of from six to ten liters. Smith and his co-workers, (112), found normal values for minute output in each of their five patients with chronic rheumatic valvular disease. While Cohn and Stewart, (29), studying mitral lesions in dogs by the Fick method, found values far above those found in normal dogs by Marshall (88) and Harrison and Blalock, (56), who used the same method.

The results of these investigations are obviously not in agreement, and because of these variances a dilemma existed for
many years concerning the relationship of cardiac failure to the cardiac output. However, Grollman has shown that most of the methods used were subject to serious inaccuracies, even when normal subjects were used, and that the errors become greatly exaggerated when these methods are used in subjects with cardiac diseases. In 1929, Grollman introduced a method involving the use of acetylene gas, this method gives the most accurate results and has largely superseded the older methods. (5-6).

Using the acetylene method, Grollman found the minute volume of the heart under basal conditions varies in different individuals from three to four and six-tenths liters. The value for a given individual is remarkably constant from time to time, and also the basal cardiac output is a function of the surface area of the body, or is proportional to the basal metabolism. (5-7).

According to Resnik and Friedman, (5-8) in patients with heart failure, the basal metabolism is from ten to sixty percent above normal, and that improvement in the cardiac function was accompanied by a corresponding reduction in the amount of oxygen consumed.

In a separate investigation Friedman and his co-workers, (46) were able to show, that with clinical improvement in cases of congestive failure as evidenced by loss of edema, and increase in vital capacity as a result of rest alone, the cardiac output per minute usually diminishes, but they were unable to demonstrate any consistent change in oxygen utilization.
occurred.

But with the administration of digitalis the cardiac output may increase, decrease, or remain unchanged, and in some patients there may be an initial rise in this function followed by a decline to or below the previous level, while in other instances the reverse changes occurred. (45).

Diuretics likewise may be followed by benefit or by alterations in either direction in the cardiac output per minute. This factor was reduced for several hours following venesection. (45)

The foregoing investigations obviously militate against the cardinal principal of the "forward-failure" hypothesis; namely, that with congestive failure, a reduction in the cardiac output occurs.

In summarizing these investigations, it is evident that a reduction in the cardiac output commonly but not invariably occurs in congestive heart failure, and the reductions in the cardiac output, when they do occur, does not run parallel with the severity of the symptoms. Moreover, the improvement of the clinical condition which follows rest and digitalis is not always attended by an increase in the cardiac output. Furthermore, venesection, which like shock produces a reduction in the cardiac output, is often a valuable therapeutic measure in congestive heart failure. (5-8).

Because of these conclusions, the "forward-failure" hypothesis is obviously untenable in explaining the clinical manifestations of congestive heart failure, excepting in such instances
as paroxysmal tachycardia, heart block, or acute myocardial disease, where there may be a marked reduction in the cardiac output. (5-5).

The majority of cases of congestive heart failure, as it will be seen in the discussion to follow, are best interpreted upon the basis of the "back-pressure" theory, which may be summarized as follows.

As the myocardium fails blood accumulated in the ventricle, which in consequence dilates. The muscle fibers become stretched to a point where they offer an increased resistance to the incoming venous blood. The intraventricular pressure rises, which is transmitted backwards resulting in a rise in the pressure in the veins which supply the affected side of the heart. The increased venous pressure leads to congestion of the organs drained by these veins, (5-5).

The heart does not fail as a whole; the left ventricle usually fails before the right ventricle by a considerable interval of time. However, death may result from the failure of either ventricle singly. (5-5)

Should the left ventricle be the first to fail, it does not adequately discharge its blood, and the pressure rises in the left auricle and in the pulmonary veins, causing engorgement of the vessels in the pulmonary circuit. The volume of blood in this area is greatly increased and the velocity of blood flow then becomes diminished. The engorged vessels encroach upon the air spaces of the lungs, and dyspnea and cough occur. (5-5) Because of a reduction in vital capacity, according
Because the pulmonary engorgement renders the lung tissue less distensible, according to Christie and Meakins. Dyspnea and cough may also occur, in the absence of left ventricular failure, when pulmonary engorgement results from an increased resistance in the pulmonary circuit due to mitral stenosis.

The systemic vessels do not become congested as long as the right ventricle is able to contract forcibly and discharge its contents against the increased resistance in the pulmonary circuit. Subsequent failure and dilatation of the right ventricle are attended by a rise in the intraauricular pressure on the right side, and in the systemic veins with resulting congestion of the liver and abdominal organs, and the vessels of the legs.

Edema and cyanosis appear due to the engorgement of the peripheral vessels and the slowing of the blood through them, for the size of the vessel has increased but not the volume flow (cardiac output) through them.

The "back-pressure" theory does not support the conception that the cardiac output is subnormal in proportion to the metabolic needs continuously throughout the duration of congestive failure. It does support the conception, that the stroke volume, e.g. the output per beat, may be reduced for a few beats, but that this is compensated for by a corresponding increase in the degree of dilatation of the ventricles.

Sir James Mackenzie objects to the "back-pressure" theory, when he says, "A great many people are under the impression that
tricuspid regurgitation occurs only in the last stage of extreme heart failure—a fallacious notion which is the outcome of the "back-pressure" theory....I have watched patients for years with a loud diastolic aortic murmur, and they never showed any trace of heart failure, which might be referred to the effects of regurgitation."(84-3)

Sir Thomas Lewis agreed with Mackenzie in saying, "In the old theory of back-pressure, the pressure was supposed to rise in the right ventricle before it rose in the veins, and the tricuspid valve was pictured as one of the last lines of defence. Incompetence of this valve was regarded as the signal for engorgement of the veins; and so tricuspid incompetence became to be used almost as an equivalent term for venous engorgement."(81-3).

These authors then believed, that the "back-pressure" theory necessarily involved the assumption of regurgitation through the auriculo-ventricular valves. Harrison, however, had demonstrated, that it is possible for the intraauricular pressure to rise, though the auriculo-ventricular valves function normally, because of an accumulation in the ventricle of residual blood. (54). Therefore, it would seem the objections raised by Lewis and Mackenzie were unsound.

Should it be that the "back-pressure" theory is correct the explanation of the clinical manifestations of cardiac failure should be sought in functions other than the cardiac output or volume of blood flow. In such functions as the venous pressure, the blood volume, the velocity of the blood
and in the vital capacity. (5-5).

The evidence bearing upon these premises will now be undertaken. If changes do occur in the functions just mentioned, the validity of the "back-pressure" theory will be supported.

Peabody and Wentworth were in accord with the "back-pressure" concept, when they demonstrated that the reduction of vital capacity resulting from congestion in the lungs, in cardiac failure was in proportion to the severity of the symptoms. (101).

Extensive investigations have been made by Blumgart, in regard to the velocity of blood flow. He found (7), that the circulation time was prolonged in the subjects with compensated hypertensive and arterosclerotic heart disease. The velocity was further prolonged with the development of congestive failure. The vital capacity was often diminished in the subjects with well compensated rheumatic heart disease, but the pulmonary circulation time and the venous pressure were normal. With subjects who had symptoms only on exertion, the venous pressure usually was normal, the pulmonary circulation time was greater, and the vital capacity was decreased. With subjects suffering from congestive failure, the pulmonary blood velocity and the vital capacity were markedly reduced but the venous pressure was elevated. Therefore the increase in venous pressure occurred later on in the progression of the disease, than did the reduction in the vital capacity and the slowing of the blood velocity.
As has been previously stated, page twenty eight, the "back-pressure" hypothesis advances the view that, in the majority of cases one ventricle, usually the left, fails before the other, or the heart does not fail as a whole. (5-5)

Blumgart and Weiss observed that congestion of the lungs occurred at an earlier stage in lesions affecting the mitral valve, such as rheumatic fever, and later in affectionations, such as syphilis, where the left ventricle had to fail before congestion appeared. They were also able to demonstrate, diminution in the velocity of blood or prolongation of the circulation time, and reductions in vital capacity occurred at a relatively earlier stage in the disease in patients with rheumatic fever, and relatively later in patients with syphilis. (11).

Harrison (54) confirms these findings by demonstrating that the vital capacity is reduce relatively early with mitral stenosis, and relatively later on in the disease with hypertension and aortic insufficiency. And states that these findings support the "back-pressure" theory, for in the latter case, the initial strain being on the left ventricle, congestion of the lungs cannot occur until there is marked dilatation of the left ventricle, while in the former case, a rise in pressure in the left auricle occurs and consequent congestion of the lungs occurs at a relatively early stage of the malady, supporting the postulation, that one ventricle fails before the other, and rarely does the heart fail in toto.

A premise of the "back-pressure" theory, has been cited
page twenty nine, that edema and cyanosis appear due to the engorgement of the peripheral vessels and the slowing of the blood through them, for the size of the vessel has increased, but not the volume flow, e.g. the cardiac output through them. The evidence has been presented concerning the reduction in the velocity of blood flow in cardiac failure, which would tend to indicate a diminished volume flow (cardiac output) through the vessel, providing the calibre of the vessel does not increase, or providing that the total volume of circulating blood does not increase, and be in accord with the "forward-failure" hypothesis. It will be seen in the following discussion that the velocity of blood flow can be diminished by dilatation of an area, without altering the volume flow (cardiac output). Also it will be noted that the total volume of circulating blood can increase in cardiac failure and usually does.

Poiseuille's law states: If the pressure head remains unchanged, the volume flow, in a unit of time, in a vessel is proportional to the fourth power of the diameter of the tube. Whereas, the velocity of flow is inversely proportional to the cross area of the vascular bed. (5-9).

The constant pressure head is maintained by the Loewen reflex, i.e. when the arterioles of an organ dilate compensatory vasoconstriction in other areas occurs, maintaining a constant blood pressure to the area where arteriolar dilatation has occurred. (5-9).

However, according to Poiseuille's law, if the total
cross area of the vascular bed of an organ is enlarged, as a result of capillary dilatation, the velocity of the blood is reduced, but the total volume of blood passing through the area is unaltered, or may even be increased. Therefore, it is evident, the size of the stream bed can increase without a diminished cardiac output. (5-9).

Evans and Gibson (35) have found that there is a definite parallelism between the blood volume, and the severity of the clinical manifestations of heart failure. They also found a similar parallelism existed between the circulation time and the venous pressure. And Hamilton et al (49) found, that in congestive failure the intrathoracic blood volume is increased and may be doubled. So in congestive failure the calibre of the vessel may be enlarged, resulting in a diminished velocity flow, without reducing the cardiac output, and also the volume of blood can and does increase in congestive failure.

The statement has been made, that a rise in the intracardiac pressure is transmitted backwards thereby increasing the venous pressure. Blumgart and Weiss were able to demonstrate a rise in the venous pressure of the systemic veins in cardiac failure, (11). The same result has also been obtained by Evans and Gibson (35) and Eyster (38). However, I have been unable to locate investigations illustrating a similar rise in the venous pressure of the pulmonary circuit, in cardiac failure. It seems plausible, that if an increase in the venous pressure does occur in the systemic system in cardiac failure, it
is also likely that it increases as well in the pulmonary system. For by what other means would it be possible for pulmonary engorgement to develop?

The evidence presented concerning the functions of velocity of the blood flow, vital capacity, venous pressure and the blood volume would seem to indicate that the "back-pressure" theory is correct in explaining the manifestations of cardiac failure. However, though the physiological alterations presented by the "back-pressure" theory do occur they do not necessarily indicate that his hypothesis is valid. The hypothesis must also explain the cardinal symptoms of congestive failure.
ENLARGEMENT OF THE HEART

The most outstanding objective sign of cardiac disease is enlargement of the heart, for as Christian states: "Physical examination shows, with few exceptions, an enlarged heart as the most significant departure from the normal. As a rule, this can be made out by palpation, percussion and auscultation. In obese patients, particularly women, in those with emphysematous lungs, and in some patients with thoracic deformity, palpation, percussion and auscultation do not yield sufficiently good evidence of heart size and one is forced to utilize the x-ray....however, for all clinical purposes in most patients simple palpation and percussion give all the needed information as to heart size. Slighter degrees of enlargement, not detectable by simple means of physical examination, are rarely of any particular clinical significance." (26-3). However, White states, that pericardial effusion or chronic constrictive pericarditis may produce the signs of congestive failure without cardiac enlargement, venous distention, edema and engorgement of the liver with a heart which is neither hypertrophied nor dilated. (122).

Today, different workers advance varied opinions as to the causes of cardiac enlargement. Boas and Landauer believe that a high metabolic rate is the principal cause (11aa). Hemingway and Fee (64) disagree and do not believe that a high metabolic rate is the cause, instead stating the enlarged heart simply consumes more oxygen. Starling and Visscher agree with Hemingway and Fee, in that the oxygen consumption is de
determined by the degree of enlargement. (116).

Other workers, such as Porter (104) and Lewis and Drury (82) ascribe enlargement as due to alterations in the nutritional stage of the heart.

Boyd states: "The usually accepted theory of enlargement of the heart, is that of work hypertrophy." and in continuing he says, "Whether prolonged increased work without a period of abnormal overload and injury can cause hypertrophy is still an open question. (16-2)

Christian, however (26-2) is inclined to favor the view, that hypertrophy is the result of disease of the heart muscle. Christian states: "To say that the heart muscle fails by reason of fatigue following sustained overwork is no real explanation for very often we have no evidence of overwork to cause the fatigue or to cause the hypertrophy preceding the fatigue. Are we really sure that the heart can undergo a work hypertrophy? There is no satisfactory evidence that physical work of any sort leads to considerable cardiac hypertrophy of the heart. We seem almost forced to conclude that hypertrophy with incident dilatation of the heart is a potential evil; that in some way, as soon as the heart becomes much enlarged, it is placed at a disadvantage and fails to do work put upon it with its previous efficiency; that once started it is a vicious circle, less efficient work causing further hypertrophy, leading to a still greater decrease in efficiency."

Boyd is in agreement with Christian as regards the production of a work hypertrophy in athletes, when he says: (96-2)
"Contrary to the usual belief, prolonged indulgence in athletics does not lead to an abnormal increase in the size of the heart." However, Steinhaus et al. recently studied under carefully controlled conditions, the effects of running and swimming on the organ weights of growing dogs. They stated: "Exercise produced a true work hypertrophy of the heart which, under the condition of our experiments, was more marked in swimmers than in runners... The cardiac hypertrophy involves both ventricles with just a little excess in favor of the left heart... There is no indication of a comparable hypertrophy of the skeletal musculature of the limbs nor of the limb bones. (118).

Yet, according to Boyd, (16-2) in patients with aortic stenosis or arterial hypertension, there is supposed to be a work hypertrophy, the individual muscle fibers increasing in size, but there is, a difficulty in this way of explanation, for there are instances of a long-continued hypertension without hypertrophy. However, except for Eyster's work, it would seem to me unjustifiable to conclude, that because a person has a valvular lesion or hypertension the work of the heart is necessarily increased.

Eyster (37) has shown experimentally that partial obstruction of the aorta for only a few days will lead to hypertrophy of the left ventricle as marked as when the obstruction is maintained for months.

The previous discussion has evidently not explained the causes of hypertrophy. All are agreed that hypertrophy does
occur, and regardless of whether it is due to overwork, deficient nutrition, or a disease process of the muscle, it is now necessary to consider the relationship between hypertrophy and dilatation.

Christian states: "So far as dilatation versus hypertrophy is concerned, I have never seen any gain from an attempt to make a distinction. Whenever the heart is enlarged, in a clinical sense both hypertrophy and dilatation are present. One may assume that increasing signs of cardiac failure are associated with an increasing preponderance of dilatation over hypertrophy. However, there is little real evidence for such an assumption. One very striking thing is that cardiac enlargement very infrequently, if ever, waxes and wanes in a way to suggest a considerable degree of dilatation that is recovered from. It almost seems true that once enlarged, the heart remains enlarged, and that enlargement after it begins progresses without regressions. If this is true, then dilatation apart from its association with hypertrophy, plays very little part in cardiac disease. (26-4).

And Sir Thomas Lewis states: "that it is not dilatation that is injurious, but that which is responsible for dilatation." (81-4)

Perhaps the conception held by Christian and Lewis, as regards the part dilatation plays in heart disease, is not entirely correct. For the law of the heart states; The energy set free at each contraction of the heart is a simple function of the length of the fibers composing its muscular walls." (5-10) And the investigations by Starling and Visscher (116) and Hemingway and Fee, (64) indicate that the amount of oxygen used by
the heart is dependent not so much on the actual work performed as on the degree of dilatation, or in other words, a normal heart with a small diastolic volume will require less consumption of oxygen per minute to do the work than a diseased heart, which has to dilate in order to do the same work. Therefore the normal heart is a more efficient heart because it can convert relatively more of the energy expended into mechanical work simply because of its smaller diastolic volume. (116).

Evans and Matsuoka were able to show that the oxygen consumption of the heart was less per minute at slow heart rates, but greater per beat, than at fast heart rates, and that the heart was a more efficient organ at slower rates because with each beat, part of the energy was required to open the valves by raising the intraventricular pressure before expulsion of blood could take place. (36)
THE PRODUCTION OF FAILURE IN ENLARGED HEARTS

The explanation of why and how the myocardium fails has never been adequately explained. Christian by his definition "Chronic Myocardial Disease" has attempted to explain, the failure as being due to a disease process. He frankly admits, however, that "during life the clinician recognizes the condition with such accuracy that in most cases the pathologist in his post-mortem studies adds but little to the diagnosis of the clinician, except for the enlargement, there is little to be found that is abnormal in the heart muscle, nothing to account for the presence of a disease process." (26-2) It would seem, therefore, that myocardial failure cannot be attributed to an underlying disease process, if the term disease process, so used, does not include pathological physiology as a distinct disease process in itself.

The Starling school have attributed the condition to lack of tone of the heart muscle or fatigue. Starling stated: "It is evident...that the word tone is properly employed as synonymous with the physical condition or fitness of the muscle fiber and its measure is the energy set free per unit length of muscle fiber at each contraction of the heart....A heart in good condition, e.g., one with a good tone, will carry on a large circulation against a high arterial pressure and nearly empty itself at each contraction while a heart with a defective tone, as in the case when it is tired, can carry on the same circulation; but only, when its ibers at the beginning of each contraction are much longer. i.e., when the heart is dilated.
In the latter case the output of blood will be the same as in the former, but both the systolic and the diastolic volumes of the heart will be increased. (116-a)

It is evident from this conception that a fatigued heart is one in which the emptying is not as complete during each filling, but that the fatigued heart can maintain a given output provided the degree of filling and the residual blood is increased, and for a failing heart to maintain a given output it must dilate. Starling in continuing states: "But the demonstration of the connection between dilatation of the heart and energy of contraction does more than merely bring the behavior of this organ into line with that of voluntary muscle. It enables us to form a picture of what is occurring in the heart in all the vicissitudes and changes in stress to which it is exposed in the course of a man's life. Thus, if a man starts to run, his muscular movements pump more blood into the heart, so increasing the venous filling, while the central nervous system, by contracting the arteries of the abdomen, increases the peripheral resistance, raises the arterial pressure and forces all the available blood through the active muscles. As a result the heart is overfilled during diastole, and is impeded from emptying itself in systole; its volume both in systole and diastole enlarges progressively until by the lengthening of the muscle fibers so much more active surfaces are brought into play within the fibers that the energy of the contraction becomes sufficient to drive on into the aorta during each systole the largely increased volume of blood entering the heart from the veins during the diastole." (116-a).
"In these circumstances therefore the heart is dilated. But in a healthy individual this condition is only temporary. A rise of arterial pressure produces a more abundant flow of blood through the vessels supplying the wall of the heart, and this increased supply of oxygen and foodstuffs improves the physiological condition of each muscle fiber, so that at each contraction it is able to concentrate a larger number of active molecules on each unit of active surface than it could previously. The physiological conditions, or what we are accustomed to speak of as the 'tone' of the heart, is thereby improved and the heart gradually returns to its normal volume even though it is doing increased work. It is only when the heart is fatigued or diseased that this secondary improvement fails to appear. Then we find that the heart remains dilated over the whole period of increased work, and if the work is prolonged this dilatation may become permanent. In a failing heart the concentration of active molecules per unit surface becomes less and less, so that this surface has to be continually increased by dilatation of the heart. If this goes on sufficiently long the dilatation may pass the optimum length of muscle fiber and the muscle then has to contract at such a mechanical disadvantage that the heart fails altogether. With the failure of the 'prime mover,' all other mechanisms of the body stop work, and the animal is dead." (118-a).

Starling then, regarded fatigue of the heart as the cause of failure and that fatigue was due to an increasing dilatation, beyond the mechanical reserve of the heart muscle fiber.
Starling also believed, that the cardiac output remained constant even though an increasing dilatation occurred. (116a), which is in agreement with the conclusions previously stated in this thesis; namely, that with certain exceptions, cardiac failure can occur without a necessary change in the minute volume of the heart.

Also, it has been previously stated that congestive failure is almost always accompanied by a rise in the venous pressure. This consensus is in agreement by most workers, especially for the systemic system, where Blumgart and Weiss (11) were able to demonstrate it. Though not proven in the pulmonary system it is a generally accepted view. Starling believes it is because of the increased venous pressure, that a constant cardiac output is maintained, even though the heart is dilated.\(116 a\)

From the results of the above investigations, it seems reasonable to conclude by saying the inefficient heart is the failing heart, for the heart maintains a normal output, but due to the change in the relationship between the output and the venous pressure, which has occurred, a greater diastolic chamber volume results and mechanical work takes place with a greater expenditure of energy, and in doing so consumes more oxygen.
THE RELATION OF THE CARDIAC RATE TO FATIGUE.

Cardiac failure is usually accompanied by tachycardia, but until the very advanced stages, it is only tachycardia on exertion. Tachycardia at rest, except in advanced heart failure, is unusual except when there is an underlying hyperthyroidism, or a definite form of arrhythmia or both. A very rapid heart rate at rest is suggestive of some of these rather than of a simple heart failure. (26-5).

Bainbridge experimentally proved the increase in heart rate is induced by arise in the pressure of blood entering the right auricle. The mechanism responsible for this, is a reflex, which today bears his name, and is carried out presumably through the afferent vagal terminations beneath the endocardium and in the walls of the great veins near their entrance into the auricle. The increase in rate is an advantage in that it lowers the venous pressure, and allows the heart to maintain a constant output with a lesser degree of dilatation. (5-12). But as has been previously cited, page forty one, Evans and Matsuoka demonstrated that a slow rate rather than a fast rate could maintain a given output more efficiently. (36). Starling and Wisscher have shown, that per unit of time the oxygen consumption was greater at fast rates than at slow rates, for a given volume of blood. (116).

Lewis states: "One of the most frequent determining factors of congestion is the onset of very rapid heart act on, as in paroxysmal tachycardia or in auricular fibrillatio ... It causes
the ventricles to expend more energy...and secondly rapid beating shortens the time between beats for recovery." (81-4).
And as Meakins said: "Probably a great decrease in the diastolic period leads to local oxygen debt, accumulation of lactic acid, decrease in glycogen stores, and increase in hydrogen ion concentration, resulting in cardiac fatigue and inefficient systolic function. (91).

Wiggers and his associates point out (123-a) that, there is a considerable blood supply to the myocardium during systole. They state, that the systolic blood flow is probably greatest in the right ventricle and in the external portions of the left ventricle. In the innermost fibers of the left ventricle the pressure is probably higher than in the aorta and hence there is presumably a cessation of the blood flow during systole. Since the duration of systole is relatively independent of the heart rate, when the output and the peripheral resistance remain the same, (5-11), it is obvious, that the total duration per minute of diastole must be very much less at a fast rate, than a normal rate. Hence at the faster rate, the oxygen need is increased, and the oxygen supply to the heart, especially to the left ventricle may be seriously interfered with.

The above discussion tends to make clear, that the diastolic interval must be sufficiently long for the process of recovery to take place through oxygenation of the heart muscle. However, it is a well known fact, that many smaller animals have very fast heart rates, many of them corresponding to the rate
of the human heart in auricular fibrillation and paroxysmal tachycardia. Since it has been indicated that the diastolic interval is greatly reduced with fast heart rates, it would seem impossible for these animals to continue their lives, unless the diastolic interval were sufficient to insure proper oxygenation.

Harrison and co-workers, studied this question. (55). They measured cardiac fiber thicknesses in various animals, and were able to show that a relationship existed between the normal heart rate of an animal, and the thickness of the cardiac fibers in that animal. The cow had the slowest rate of sixty, and the thickest mean fiber diameter of seventeen and six-tenths micra. While the rat with a rate of three hundred and forty per minute had the smallest mean fiber diameter of eleven and two-tenths micra. For a man with a normal heart, the mean fiber thickness was seventy three micra and a pulse rate of seventy three. But a man with an enlarged heart without failure with a pulse of eighty four, had a mean fiber thickness of twenty four and five tenths micra. Whereas, in the case of a human heart, which had failed the mean fiber thickness was thirty one and eight-tenths micra, the pulse rate was but seventy six, however this patient had been digitalized. These workers believed that in the animals with smaller mean fiber thicknesses, oxygenation of that fiber could take place more rapidly, in other words, in a shorter diastolic interval, thus accounting for the fact that smaller animals were able to live their lives with fast heart rates, in which the diastolic
interval is very meager. Should this observation be correct, it also would indicate (not prove) that in man, hypertrophy of the heart muscle fiber would require a greater diastolic interval, or slower pulse rate, for recovery to take place, than in the normal heart.

Starling held (116-a) that dilatation of a heart, even the temporary dilatation of a normal heart during exercise, was a response which offered a chemical advantage because of the greater surface exposed to the active molecules, but that dilatation placed the heart at a mechanical disadvantage. It has been advanced in the previous discussion, that because of the lessened mechanical ability of the stretched fiber, that fiber by some means, as yet unknown hypertrophies. The hypertrophy offers the heart in turn a greater mechanical advantage, but the former chemical advantage of easier oxidation is again insufficient for the requirement of the organ. In order to regain this advantage the heart muscle again dilates, the fiber stretches, but more so than formerly, because the muscle fiber is now greater in diameter. (117-a) It would seem by this chain of events that a vicious cycle is inaugurated in failing hearts by processes, which once compensatory and benign, become malignant, producing congestive heart failure and its many manifestations, providing the conceptions of Starling and the other workers are correct in this regard.
MINERAL CHANGES IN FAILING HEARTS

Wilkins and Cullen (125) compared the potassium, phosphorus, sodium, chlorides, magnesium, calcium and total base contents of a series of normal hearts from persons dying accidental deaths, with those of patients dying from congestive failure. The latter group showed a diminution in the content of potassium, phosphorus and magnesium, but an increase in sodium in both ventricles. The left ventricle was the richer in both groups of hearts in potassium, phosphorus and magnesium, but poorer than the right ventricle in chloride and sodium. Calcium did not show any consistent findings, while the total base was usually lowered in the congestive failure group. In general the failing hearts were richer than normal in those elements which are normally more abundant in tissue fluids, and poorer in the substances which are normally more abundant in the tissue cells. The significance of these changes had to date not been investigated.

According to Hermann, and his co-workers (68) the creatine content of hypertrophied cardiac muscle is diminished in congestive failure hearts, but normal or elevated in hypertrophic hearts, in which failure had not occurred.

The fact that creatine plays some part in the contraction of muscle, may indicate that the development of failure and fatigue may be favored by a loss of creatine. However, this proposition is purely hypothetical, and I am unable to find evidence pointing to the probability of this occurrence.
According to Harrison (51), congestive failure may be associated with many different clinical manifestations, but in practically every patient with congestive heart failure, three abnormal signs appear during some stage of the disease. These are cardiac enlargement, which has been discussed, dyspnea and edema.

Dyspnea is important because it is ordinarily the first and often the last subjective manifestation of left sided heart failure, and it usually causes the patient more distress than the other symptoms combined. Furthermore the index of prognosis and guide to treatment can often be determined by the degree of dyspnea present (51, 60).

Harrison classifies dyspnea as follows: (51, 60) but states that the same patient may suffer at the same time from several of the clinical types.

I----Dyspnea due to cardiac disease per se.

A--Dyspnea on exertion.
B--Dyspnea at rest.
   1-Nocturnal dyspnea.
      a--occurring before the onset of sleep.
         1-Orthopnea.
         2-Evening Dyspnea.
      b--occurring after the onset of sleep.
         or Paroxysmal dyspnea.
            1-Cardiac asthma.
            2-Cheyne-Stokes Respiration.
   2-Continuous dyspnea.

II----Dyspnea due to Complications.
DYSPEAN EA IN EXERTION

Dyspnea in exertion, occurs in all types of cardiac disease regardless of the underlying cause. It is a particular feature of certain chronic heart sessions; e.g. mitral stenosis. The patient is aware that exertion which previously could be performed without distress, now causes some panting. The symptom is progressive in nature, and the rate of progression varies with the person and the underlying cause of the heart disease. The rate is most rapid with cases of syphilitic insufficiency, and least rapid with congenital heart lesions. However, other factors also influence the rate of progression, such as overindulgence, in any form, superimposed infection and other precipitating factors, eventually the patient realizes that the symptom occurs with the slightest effort, and he is only comfortable at rest. (60)

The proponents of the "forward-failure" hypothesis conceived breathlessness to be essentially as Sir Thomas Lewis states: "Breathlessness is to be ascribed to a deficiency in the flow of aerated blood to the head and neck; at first the deficiency is confined to those exercises in which normally the cardiac output is much above resting values; at last there is a deficiency in the physiological quantity of aerated blood expelled by the heart while the body is at rest. The deficiency, in the later stages, consists not only of inadequate flow, but also of insufficient aeration. (81-1). This concept holds, therefore, that a person becomes short of breath during exertion because the supply of oxygen and the elimination of
carbon dioxide do not keep pace with the need of the tissues, and the dyspnea is a compensatory mechanism for the deficiency of the circulation.

The "forward-failure " school supported these views with the results of experiments performed by Gesel, who has shown the blood flow through the brain to be a factor in the control of the volume of breathing. (60). And the investigations of Hill and Lupton (69). According to them, muscular exercise produced lactic acid. Most of this lactic acid would be reconverted to glycogen by the available oxygen, but during exercise the oxygen supply was inadequate, and an oxygen debt resulted. Therefore the lactic acid which was not reconverted tended to cause a muscular acidosis. The "forward-failure" school, then, believed that the oxygen debt was greater in persons with cardiac failure because of the diminished ability of these patients to increase their cardiac outputs. However Hill and his coworkers stated that the ability to acquire an oxygen debt depended on the power of the tissues to buffer lactic acid. (69).

Harrison and Pilcher, were able to show, that patients with cardiac failure have much smaller oxygen debts following the severest muscular exertion of which they are capable, than do normal persons at the end of maximum exercise. They believed that in these patients muscular exercise is checked by rapid breathing long before the exercise has become sufficiently severe to produce a large oxygen debt. (61). If the results of this investigation are correct it is not the oxygen debt which causes the dyspnea in these patients. Harrison and Pilcher believed, however, that the buffering power of the skeletal muscles was diminished in patients with cardiac disease. (61). And
because of this it may be possible for acidosis of the blood to cause the dyspnea. (61).

But Cullen et al (30) in order to determine whether acidosis of the blood, following exercise, was the cause of dyspnea in cardiac disease, withdrew arterial blood immediately before exercise, during each two minutes of exercise and during the minutes minutes following exercise from normal patients and those suffering from mild congestive failure. They found, that neither during, nor after the exertion were there increases in hydrogen ion concentration and carbon dioxide tension or oxygen decreases in the oxygen saturation of the blood. This observation was unique in that it concludes that the increased ventilation produced by mild exercise is not due to alterations of the blood causing an acidosis, which in turn stimulates the respiratory center. Furthermore, since Gesel, had shown the blood flow through the brain is a factor in the control of respiration, (60) (30). Cullen and his co-workers took blood from the internal jugular vein before and immediately after exercise. They found the jugular venous blood usually had a slightly lower carbon dioxide tension and was usually slightly more alkaline after exercise than at rest, but acidosis was not evident. (30)

The evident conclusion from such work is, that stimulation of the respiratory center by oxygen want or carbon dioxide excess is not, in the absence of cardiac failure, responsible for the dyspnea, since the oxygen saturation of the arterial blood is
not reduced to any important degree and the carbon dioxide tension is about the normal level, or, even may be below that level. (5-13).

According to Drinker and his coworkers (27-a) congestion of the lungs leads to diminished expansibility of these organs, causing a diminution in vital capacity, which in turn decreases the maximum possible ventilation and thereby predisposes to dyspnea, because this symptom occurs when the actual ventilation becomes more than a certain fraction of the maximum possible ventilation. Christie and Meakins (27) likewise consider diminished distensibility of the lungs, resulting from pulmonary engorgement as the prime cause of cardiac dyspnea. They agree with Drinker et al., in that the reduction in the vital capacity is roughly proportional to the dyspnea, but the two do not bear the relationship of cause and effect, since the subject's vital capacity is always greater than the volume of air required for the exertion which causes the dyspnea. Because, however, of the diminished distensibility—the stiffness of the lung—a greater inspiratory effort is expended in breathing the extra volume of air which the muscular exertion demands. (27). In other words, a stiff lung requires a greater inspiratory effort to distend itself. And whereas, the elastic lung is able to expire air by a passive act, this stiff lung has to squeeze the air from the chest, and the intrapleural pressure becomes, therefore, positive near the end of expiration. The decreased distensibility of the lung, for the same reason that
it increases the difficulty of enlarging the volume of tidal air, reduces the vital capacity. And dyspnea and vital capacity are, therefore both effects due to a common cause. (27).

The reduced distensibility will also have the effect of increasing the sensitivity of the Hering-Breuer Reflex with the production of shallow breathing. The drug morphine is beneficial in these instances because it reduces the sensitivity of the vagal endings. (27).

Christie and Meakins believe with the marked slowing of the circulation in congestive heart failure the effect of oxygen lack and carbondioxide excess may be a factor in addition to the pulmonary factor. But they believe, this is a mechanism of very minor importance. Even so, they believe an arterial anoxemia may exist, because of unequal ventilation of the alveoli, with a normal or even a subnormal carbon dioxide content of the arterial blood, even in the absence of pulmonary edema. But they state, that when this occurs the factor of oxygen lack becomes of more major importance in the production of dyspnea. (27).

Harrison et al (60) agreed with Drinker et al (27-a), that pulmonary congestion may cause dyspnea of some types, but not that of exertion, for exercise did not produce a greater degree of pulmonary congestion in normal persons or patients with mild cardiac symptoms, to account for an increasing breathlessness with exertion. They did concede, that pulmonary congestion was present, however, it did not increase in this instance.

Harrison and his co-workers, noting that the increase in
commenced almost at the onset of exercise, believed dyspnea on exertion was due to a nervous mechanism. They actively and passively exercised the muscles of the arms of their subjects, in which the blood supply to and from the muscles, had been shut off by pressure cuffs. They noted the respirations immediately increased. (60)

Barrison et al, then amputated the hind leg of a dog, which previously had demonstrated increased respiration with passive movements of that leg. Severing all connections between the leg and the trunk, except the sciatic nerve and the femoral vessels, which were clamped, with passive exercise of the leg an immediate increase in breathing was noted. Cutting the spinal cord at the fourth dorsal level caused the increase in breathing to cease even though exercise was continued. These workers concluded, that dyspnea on exertion was reflexic in origin in the normal person and in the patient with mild cardiac disease. But this did not explain why the person with cardiac failure had a greater increase in ventilation than does the normal individual. (60).

Barrison and associates believed, since patients with congestive failure had a higher venous pressure than normal, the pulmonary congestion was responsible for the higher venous pressure of these individuals, even though the pulmonary congestion did not increase significantly with exercise. And it is because of this increased venous pressure in the patient over the normal person, that a greater increase in ventilation occurs in such individuals. In an investigation they suddenly raised the venous pressure by injection of fluid, and by inflating a balloon in the
right auricle, and were able to demonstrate that the increased venous pressure resulting, caused an increase in the ventilation rate as long as the vagi were intact. Upon cutting these nerves the increase in venous pressure had no effect. They concluded that venous pressure causes reflex stimulation of respiration, and because the patient has some pulmonary congestion he is more likely to feel respiratory distress at any given level of ventilation than the normal individual. (57).

These investigations seem to indicate, muscular exercise in both the patient and the normal individual, causes an immediate increase in ventilation by means of a reflex. Somewhat later a further increase occurs in respiratory rate due to a rise in venous pressure instituted by means of the Bainbridge reflex. Since the patient with cardiac disease has a greater increase in venous pressure he demonstrates a greater increase in ventilation that does the normal person. Furthermore, after exercise the patient because of the continued stimulation from the increased venous pressure, which persists for some time after exercise, returns to his resting respiratory level later than the normal subject.

The previous discussion of dyspnea on exertion seems to indicate, that this sign is not due to stimulation of the respiratory center by an increased hydrogen ion concentration, but is possibly due to pulmonary engorgement causing a less distensible lung, or due to a reflex from the active muscles. And dyspnea appears sooner and persists longer in cardiac patients because of the increased venous pressure as compared to the normal individual.
Orthopnea is a type of breathing occurring in advanced cardiac disease. The breathlessness appears or becomes more pronounced in the recumbent position, for the patient becomes dyspnea on lying down. (5-145).

Many different theories have been proposed to explain the more difficult breathing in the recumbent position.

Krehl attributed the condition to a diminished cerebral blood flow. Believing that the normal gaseous interchange is reduced in cardiac failure, between the blood and the respiratory center. (71).

Haldane et al, believed the condition due to a deficient aeration of the pulmonary blood in the recumbent position. A normal person, to them, could compensate for the uneven expansion of the lungs upon lying down, but an individual with cardiac failure could not compensate because of the reduced vital capacity, and therefore developed anoxemia and resulting dyspnea. (48).

Field and Bock considered orthopnea as due to an increase in the cardiac output in the recumbent position, which was caused by an increase in the degree of pulmonary congestion. (40). However, Grollman demonstrated that the cardiac output was approximately the same in the two positions. (47).

Harrison et al, believe the assumption of the recumbent position causes an increase in congestion of the lungs, further diminishing the vital capacity of the patient, whose respiratory reserve was already lowered below normal. The increasing
congestion causes a reflex over the vagus nerves to the respiratory center, which in turn increases the respiration. \(57\).

Christie and Meakins (27) insist dyspnea and the reduction in vital capacity are due to a common cause. That cause being an increased distensibility of the lung resulting from an increase in the degree of pulmonary congestion. They believe sitting up causes a draining of the the blood from the chest relieving pulmonary congestion. The lung then becomes more distensible and the Hering-Breuer reflex becomes less sensitive, in turn slowing the respiratory rate.

Whether orthopnea is due to a decrease in the lung distensibility, or due to a reflex over the vagus nerves, the weight of evidence suggests, as in the case of dyspnea on exertion, the condition is due to an increase in the pulmonary congestion upon lying down, rather than to a deficient aeration of the respiratory center from diminished cerebral blood flow, or diminished carbon dioxide tension, which are advanced by the proponents of the "forward-failure" theory.
THE PRODUCTION OF EVENING DYSPNEA

Harrison and his coworkers have given the name evening dyspnea to dyspnea, which develops gradually during the day, reaching its maximum in the evening hours just before the patient goes to sleep. According to them, it is not paroxysmal in nature. They attributed this condition to an increasing pulmonary congestion developing during the day, resulting from an increased bodily metabolism during the waking hours. They found the vital capacity was less in the evening than in the morning, and assumed a vagal reflex stimulated the respiratory center causing the increase in rate of respiration. (63).

Again, Christie and Meakins (27) believe, that the increased pulmonary congestion leads to a less distensible lung, and results in a more sensitive Hering-Breuer reflex.
THEORIES AS TO THE PRODUCTION OF CARDIAC ASTHMA.

Cardiac asthma is the term applied to paroxysmal attacks of dyspnea occurring, usually at night, in patients with heart disease, especially those with an underlying hypertension or an advanced arteriosclerosis. (5-15). However, McGinn and White noted mitral stenosis to be frequently associated with cardiac asthma. (90) Assuming the upright position tends to relieve the dyspnea. The cause of the attack is unknown, though several theories have been advanced to explain its production. (5-15)

W.G. Harrison, Jr. and associates stated: this condition must be clearly differentiated from other paroxysmal seizures which may occur in persons with an entirely different type of cardiac disease, and which may simulate attacks of cardiac asthma. For instance, cor pulmonale which results from chronic pulmonary disorders, such as asthma and bronchiectasis, and in which the seizures are due either to the associated bronchial asthma or to the effect of coughing induced by bronchitis. The seizures, though they may occur during sleep, are never followed by acute pulmonary edema. Cor pulmonale with asthma can be differentiated by some other clinical findings, such as clubbing of the fingers, marked cyanosis, the presence of persistent wheezing throughout the day, allergic history, and a history of a chronic cough. The predominance in the x-ray of right ventricular enlargement is another point in differentiation. (62)

Plotz states that the differentiation of asthmatic heart
failure from bronchial asthma is difficult, especially when there are moist as well as wheezing rales, or when there is some degree of right heart failure present. Response to adrenalin will not differentiate, nor will measurements of the venous pressure. But the most reliable diagnostic feature is the circulation time, which is reduced in cardiac asthma. (103).

In 1878, Welch concluded that pulmonary edema was a result of a difference in the amount of blood pumped by the two ventricles. The right ventricle pumped more into the lungs, but the dilated left ventricle was unable to pass on the blood it was receiving from the auricle and the pulmonary circulation. (62-a).

Weiss and Robb (121) found no constant alteration in the cardiac output during the seizures to account for them on a basis of an increase in the cardiac output. They found that during the attack, there is engorgement of the pulmonary vascular bed, due to left ventricular failing (not complete failure), a tendency to pulmonary edema and a marked reduction in the arterial oxygen saturation, as well as, a reduction in the vital capacity.

Fraser et al, discounted the theory that an increased hydrogen ion concentration of the arterial blood was responsible for the attacks, stating; an increased hydrogen ion concentration occurred only in moribund patients or in those with extensive pulmonary disease. (43).

Gollwitzer-Meier believe the passage of water into the
blood stream at night from the tissues led to pulmonary engorgement in individuals with failing left ventricles. The engorgement resulted in a decrease in the residual air, which in turn caused a reflex stimulation of breathing. Gollwitzer-Meier believed morphine and pituitrin were beneficial in this condition because they tended to make the tissues hold water. (121-a).

Wassermann believed paroxysmal dyspnea was reflexic in nature. The reflex arose in the aorta, from a rise in blood pressure and an increase in pulse coming on just before the attacks. He was able to produce an antagonistic reflex by pressure on the carotid sinus. (123-b).

With cases of mitral stenosis, McGinn and White, believed the mechanism of producing acute pulmonary edema, which may or may not be accompanied by cardiac asthma to be first a speeding up of the heart, through excitement, effort or paroxysmal tachycardia. The strong right ventricle pumped more blood into the pulmonary circulation, than could be passed through the stenosed mitral valve in the same unit of time, and engorgement was the result. (90).

Christie and Eakins suggest the seizures are due to pulmonary congestion occurring suddenly, thereby producing a less distensible lung, and consequent stimulation of the vagal endings setting up the Hering-Breuer reflex. (27).

W.G. Harrison Jr. and co-workers believe, that cardiac asthma is the result of a combination of two factors, which may occur simultaneously. The first is the diminished respiratory
reserve present in these patients, due to pulmonary congestion. The second factor occurs after the onset of sleep, and is precipitating in nature, when the exciteability of the nervous system is decreased. At this time the precipitating factors, which are unpleasant bodily stimuli reach an intensity beyond which the subject would permit if awake. (62). They mention as precipitating factors, cough, which is the most common, nightmares, and unpleasant dreams; abdominal distention, constipation, desire for urination, the amount of activity indulged in during the preceding day, excessive environmental heat, and the position of the body. They believe, that after a variable time these stimuli become strong enough to awaken the patient, and the respiratory rate is then suddenly increased because the nervous system becomes suddenly more exciteable in an individual with an already diminished respiratory reserve.

The subsequent course of events, according to W.G. Harrison et al, depends on a balance between two opposing groups of factors, such as expectoration of mucous in coughing, or the relief of apprehension from nightmares etc. Combined with the assumption of the upright position, tend to diminish the respiratory volume and favor abolition of the attack. But on the other hand, a greater venous return to the heart is favored by the greater ventilatory movements, and an increased degree of pulmonary engorgement is produced which causes further stimulation of respiration. Also in these cases, the vicious cycle inaugurated will predominate over the factors which would tend
to relieve the attack, and the seizure becomes progressively worse unless morphine is given, which decreased the sensitivity of the respiratory center, breaking the cycle. If this fails the lungs become more and more congested and in time acute pulmonary edema sets in. The edema results in anoxemia which stimulates respiration further, and edema here causes cough which further aggravates the condition. (62).

The foregoing discussion concerning the various theories responsible, indicates the true mechanism of cardiac asthma is as yet an argument among the different investigators, and that further experimental proof is necessary before the correct answer is known.
THEORIES as to the PRODUCTION OF CHEYNE-STOKES RESPIRATION.

Cheyne-Stokes respiration, or periodic breathing is characterized by its waxing and waning. E.g. a period of breathing occurs in which the individual respirations are small and slow to start with but gradually increase in depth and rate to a maximum and then, subsiding again, finally cease for a time. The hyperneic and apneic phases last each for about thirty seconds. A tendency to this type of breathing is commonly shown by healthy infants and occasionally by normal adults during sleep. The most common clinical conditions in which periodic breathing occurs are advanced renal and cardiac disease, asthma, and cases of raised intracranial pressure. It is also seen in severe pneumonia and in morphine administration, following chloral poisoning or a general anesthetic. Clinically Cheyne-Stokes respiration is usually a grave omen and is probably the result, in most instances, to damage to the respiratory center due to oxygen lack. (5-15).

Periodic breathing must be differentiated from cardiac asthma, since the two are often confused, however they may both occur in the same patient at different times. Periodic breathing usually is especially marked just at the onset of sleep, while cardiac asthma appears after the patient has been sleeping for an hour or more. Periodic breathing is only rarely complicated by acute pulmonary edema, which is frequent
with cardiac asthma. Periodic breathing usually appears in somewhat older patients, and most important the breathing is irregular, while in cardiac it is regular. (58).

Harrison and associates found that breathing was usually regular while the patient was awake, but as the patient began to doze, periodic breathing commenced and usually lasted for about thirty minutes. With deep sleep breathing again became regular. They found also, that with the onset of sleep apnea would appear, but in about twenty seconds the patient would wake up and the hyperpneic phase commence. As the patient again commenced to doze the apneic phase would again appear. They also noted any factor which either causes the patients to approach the waking state precipitated periodic breathing. Coughing was the most frequent precipitating factor, desire for urination another. They concluded that periodic breathing is related to the transition state between wakefulness and sleep. (58).

Harrison et al, were unable to find any constant changes in the blood gases, in their subjects. The hydrogen ion concentration was within the normal range, some subjects displayed an anoxemia, while others had a very high arterial saturation. (58).

Though periodic breathing rarely occurs in forced breathing, Douglas and Haldane (34) induced it in normal persons by voluntary overventilation, they believed that oxygen want acted as a stimulus to the respiratory center, and also increased the latters's sensitivity to carbon dioxide. They considered the
mechanism being, as the respirations increase in vigor, the carbon-dioxide tension of the blood falls below the level at which the center is stimulated, and apnea ensues. The apneic period increases the degree of oxygen lack and prevents the elimination of carbon dioxide; the center is stimulated and the breathing returns, but ceases again when, through the absorption of oxygen and the blowing off of carbon dioxide the center is no longer stimulated. (34).

Anthony and his co-workers, believed the lack of carbon dioxide was the important factor in periodic breathing, since they were able to abolish it in almost every case by the administration of carbon dioxide. They pointed out that anoxemia was a factor of minor importance, since its administration may, but usually does not, abolish periodic breathing, and secondly patients may have an extreme anoxemia for long periods of time without periodic breathing, providing their carbon dioxide tensions are right. They demonstrated administration of oxygen prolonged both the apneic and hyperpneic phases, but the latter phase was not as pronounced as with ordinary air inhalation. (1).

Eyster(38) found periodic alterations in blood pressure which passed alternately below and above the level of the intracranial pressure, this was especially true in patients with an increased intracranial pressure. In such cases, Eyster believed, periodic breathing was due to an intermittent blood supply to the respiratory center.

Meyer and Middleton showed, a rise in venous pressure
occurred during the apneic phase and a decline occurred in the hyperpneic phase. (96). They did not attribute fluctuations in the amount of congestion in the lungs as a cause of periodic breathing by stimulation of the respiratory center over the Hering-Breuer reflex, because many individuals with outspoken periodic breathing do not show alternating increasing and decreasing congestion, which would be necessary to alternately set off the Hering-Breuer Reflex.

In summarizing the foregoing discussion of periodic breathing, it is evident the original cause leading to the change in the blood gases has not been clearly identified. Some investigators believe the breathing is initiated by overventilation, which in turn causes a change in the blood gases, and once the change has occurred in the blood gases, which accounts for further production of this type of breathing.

The majority of investigators consider a change in the carbon dioxide tension more important than anoxemia, which most agree plays some part. Other workers believe the transition into the sleeping stage, causes some incoordination between the nervous and chemical mechanisms controlling respiration, and the blood gases therefore lack the equivalent balance necessary at each phase of the normal respiratory cycle to maintain normal ventilation. (58).
THE PRODUCTION OF CARDIAC EDEMA.

The third major symptom, in congestive heart failure is edema. The fallacy of the common assumption that most edema of the legs in ambulatory patients is cardiac edema has been pointed out by Foote et al. Out of one hundred cases of dependent edema in ambulatory patients, only thirteen of the patients possessed definite cardiac edema. In these patients, the majority of edematous legs were due to varicosities, obesity, and postural factors. However in a series of bedridden patients with dependent edema, sixty cases were definitely cardiac in nature, out of a possible one hundred.

Many different theories have been proposed to explain the occurrence of edema in congestive failure.

Mackenzie (84-2) states: "The causes of dropsy are still obscure. The fact that it is found in heart failure in dependent parts of the body indicates that certain forms of it are due to a diminution of the force which propels the blood through the capillaries, and there is no doubt that it is of frequent occurrence where the heart's force is greatly enfeebled, as in auricular fibrillation with numerous small and ineffective beats." He therefore, believed that certain forms were due to an inadequate circulation through the tissues.

Martin Fisher states: "When through any disease process, myocarditis, a valve defect, the normal efficiency of the circulation is cut down, it is obvious that those portions of the body most distant from the heart will be the first to suffer from the chemical effects of a lowered circulation. The immediate result is that the carbonic acid normally produced in the tissues is not carried away. But oxygen also to be carried into
the tissues in normal amount and so lactic and other organic acids accumulate in the tissues. Because of the action of these acids upon the colloids of the involved cells, their hydration capacity is increased and they now suck water out of their surroundings, the blood chiefly. An edema due to a circulatory failure is therefore in essence a toxic edema, with the chief toxic agent represented by an abnormal production or accumulation of acids in some part, or ultimately in all the parts, of the living organism." (41). Fisher evidently believed decreased circulation, increased the water binding power of the tissues, due to the accumulation of toxic acids in the cells.

The "back-pressure" theory holds, that cardiac edema is due to a rise in pressure in the systemic capillaries. Cohnheim (41-a) was the first to support this view experimentally.

A knowledge of the mechanism of edema in general is necessary for an understanding of the factors producing cardiac edema, i.e. the understanding advanced by the majority of investigators. However, due to the great complexity of the subject, it is unwise in this thesis to consider each at length, therefore for the sake of brevity, the various mechanisms will be mentioned, with a brief explanatory note concerning them.

The normal interchange of fluid between the vascular system and the interstitial spaces is dependent upon two major factors, one of these is the capillary blood pressure, the
other the colloid or osmotic pressure. (98).

The capillary blood pressure may increase in two ways. Dilatation of an arteriole allows for a higher pressure to be transmitted into the capillary. Providing the dilatation persists for a sufficient length of time, edema of the tissues in that area will result. Slowing of the capillary blood flow by increasing the venous pressure will also increase the pressure in the capillaries until the oncoming arterial pressure is high enough to overcome it. (5-16). The level of capillary pressure necessary to cause edema is not in agreement. According to Minishe (98) it is between thirty five and thirteen millimeters of mercury. But Krogh found that a venous pressure greater than fifteen to twenty centimeters of water would produce edema. (73). While Landis and his co-workers found that edema would result with venous pressures as low as thirty centimeters of water. They also found that the fluid loss was in direct proportion to the height of venous pressure. (75).

The osmotic pressure of the blood is greater than that of the tissues, by virtue of the large-sized, non-diffuseable plasma protein molecules, principally albumin. If this pressure is great enough it will tend to hold the water in the tissues. (12). But any condition which diminishes the concentration of the plasma proteins will diminish the attracting force of the blood for water and thereby allow the driving out force of the capillary blood pressure to predominate and edema will result. Minishe states (98) that the osmotic pressure approximates
twenty five millimeters of mercury. Landis et al, found however, that a venous pressure of eighty centimeters of water was necessary to cause a loss of protein through the capillary walls. (75).

The normal functioning of this system depends upon a third factor, the intactness of the semipermeable membrane, or the capillary wall. This factor varies with the other conditions present at that time. Krogh pointed out, that dilatation of a capillary causes its wall to become more permeable. (72).

It is therefore evident, that the capillary dilatation resulting from an increased venous pressure would tend to the production of a greater edema. But this will take place only up to a certain point, for Landis and Gibbon illustrated that the filtration rate due to experimental venous congestion, gradually diminished as edema develops, or that a state of equilibrium was approached, as fluid continued to pour out. (76). Landis, in another article, demonstrated that anoxemia made the capillary wall more permeable (74). Barbour and Hamilton also believed that anoxemia of the capillary wall, due to arteriolar constriction would cause edema. (2).

A fourth physical factor in the removal of fluid from the blood stream, according to Minish (98), is the influence of salts. For example, the sodium ion requires the retention of water, to maintain an isotonic level. Loeb et al, showed that the different salts will have different effects, and also the same salt may have a different effect in different
individuals. They showed, that the sodium salts are particularly responsible for edema formation, whereas ammonium and potassium salts may act contrawise. (77).

A fifth factor in the process depends upon the ability of the lymphatics to remove fluid from the reservoir of fluid in the tissues. The degree of edema will be greater, when the part in question is active rather than at rest. This is because with activity, the arterioles of a part dilate and increase the capillary pressure. (98).

In summary, some of the more important theories concerning the formation of edema in general have been mentioned in order to understand the mechanism behind its formation in congestive failure.

According to Blumbart et al (11) the venous pressure is elevated in right-sided heart failure, resulting in a damming of blood in the capillaries. Since damming of blood in the capillaries causes an increase in capillary pressure, edema results. According to Minish (98), the plasma proteins do not increase sufficiently to compensate, however the lymphatics drain the fluid away for a time. As the venous pressure continues to rise the formation is greater than the drainage.

The edema occurs in the dependent portions for it is here, that the venous pressure is the greatest, and too the effect of gravity is such to prevent the upward flow of lymph. (98).

The foregoing paragraph essentially explains the mechanism of cardiac edema in congestive failure, as it is today
understood. However, there is one added factor according to Fremont-Smith (44). This factor is a renal factor, an alteration in the filtration or absorption of the fluids passing through the kidney in patients with congestive failure. Fremont-Smith showed that the decrease in urine output in these cases is not due to a decrease in the water content of the blood. He also showed that ingestion of water in these cases dilutes the blood more than in the normal person, but there is less marked resulting diuresis.

According to Levine, (79), the accumulation of edematous fluid in the dependent parts is usually a late manifestation of a failing heart. For the majority of the causes of cardiac disease place the initial strain on the left side rather than on the right, and it is not until the strain is on the right side, that dependent edema appears. According to Levine (ibid) there are however, several types of cardiac disease which affect the right ventricle to a greater degree than the left. Such conditions as mitral stenosis, adhesive pericarditis, congenital lesions and extensive disorders of the lungs and bronchi, kyphoscoliosis, and failure of the right heart muscle.

Occasionally in cardiac disease, there is a tremendous abdominal ascites, but little edema of the legs. Salvesen and Linder (111) have explained this on the basis, that the peritoneal capillaries, have relative little resistance to stretching their walls, and secondly the fact that these capillaries are more permeable to plasma protein than those
of the extremities. However it would seem to me, that this second factor would have little effect, and to make the major factor in the production of ascites in these patients, is an increase in venous pressure being transmitted back through the more extensive venous bed, such as the portal system and other large veins in the abdomen, and secondly the possibility that the venous pressure if high enough would obstruct the outflow of lymphatic drainage from the thoracic duct, or in other words a less adequate lymphatic drainage, than that present in the legs. However, I have no evidence to support these views.

The investigations cited by the various workers would tend to fix the blame for cardiac edema principally upon an increased venous pressure, which is in accord with the "back-pressure" theory of congestive heart failure. While the weight of evidence supporting the "forward-failure" views does not seem to be as great, in this instance. The latter view is essentially a mechanism, whereby edema is a manifestation of a diminished supply of blood to the tissues, and in consequence the capillary wall suffers from anoxemia, thereby becoming more permeable to the fluid in the blood stream.
THE NATURE OF CONGESTIVE HEART FAILURE

The dynamics of congestive heart failure and the mechanisms of its cardinal manifestations have been considered at length and with some detail. The interpretation of the nature of congestive failure requires a synthesis of the various hypotheses previously presented.

According to Parsons-Smith, (100), "general consensus associates the development of congestive failure with a diminution of the cardiac output to such an extent that blood supply to the tissues becomes insufficient for their requirements; but there are also other factors, which have been previously accepted related to variations in the blood chemistry induced by the retarded flow in the capillaries, by which carbon dioxide pressure and hydrogen ion concentration in the tissues and respiratory center are abnormally raised and oxygen content becomes relative deficient for the normal processes of metabolism. Recent research indicates that the manifestations of cardiac failure cannot be entirely accounted for by the diminished output theory or by alterations in the blood chemistry; other factors are obviously concerned, and evidence is gradually accumulating that certain of these may be essentially back-pressure phenomena. In the advanced stages of heart disease and after severe exercise there may be discrepancies in cardiac output and blood chemistry which amply explain the failure symptoms; but such changes are not manifest in earlier, uncomplicated stages of the condition, when breathlessness and
moderate deficiencies of exercise tolerance are intimately associated with variations in venous pressure and reflex nervous stimuli in the lungs, heart, and elsewhere." (100).

"The back-pressure mechanism associates pulmonary congestion with failure of the left ventricle and venous stasis in the systemic circulation with incompetence involving the right heart chambers." (100).

Thus Parsons-Smith adequately summarizes the evidence heretofore presented in this thesis. Failure of both sides of the heart may be either myocardial or mechanical in nature. Myocardial failure being due to dilatation of the ventricles resulting from resistance of residual blood. Mechanical failure, due to disease of the mitral valve, tricuspid valve, or an increased pericardial pressure preventing adequate filling of the right side of the heart.

As regards the pure myocardial congestive failure, it results when the degree of cardiac dilatation required to maintain a normal cardiac output produces an increased venous pressure sufficient to be detectable as congestion in the vascular system. This is the essence of the "back-pressure" mechanism, responsible for congestive heart failure.

I have placed the greater emphasis on the "back-pressure" theory throughout this writing, for recently it has been more generally accepted by the majority of authoritative investigators, and whose conclusions make up the body of this paper.
THE MINOR SIGNS OF CONGESTIVE HEART FAILURE

I---------Tachycardia.

II---------Gallop Rhythm.

III--------Auricular Fibrillation.

IV---------Heart Sounds.

V--------Murmurs.

VI--------Blood Pressure Changes.

VII--------Character of the Pulse.

VIII-------Fever.

IX--------Chills.

X--------Cyanosis.

XI--------Anorexia.

XII--------Cough.

XIII-------Hemoptysis.

XIV--------Pain.
THE MINOR SIGNS OF CONGESTIVE HEART FAILURE

I-Tachycardia--Regarding this symptom little need be said. As has been previously stated, Bainbridge experimentally proved the increase in heart rate is induced by a rise in the pressure of blood entering the right auricle. The mechanism responsible for this is a reflex. (5-12). Therefore it is evident that an increased venous pressure resulting from congestive failure will increase the rate of the heart.

II-Gallop Rhythm--According to Dock, (33), gallop rhythm is a sign that one or both of the ventricles are dilated. It occurs rather early in dilatation however and is an immediate sign of impending failure. He was able to show, that this sign is not due to a sudden stretching of the ventricular muscle, but that both the protodiastolic and presystolic sounds are due to a sudden increased tension on the valve leaflets, from ventricular rebound. Ventricular rebound results from a very rapid inflow because of elevated auricular pressure, and this in turn becomes raised whenever the ventricle is dilated.

III-Auricular Fibrillation--Brill states, that occasional patients apparently derive some advantage from auricular fibrillation associated with congestive heart failure, since response to digitalis is better. Some patients despite digitalization, continue with auricular fibrillation. These individuals are usually those with thyrotoxic heart disease,
in which thyroidectomy or quinidine will suffice. The irregularity is not harmful, but the tachycardia is disadvantageous from several aspects, as it may precipitate heart failure, cause emboli formation etc. And the pulse deficit allows for wasted energy in an organ with a diminished reserve. (20).

IV-Heart Sounds--Lewis states; that the first sound like the second sound is dependent not on muscular contraction, but due to increased tension of the valve leaflets. (80). According to this interpretation, it would seem that the intensity of the heart sounds would not be significant in congestive myocardial heart failure, but would be significant in mechanical heart failure due to valve disease.

V-Murmurs--Christian states: "Murmurs play very little part in diagnosis of Chronic Myocardial disease. The significant thing is that with very marked degrees of cardiac failure there may be no murmurs at all." (26-4).

VI-Blood Pressure Changes--This depends upon the underlying conditions responsible for the congestive failure. It is a well known fact that blood pressure declines with prolonged tachycardia, and that it is elevated in hypertension. According to Mackenzie, (84-4) because of these variations the significance of blood pressure in heart failure aside from a conception of the underlying cause, is little.
VII—Character of the Pulse—According to Christian, (26-5). "The size and form of the pulse is of little clinical importance in these patients. As a rule, the pulse gives very unsatisfactory evidence of heart function, as many of these patients have high blood pressure, the pulse usually is of increased tension. As so many of these patients are elderly, the arteries frequently show the changes of arteriosclerosis, The most significant finding in the pulse is pulsus alternans. If carefully searched for, it will not be infrequent in the later stages of the disease. When found, it is indicative of a poor prognosis. It may be constant or appear only following an extrasystole. The latter type is of less evil prognosis."

VIII—Fever in some degree occurs in a large proportion of patients with congestive heart failure. Kinsey and White reviewed two hundred cases of congestive heart failure to determine the incidence and cause of fever in this condition. They stated: "Although congestive heart failure alone may possibly explain up to one degree of fever, there was almost invariably some underlying complication to account in general for fever... In order of frequency the four most common complications were: pulmonary infarction, pulmonary infection (especially bronchopneumonia) active rheumatic infection and acute corona thrombosis. Fever of any grade in a case of congestive heart failure should be considered a probable evidence of some complication, which not only frequently explains intractability to treatment but also, in some cases, may be the cause of death,
which rarely occurs with heart failure alone." (70).

Another mechanism which may produce fever in patients with congestive heart failure was pointed out by Steele, (117), who believed that vasconsuction of the vessels in the skin prevented heat loss and caused a subnormal skin temperature, when the rectal temperature was abnormally high.

Chills--I have been unable to locate any observations regarding the incidence and significance of chills in patients with congestive heart failure. However, simple reason would indicate, that since a chill is apt to occur with infarctions and blood stream infections, a chill is apt to be a precipitating factor and an evil omen in congestive heart failure, though it in itself may not be a sign of heart failure.

Cyanosis--According to Harrison, cyanosis is not a constant feature, but is frequently present and may be caused by arterial anoxemia resulting from pulmonary edema or emphysema, by distention of the small skin veins from increased venous pressure. (51).

Anorexia--Boshes states; that anorexia, nausea and vomiting, may occur in the late stages of congestive heart failure, or they may occur from digitalis or theophylline or morphine in the course of treatment. (14).

Cough--Cough is a frequent symptom in patients with pulmonary congestion secondary to left ventricular failure or to mitral disease, and may be due either to the congestion and edema of the lungs, or to secondary, low-grade infections. (60).
Coughing is a form of muscular exercise and throws a strain on the whole heart as does any other form of bodily activity. In addition coughing causes a rise in pulmonary pressure placing a burden on the right ventricle especially. Therefore coughing is both a result and a precipitating factor of congestive heart failure. (60 ibid).

XII-Hemoptysis— "Rusty Sputum" is common in patients with mitral stenosis and in patients with pulmonary congestion due to left ventricular failure secondary to aortic insufficiency or to vascular disease. The indurated lung of long standing congestion, such as most frequently occurs in mitral stenosis, is more frequently associated with hemosider deposits in the cells and hence with brownish "rusty sputum" than with the pink frothy sputum of pulmonary edema. (17).

XIII-Pain—This is a frequent occurrence in patients with congestive heart failure. It occurs usually in the right upper quadrant and is due to engorgement of the liver. The pain is often misleading and may lead to a false diagnosis of gall bladder disease. Occasionally accompanying it there may be jaundice and the other manifestations of liver disease. (14).

The more common of the minor symptoms of congestive heart failure have been briefly discussed. They are more important from a prognostic standpoint, than a diagnostic, for the clinician rarely interprets a condition of congestive heart failure from these minor manifestations. (51). However, prognostically they give a clue to the course and stage of the disease, as well as an indication for treatment. It is for this reason that I have mentioned them, though briefly.
TREATMENT OF CONGESTIVE HEART FAILURE

I-------Pharmacologic Action of Digitalis.

II-------Indications for Digitalis.

III-------Contraindications to Digitalis.

IV-------Digitalis Doseage.

VI-------General Management of Congestive Heart Failure.

VII-------Management During the Asymptomatic Stage.

VIII-------Management of Left Ventricular Failure.

IX-------Management of Right Ventricular Failure.
TREATMENT OF CONGESTIVE HEART FAILURE.

The treatment of congestive failure since the time of William Withering has been closely concerned with the use of digitalis. Because this drug plays a very important part in therapy, this discussion will begin with a consideration of the effects of that drug. Needless to say, digitalis since its introduction, has been the subject of enumerable studies, so many in fact, that it would be impossible in this paper to consider the conclusions derived by the various investigators. Therefore, I will be unable to consider but a few of the more notable investigations as regards the pharmacologic action and therapeutic indications of this important drug.

Primarily the action of digitalis on the heart is to produce an increase in its efficiency. As has been cited, Starling and Visscher, showed that an inefficient heart is a dilated heart, because it is then it consumes more oxygen than the normal heart to perform a given amount of work. (117).

Digitalis produces a beneficial effect, according to Bodo, (13) and Cohn and Steele (28), and most other investigators agree (26-6), because it produces a diminution in the size of the heart, and a diminution in the degree of dilatation. Peters and Visscher state; that the essential action of digitalis is the production of an increased mechanical efficiency. (102). This then, is the 'prime' action of digitalis in congestive heart failure.

The decrease in the rate of the heart appears to be of
great importance, especially with cases of auricular fibrillation, for previously this thesis has brought out the harmful effects of tachycardia in congestive heart failure; namely, by expending useless energy in an already failing organ. Clark states: "Digitalis stimulates the vagal centers and thereby causing slowing of the heart and a decrease in the rate of auriculo-ventricular conduction." (24-2). Or in other words the drug diminishes the responsiveness of the auriculo-ventricular node to impulses arriving at it from the auricles, thereby slowing the heart rate.

As regards the action of digitalis on normal rhythm, Clark states: "It is generally agreed the beneficial effect produced is more dramatic in cases of auricular fibrillation, than in cases of heart disease with normal rhythm. It is now agreed, however, that digitalis if given in adequate dosage produces a marked beneficial action in the latter cases." (24-3) And Luten concluded that clinical benefit was produced as frequently in cases of normal rhythm as in cases with fibrillation. (83). While, Christian pointed out that digitalis must obviously produce some beneficial action apart from depression of conduction, because it produced marked benefit in cases of auricular fibrillation in which the frequency of the untreated ventricle was not much above eighty. (26-7).

A fourth action of the drug, according to Christian, is an indirect effect in improving the nutrition of the heart muscle. It does this by increasing the blood flow through the
coronary arteries as a result of the slowed rate of contraction of the heart muscle with its prolongation of ventricular diastole. (26-6).

The influence digitalis has on the cardiac output is debateable. Bodo states, that the output is not changed. (13). Stewart and Cohn (119) studied seven patients and concluded that digitalis regularly caused an increase in the output of the heart.

Dock and Tainter (33) believed that the method of Stewart and Cohn was in error, and they concluded from their observations, that the cardiac output was reduced when digitalization took place. They believed the decrease in the cardiac output was due to a decrease in the venous pressure. While Rytand (110) demonstrated, that digitalization does decrease the venous pressure. The weight of evidence apparently demonstrates that digitalis does not increase the cardiac output, producing a beneficial action. It apparently decreases the cardiac output by decreasing the venous pressure, which is in accord with the "back-pressure" theory. However, out of fairness, it should be said, that it has never been absolutely proved, that the cardiac output increases or decreases, my conclusions were derived mainly because the majority of investigations supported this view.

Fremont-Smith stated, that there is a renal factor in cardiac edema. An alteration in the filtration or absorption of the fluids passing through the kidney in patients with congestive failure.
Fremont-Smith demonstrated that ingestion of water in these patients dilutes the blood more than in the normal person, but there is less marked resulting diuresis. (44).

According to Clark (24-4) and a fact, which is generally well known, "Digitalis has a very strong diuretic action in such cases (cardiac edema). As the circulation improves the quantity of urine secreted rises rapidly and the dropsy disappears. Digitalis produces little or no diuretic action in normal persons, and therefore has probably no direct action upon the kidney in therapeutic doses. Moreover digitalis when it fails to produce a beneficial action on the circulation in a case of heart disease, produces very little diuretic effect. The digitalis glucosides have, however, some direct action on the kidney, for Gremels showed that digitoxin produce diuresis in the heart-lung preparation, when the arterial pressure was kept constant." From this point of view, it appears, as though digitalis produces a diuretic effect by improving the circulation through the kidney, allowing for a proper functioning of the filtrating and absorbine mechanisms.
INDICATIONS FOR DIGITALIS

Paul White states: "Digitalis is indicated only for persons with clear evidence of heart failure or in whom the heart failure threatens or is in doubt and for persons with auricular fibrillation or flutter that does not clear up spontaneously or respond to quinidine....Dyspnea does not indicate use of digitalis, because conditions such as bronchitis, asthma with emphysema, nervousness and obesity may be responsible. Dyspnea is not due to heart failure or obstruction, as from mitral stenosis, if the heart size is normal. However, according to Harrison et al (59), the indication for this drug in the majority of persons with cardiac disease is the presence of the manifestations of congestive heart failure, when the patient is at rest. I.e. unless the heart failure is of mechanical rather than myocardial origin, as in mitral stenosis, where digitalis produces little if any benefit. The most constant and dramatic effect in persons with regular rhythm consists in the abolition of seizures of paroxysmal nocturnal dyspnea.(ibid). Harrison et al plainly differ from White, as to the indication of digitalis with dyspnea. Their observations constituted objective evidence that digitalis may produce improvement in patients without manifest congestive failure or cardiac enlargement per se, but with diminished cardiac reserve, and seemed to furnish an answer to the question as to when the administration of the drug should begin. "Whenever the minimum amount of activity,
which is compatible with a given patient leading an economi-
cally useful existence produces dyspnea, digitalis is indi-
cated, and digitalis should not be withheld from patients
who have recovered from congestive failure. Even under the
most favourable circumstances, such individuals nearly al-
ways suffer from some shortness of breath with moderate
exertion; and consequently they should continue to receive
the drug. Withholding it in such cases is likely to lead to
another 'break in compensation' with a few weeks. The imp-
ortant fact that digitalis is not only helpful in combating
congestive heart failure, but is also useful in preventing it
does not seem to have been sufficiently widely recognized."
(59).

Digitalis is then indicated, providing the above views
are acceptable, in those patients with congestive failure,
or in whom failure threatens. There is as yet some argument
as to when the drug should be started. White believes in
withholding the drug until actual cardiac enlargement has
begun. (124). Harrison et al, believe it should be given
whenever dyspnea is due to a diminished cardiac reserve,
regardless of whether the heart is enlarged or not. (59).

All clinicians agree that the drug should be administered
to auricular fibrillation, which does not quickly cease by
other means. (24-3). Christian believes the drug is indicated
in cases of prolonged paroxysmal auricular tachycardia. (26-1)
In pulsus bigeminus, if present before digitalization (26-9),
and in auricular flutter. (ibid). The majority of writers agree
that once digitalization has been instituted in congestive failure it should be maintained after improvement in the clinical picture appears, purely as a prophylactic measure.
CONTRAINDICATIONS TO DIGITALIS

The most common contraindication to the use of this drug in persons with congestive heart failure is the presence of digitalis intoxication, as revealed by anorexia, nausea, or vomiting, or by the presence of coupled beats due to extra systoles alternating with normal beats. (24-5). However, Christian states, that the drug can be given if the pulsus bigeminus is present previous to administration. (26-9).

Blumgart and Altschule investigating the consensus that digitalis should not be used in heart block, state: "The presence of partial heart block does not constitute a contraindication to the use of digitalis." (8). Arrison et al agree, and believe that a mild heart block is not a toxic manifestation but a desirable therapeutic effect. (59).

White states that the drug is contraindicated in palpitation resulting from conditions other than cardiac diseases, or in cardiac failure secondary to chronic pulmonary diseases. He believes the drug should not be used in cases of pulmonary embolism, infarction, thyrotoxicosis or highly emotional states. White also maintains the drug should not be used in the treatment of tachycardia, unless it results from auricular fibrillation or flutter. Nor in bradycardia, or cyanosis, since the latter is usually due to congenital heart defects; or pulmonary congestion resulting from mitral stenosis. (124).

Niles and Wycoff (99) state, that many physicians use the drug in the treatment of pneumonia, where congestive failure rarely occurs, and that the use of digitalis in this instance
is harmful.

Harrison et al hold the drug should not be administered in acute conditions of the myocardium. In coronary it tends to produce ventricular tachycardia and should not be used for that reason. (59).
According to Christian (26-11) "Failure to obtain digitalis effects is by far a more serious error than to obtain a mild or even fairly severe toxic action. Damaging toxic digitalis effects in my experience are extremely rare and can be easily avoided."

Harrison et al. fix the dosage at one and two-tenths to two grams of the powdered leaf or its equivalent, over a period of forty eight to seventy two hours, followed by a maintenance daily dose of one-tenth to three-tenths gram, depending on the potency of the preparation, the size of the patient, and more especially the size of the heart. (59).

Christian uses three methods of digitalizing. The single large dose method for the very occasional patient who is extremely ill, and has never had the drug previously. The average total dose for man by mouth is fifteen-hundredths of one cat unit per pound of body weight. Christian prefers the second or modified large dose method for the majority of patients. The total dose here is from two to two and one-half grams, depending on the size of the patient. One-fourth of the total dose is given initially, followed by the same amount in four hours. The remainder is given at the rate of one-tenth to two-tenths grams every four hours. Thirdly the divided dose method for patients who are only moderately uncomfortable, whereby two-tenths gram of powdered leaves is administered threetimes a day until the signs of digitalis action appear. (26-11).
GENERAL MANAGEMENT of CONGESTIVE HEART FAILURE

Felter states: "Congestive failure is a late indication that nine-tenths of the cardiac reserve has been used up." He emphasizes that more attention must be paid to prophylaxis in heart disease in an effort to preserve the cardiac reserve force from excessive wasteage. (39)

In cardiac diseases, as in other diseases, the first aim is to remove the cause of the disorder. In cardiac disease this is rarely possible. As has been previously stated, the etiological causes of heart disease can rarely be treated adequately. Rare causes such as myxedema (25-a), beri-beri, (25-b), and diptheria (25-c), can be treated medically. Causes of cardiac disease which offer opportunity for cure by surgical methods are thyrotoxicosis, (107), cardiac compression (4), and arteriovenous fistula. (32).

Previously it has been mentioned, that the patient passes through several stages in the course of the disease. In all stages, according to Lewis (81-5), the general attitude of the physician, and his management of the psychological aspects of the problem are of great importance. The patient and his friends should be told the truth about his condition, and any unnecessary fears should be tactfully relieved.
MANAGEMENT DURING THE ASYMPTOMATIC STAGE

Heart failure must be prevented, and according to Burwell, the greatest effect can be obtained in the asymptomatic period. The primary disease process must, if possible, be prevented from progressing, and another disease imitable to the heart form being superimposed. Also the precipitating factors must be avoided. The patient should avoid exercise which produces dyspnea. The nutritional state is important; those with rheumatic infections should be maintained on well-balanced diets. Those with hypertension and obesity reduced. (21).

Lewis states (81-6) pregnancy is definitely contraindicated in persons with limited cardiac reserve.
THE MANAGEMENT OF LEFT VENTRICULAR FAILURE.

This stage of the disease is characterized by shortness of breath at rest. Herrmann states: "Paroxysmal nocturnal orthopnea may be the earliest symptom and acute pulmonary edema may be fatal. In cases of this type with regular cardiac rhythm, the effects of digitalis are remarkable, for the paroxysmal attacks are usually relieved and ventricular tone improved. Aminophylline intravenously, seven and one-half grains, may be theoretically dangerous but has been used without difficulty. (67).

With profuse pulmonary transudation, tracheal bronchial catherization with suction may prevent death. (67). Tourniquets on all four extremities usually stop an attack by trapping venous blood peripherally and thereby limiting the output of the right ventricle. Phlebotomy or venesection acts similarly. (19).

Morphine grains one-fourth is specific. Anxiety is allayed, excessive pulmonary reflexes are interrupted, cough stops and sweats and pallor disappear. Pure or crystalline digitalis glucosides intravenously are powerful left ventricle muscle tonics in severe attacks of pulmonary edema; digiland C or Lanatosid C, one and one-half, to two milligrams, or strophanthin, five-tenths milligrams, providing digitalis has not been previously administered during the past two weeks. (67).

In regard to the treatment of dyspnea, of the periodic type, Miller and Fulton stated: "Contrary to usual experience, caffeine dodiobenzoate was the only measure which restored
normal breathing and coincidentally abolished the transient heart block which occurred during the apneic phase. Oxygen administration resulted in subjective improvement without affecting the respiration. (97).

In this stage of the disease, bed rest and other supportive measures are obviously a necessity. And the precipitating factors of paroxysmal dyspnea should be eliminated if possible, i.e. prevention of coughing, excessive environmental heat etc.
THE MANAGEMENT OF RIGHT VENTRICULAR FAILURE

Patients developing edema, should be kept at rest, and except when dyspnea necessitates it, should not sit up, for then the edema is allowed to accumulate in the dependent portions of the body. McMahon states that diuretics are essential, (86). The action of digitalis in this respect has already been mentioned. According to Marvin, the underlying heart failure should be treated adequately before treating the edema, for this alone may cause its disappearance. If, however, hydrothorax is present and interferes with respiration, paracentesis is indicated, and if edema elsewhere causes extreme discomfort, mercurial diuretics should be immediately used. (89).

Theophylline may be administered in three to five grain capsules several times daily but provokes nausea and vomiting. Theophylline sodium acetate (fifteen to thirty grains daily in three to four equal doses) and theophylline ethylene diamine (one and one-half to three grains three times a day) are better tolerated. Theobromine (five to ten grains three times per day for several days) is less powerful but well tolerated. Theobromine with sodium salicylate (diuretin) is given in large doses (forty to sixty grains). Theobromine calcium salicylate is potent and may be continued for days if necessary in doses of three to six tablets, seven and one-half grains each, daily. (89).

Organic mercurials are most potent. Salyrgan, is effective intramuscularly, intravenously or in rectal suppositories,
and its effectiveness is increased if ammonium chloride or nitrate (three to eight grams daily) is orally administered three to four days prior to injection. Its diuretic effect may occasionally be increased by combining magnesium sulfate (six to fifteen cc, of fifty per cent solution) with it intramuscularly. Combination with theophylline is more potent than either alone. (89).

Marvin states, that acute nephritis or ulcerative colitis contraindicates the use of mercurial diuretics. (89).

Congestive heart failure necessitates a restricted diet. Progermand Magendantz (106), restricted the diet to three hundred and fifty six calories for one or two weeks, then six hundred calories until ten percent of the body weight had been lost, then continuing with twelve hundred calories. In some instances a diet comparable to the Karrel diet was followed. In all of their cases the metabolic rate, cardiac output, blood pressure and heart rate were reduced, with an increase in vital capacity and in ability to perform work.

Following recovery from an episode of decompensation, the patient is portentially in danger of another break in compensation. Therefore, the patient should be checked frequently for signs of a break. He must avoid exercise which produces dyspnea, protect himself from colds, infections and anything which may precipitate another episode.
The immediate prognosis of congestive heart failure was studied by Boyer et al. (18) and was found, in general, independent of the underlying type of heart disease. The precipitating cause of failure, however, was prognostically important not only, because some precipitating cause were uncontrollable, but also because the apparent benignity or malignancy of any precipitating factor is a fair measure of myocardial reserve before actual onset of congestion.

Thus when failure is precipitated by a relatively mild respiratory infection, the myocardial reserve must already have been very low. Auricular fibrillation with a rapid ventricular rate can precipitate failure in a diseased heart with high reserve and probably even occasionally in a heart which is otherwise apparently normal. Consequently, with adequate control of the heart rate, much myocardial reserve may be regained, although naturally, tachycardia of any sort may also excite failure when the reserve is low. (18).

Prognosis may be modified by presence or absence of complications. Most common complications were embolism (peripheral or pulmonary), anemia, diabetes, cerebral vascular accidents and pneumonia. (18).

Age was also a factor. The peak of failure incidence lies between ages forty and seventy. The outcome was fairly constant for all ages and corresponded closely to the outcome for all types of heart disease, with exception of three peaks. Seventy five percent of a small group of children aged one to
ten did poorly, all but one having severe rheumatic infection with failure. The second peak occurred during the fifth decade and the third in patients over seventy. (18)

As regards the degree of enlargement, patients with slight enlargement did well, whereas the outcome became progressively poorer as the degree of enlargement increased. (18).

As regards the remote prognosis, Birchard, of the Sun Life Insurance Company gives a formula to determine remote prognosis. If under sixty-five years of age, the age is subtracted from eighty and the result multiplied by eight-tenths; at ages over sixty-five the formula is one hundred and five minus the age, divided by four. Each ten percent of extra mortality has the same effect as becoming a year older, and reduces his expectation eight-tenths of a year. The older rules, as to systolic blood pressure are declared fallacious in the assumption that normal systolic pressure is practically the same at all ages; the high limit of normal pressure is under one hundred and thirty millimeters of mercury. Elevation of systolic blood pressure of any given amount is more serious in the forties of life than in the twenties. For a systolic pressure of one hundred and forty-five millimeters, the mortalities will be approximately at thirty years, forty percent in excess of normal; at forty-five, fifty percent; and at sixty, sixty percent. (6).

The practical result of diastolic pressure constantly maintained at ninety give no excess of mortality; at one hundred the mortality is sixty percent in excess of normal, and at one
hundred and five, one hundred and fifty percent in excess.
Without other blemish of any kind this patient is about
fifteen years older than he thinks he is, and his life ex-
pectancy is reduced by about twelve years. (6).

Providing patients are classified by the frequency with
which the extrasystoles appear in arrhythmia of the pulse,
it is found that five extra systoles or less per minute, fif-
teen per cent extra mortality; five to ten per minute, twenty
five percent extra mortality; over ten extrasystoles per min-
ute, fifty percent extra mortality. (6).

In a large group of such patients, incidence of death
from heart disease has been two and a half times the normal.
A group of forty seven thousand with tachycardia due to so-
called "nervousness," the pulse rate being above ninety and
under one hundred, all in excellent health otherwise, gave
a death rate forty seven percent in excess of normal. Stat-
istics show that three hundred and sixty six thousand persons
with rates of fifty five to sixty five gave death rates
fifteen percent below the average for normal lives. (6).

In my opinion, it seems as though the best guide to
prognosis in the individual case, would be the response to
treatment, and the rate at which the process has progressed,
determined from the history and the clinical observation.
I do not have any evidence to support this view, excepting
the fact, that if a patient responds favorably to treatment
in most disease processes, the prognosis is likewise more
favorable.
SUMMARY

The foregoing pages have been concerned with the clinical and experimental observations of the various investigators in regard to the pathogenesis and treatment of congestive heart failure. Because of the immensity of the subject many important contributions, in which the basic deductions were similar to those cited, have been omitted.

The theme of the discussion has emphasized the fact, that the final result, regardless of the primary disease process, is to render the heart inefficient in the performance of its work. Congestive Heart Failure is seen as a syndrome, with the most important objective sign being cardiac enlargement, while the most important subjective manifestation is dyspnea.

The chief sign of left heart failure is a diminished vital capacity due to pulmonary engorgement. While increased venous pressure, edema, liver enlargement, and ascites are manifest in right heart failure.

The advocates of the "forward-failure" theory, attribute the clinical picture to a diminished blood supply to the tissues. Recent evidence, which has been extensively cited in this paper, indicates, though does not actually prove, that this cannot be explained on this basis.

The alternate, or "back-pressure" theory is today favored by the majority of investigators. According to this theory the essential factor in producing the clinical picture is accumulation of blood in the vascular areas which drain toward the failing heart, due to a rise in pressure in the veins. This theory
holds that the heart does not fail in toto, but that the left side fails in most instances first, the velocity of blood flow through the lungs is then diminished, while the cardiac output remains constant. In the systemic system the rise in venous pressure produces edema, liver enlargement and ascites.

The production of dyspnea, from recent evidence apparently is due to nervous reflexes, rather than diminished cerebral blood flow. However, the argument continues among the different workers in this respect.

Cardiac enlargement is a two fold process. One, hypertrophy, which is dependent on overwork, and results in a mechanical advantage, but which also results in a decreased chemical advantage. The second process, dilatation is to increase the chemical advantage. At the outset the two processes are advantageous, but later because of the intercompensation for each other, an enlarged myocardium results, which requires more oxygen than formerly. The heart, then is consuming more oxygen relatively than the energy it can produce, and therefore is inefficient. If oxygen is not available for the metabolic needs the muscle fails. This is myocardial failure, as distinguished from mechanical failure due to valvular conditions, which result in back pressure, and which eventually may become myocardial failure.

I have indicated my conclusions concerning congestive heart failure in the preceding paragraph. I am more inclined to believe the mechanisms proposed by the "back-pressure theory"
because of the evidence offered in support by the investigations cited. However, I do not wish to convey the impression, that the "back-pressure" theory had been proven, and that the "forward-failure" hypothesis has been cast aside.

I stated in the introduction, that I chose this topic, because I wished to coordinate, in my own mind, the facts I did know concerning the heart, into a clinical picture, the manifestations of which would be explainable upon a physiological basis. In other words to learn something about that process known as Congestive Heart Failure. I feel, that I have managed to derive a present day concept-ion of the process concerned, and it is my desire, that the discussion entered into in these pages, is sufficiently clear to the reader in this regard.

"THE END"
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