THE PATHOLOGICAL PHYSIOLOGY OF CHRONIC CARDIAC FAILURE

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INTRODUCTION

Cardiac decompensation has and will continue to present some of the most important, as well as the most interesting, problems of medical practice. It is often quite simple for the physician to make the diagnosis of heart failure, or even to recognize the etiological background; but, not infrequently, little thought is given to the impaired physiology present. With an understanding of the pathological physiology therapy can be instituted with a much cleared conception of its value. To understand fully the physiological basis for the signs and symptoms of chronic decompensation, it is first necessary to comprehend much of normal cardio-vascular dynamics.

Naturally, since the scope of chronic cardiac decompensation is so great, this article must have certain limitations. Thus the etiology, pathology, diagnosis and therapy of this condition are not at present our concern and will not be discussed here. Acute cardiac collapse which produces a different clinical picture and depends on different functional disturbances also will be omitted. We will consider mainly the impaired physiology of cardiac decompensation, which cannot help but include a comparison of the "forward-failure" and "backward-failure" theories of the pathogenesis of the clinical manifestations. Assuming from the start that there has been wide controversy on most points under consideration, it will be impossible to state in detail the important experimental works; but, on the whole, a comparison alone of viewpoints will be considered. This paper will, in main, present

a review of some of the ideas of prominent investigators along the line of cardiac decompensation. At many points it must be left to the judgement of the reader to determine the most plausible explanation of the problems at hand.

Depending mainly on etiology the right or the left side of the heart is usually involved alone at first. However, cardiac failure is a progressive thing and usually eventually involves both sides of the heart; thus it will not be attempted to divide conclusively left-sided or right-sided failure. This division may be justified on a theoretical basis for explaining signs and symptoms, but never entirely on a practical basis because of the interdependence of the heart chambers. Mackenzie stressed the failure of the heart as a whole, and believed no chamber could fail without affecting the others; however, he likewise felt that certain signs and symptoms were due primarily to failure on one side or the other. On the other hand Koyz and Mendlowitz in their experiments feel that one must define heart failure in terms of a single chamber rather than the heart as a whole.

It is noted by many that discussions dealing with congestive heart failure too often are confined to a consideration of the heart alone. Such a limitation, obviously, disrupts the continuity of the theme, owing to the fact that decompensation results in circulatory changes that influence the functions and conditions of various organs and tissues of the body. There will thus be an attempt made to consider changes other than those in the heart, but the prime importance of the cardiac changes must at no time be forgotten.

HISTORY

The knowledge about the heart and its diseases began back in the time of Hippocrates. Galen first studied circulatory physiology, but along with good experimentations he developed numerous inaccurate theories. It remained for William Harvey to demonstrate the true nature of the circulation. Stephan Hales was the first to measure the blood pressure. In the 17th and 18th centuries early studies in cardiac pathology were made by such men as Lancisi, Morgagni and Baille.

The modern period began with Corvisart, Napoleon's physician, who made progress in diagnosis; and also saw the need to correlate clinical, pathological and physiological findings. T.R. Harrison believes that James Hope deserves the credit for the first clear conception of the "back-pressure" idea. H. M. Korns states that Robert Adams deserves credit for formulation of the "back-pressure" theory in 1827, while James Hope substantiated it four years later.

William Stokes an Irishman, believed that too much stress had been put on the importance of valvular lesions, and was the first to insist on the paramont importance of the cardiac muscle in heart disease. Julius Cohnheim first made careful studies on cardiac failure produced experimentally; he felt that the manifestations of cardiac failure were dependent on a "forward-failure" (diminished output) as well as on a "backward-failure". Mackenzie insisted on the importance of the cardiac muscle, and had a great deal to do with the acceptance of Stoke's conception. However, he remained unconvinced of the importance of the

mechanical factor of the "back-pressure" hypothesis and became the foremost exponent of the opposite or "forward-failure" theory.

Starling, Patterson and Piper demonstrated that the mechanical energy set free by the heart when it passes from the resting to the contracted state depends on the length of the muscle fibers, and that the venous pressure is the major factor in controlling the amount of blood pumped by the heart. Some investigators believe that this work of Starling has practically decided the question of "forward-failure" and "backward-failure" in favor of the latter. Korns and many others feel that the excellent studies of T. R. Harrison and his collaborators have done the most to round out modern conceptions of congestive failure. It cannot be overlooked that at present there are still those who strongly oppose Harrison's support of the "back-pressure" theory. In the following pages an attempt will be made to compare the views and evidence of some of these recent investigators.

THE TWO OPPOSING THEORIES

As already has been mentioned, two theories have been advocated by which to explain the signs and symptoms of chronic cardiac failure, namely: the "forward-failure" and "back-pressure" theories. There has been much confusion and controversy as to which of these more correctly accounts for the complex changes that take place in chronic congestive failure. Both hypotheses have strong proponents and opponents; but T. R. Harrison has done more to swing opinion in favor of the "back-pressure" theory than any other man. Up to the time of his clearly defined discussion the majority of the clinicians in England and the United States firmly believe in Mackenzie's"forward-failure" hypothesis. Altschule, on the other hand, feels that neither theory can accurately explain all of the changes, and that both theories neglect the chemical changes which he believes are so important in the genesis of the signs and symptoms of cardiac decompensations.

It is generally accepted that the clinical manifectations of chronic cardiac failure are, in the end, dependent upon exhaustion or fatigue of the heart muscle itself. The "forward-failure" theory presupposes that the clinical findings are due to an inadequate blood supply to the tissues because the heart is unable to pump a sufficient amount of blood. In the words of Harrison and the "back-pressure" theory "holds that the clinical phenomena of heart failure are brought about by dilatation of one or more of the chambers in the heart with a consequent engorgement of these portions of the body on the venous side

of the affected chamber". According to K. S. Smith the term "back-pressure" was originally used to convey the idea that regurgitation of blood through valves of the heart is the cause for the over-burdening of the venous (inflow) side of the circulation, and that tricuspid insufficiency is necessary because venous engorgement develops. Harrison, in support of this theory, has recognized and demonstrated that engorgement occurs quite apart from valvular damage or imcompetence.

The "forward-failure" theory is easy to understand and appeals to common sense; because it explains, on one basis, all of the phenomena of cardiac failure. This theory assumes that the cardiac output per minute is lowered in persons with congestive heart failure; that procedures which cause lowering of cardiac output, in proportion to the metablois needs, result in an increased severity of the symptoms of failure; and that clinical improvement is associated with increase in the ourput of the heart. Studies of cardiac output and its relations to these theories will be considered in the pages to follow.

Harrison summarizes the "back-pressure" theory in its simplest form as follows: "Overwork of the heart leads to enlargement which usually is brought about by both hypertrophy and dilatation of those portions of the heart which are subjected to the increase in work. If dilatation of a chamber becomes extreme, there results 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." The relation of cardiac output, velocity of blood flow, blood volume and venous pressure to this theory will be reviewed later.

Thus the latter theory states that the symptoms develope in the organs which feed blood toward the failing chamber of the heart; while the former indicates that the symptoms develope in the organs which receive blood from the failing chamber. Thus an alteration in intra-capillary pressure is the point of prime importance in the "back pressure" idea, whereas a change in volume-flow is the outstanding feature of the "forward-failure" thesis. In the following chapters we will try to determine which of these theories most nearly suffices to explain the cardinal clinical manifestations of cardiac failure.

PHYSIOLOGICAL CHANGES WITHIN THE HEART ITSELF

Failure of the heart affects the body as a whole, but as "cardiac failure" denotes, the changes start in the heart; thus it is no more than correct that we consider the impaired physiology within that organ first before going on to consider the pathogenesis of the signs and symptoms of congestive failure. Naturally without the impaired physiology in the heart the subsequent changes in other tissues would never occur.

Bedford considers "the heart as comprises of two separate pumping units, right and left, between which is interposed a vascular sponge in the form of the lungs, which by virtue of their ready capacity to take up additional blood, play an important part in the mutual adjustment of the two sides of the heart." Under normal circumstances these two pumps work in exact harmony; the leftventricle quickly adapting its output to correspond to the volume of blood delivered to it by the right, which thus sets the pace. Therefore Starling's Law of the Heart again can explain the physiological adjustments by which the two ventricles are maintained in equilibrium. Since the more powerful ventricle is in front of the lungs, nature has guarded against their being flooded under normal conditions, but when, as occurs in certain dosorders, the left ventricle is overworked, it sometimes fails to keep pace with the right ventricle, and the blood accumulates behind it in the lungs.

As already stated, the stress has come to be placed more and more on the state of the cardiac muscle. In the words of Harrison heart

failure begins"when, in order to perform a given amount of work the diastolis volume of the heart increases. Expressed otherwise it maybe said that the reserve power of the heart is beginning to fail when the sizeof the heart is increased in proportion to its output. Similarily congestive failure may be defined as a state in which venous pressure is increased disproportionately to the cardiac output, or as a condition in which the heart can maintain a given output only when driven to do so by a greater filling pressure. Heart failure is to be attributed, in the main, to inefficiency rather than to insufficiency of the myocardium."

The theory of myocardial inefficiency rather than insufficiency is becoming popular and generally accepted. With this theory in mind we may best consider the heart as a mechanical pump which is subjected to increased burden if there are incompetent valves, inflammation of the myocardium or increased peripheral load. Like any machine its effectiveness is measured by the total energy which it uses that it is able to put to useful work. Visscher feels that the maximum efficiency of the heart as a machine is 25%, the other 75% being dissipated as heat in the cardiac muscle. The normal heart has a large reserve power, which is manifest in the difference between the maximum work capacity and the work the heart does at rest. Thus, as would be expected in cardiac decompensation where there is aonstant decrease in the reserve power, the most prominent clinical feature is the progressive decrease in the amount of physical exercise which the patient can tolerate. Visscher also mentionsthat the limitation in the total energy liberated in congestive failure could possibly be due to an insufficiency, which

would correspond to the lack of fuel which might be supplied to a steam engine; thus in certain conditions as fibrosis or infarction of the heart, the cardiac muscle may be insufficient to carry out work rather than being inefficient. However, he considers it more probable that the limitations in the maximum amount of work be due to a decrease in the efficiency with which the expended energy is put to work. Thus it might be well that a decline in the mechanical efficiency of the heart muscle as a machine might be the basis of decompensation. Visscher states that in the isolated dog heart, when decompensation is present, its ability to liberate energy does not diminish but its capacity to convert the energy to work declines. Starling and Visscher found the oxygen consumption of the heart to be determined by the diastolic volume. This illustrates that the oxygen utilized by the heart is more dependent on the degree of dilatation than on the actual work performed. Thus a healthy heart doing a given amount of work with a small diastolic volume will require less oxygen per minute than a poor heart which has to dilate to do the same work. The dilated heart is therefore an inefficient heart because it can convert relatively less of the energy expended into mechanical work.

Kotz and Mendlowitz differ with the above investigators on the point of mechanical inefficiency being the basis for decompensation. They have done work with an isolated heart circuit in which they can cause failure with little or no change in the total diastolic volume. They found that, with the development of heart failure, and with a relatively unchanged diastolic volume, there is a progressive decrease

in the work and oxygen consumption of the heart and little change in its mechanical efficiency. Also, when the work of the heart was kept constant, they found no change in the oxygen consumption or mechanical efficiency despite a progressive increase in the diastolic volume. They felt that heart failure had to be defined in terms of a single chamber rather than the heart as a whole. This failure in a chamber was thought to be due to an increased load, a decrease in the contractile power or both, of such degree that the chamber begins to fail to do work which is placed upon it. They feel, therefore, that "the loss of contractile power is manifected by a reduction in the total energy release and hence work at a given diastolic volume and (except terminally) not by a decrease with which the liberated energy is utilized for mechanical work."

Back suggested that heart failure may happen for one of two reasons, namely: weakness of the heart beat, or increased resistance to the discharge or to a combination of both. He further states that when the heart "fails to adequately discharhe its contents, it does so because its beat is insufficently powerful to overcome the resistance its meets; therein is the cause of heart failure." He speaks of congestive heart failure as a"functional condition" almost always associated with organic heart disease, and indicates that cardiac failure means the inability of the heart to discharge its contents adequately and maintain a satisfactory circulation. Apparently Back remains rather vague in his explanation of why the beat is insufficient, and whether or not he considers the beat due to an inefficiency with which the expended energy is used.

As stated, most investigators agree with Harrison and disagree with Kotz and Mendlowitz, and thus attribute failure to inefficiency of the myocardium. However, at this point, another obstacle arises, and that is in trying to explain why or how the myocardium fails. There has been no entirely adequate answer as yet, and the vagle conceptions we have will be mentioned later in this chapter.

The cardinal objective sign of cardiac disease is enlargement of the heart, and it should be considered at this time. It has long been known what diseases cause cardiac enlargement, but there has been much dispute as to how it occured. The enlargement may be seen as hypertrophy, dilatation, or, as usual, a combination of both. It is most widely accepted by the investigators in this field that the heart dilates or hypertrophies because of an increase in the work it must perform. This latter statement is true if we consider that hypertrophy occurs indirectly as a result of increased work, and view dilatation as the basis on which hypertrophy arises. Eyster's excellent work on cardiac dilatation and hypertrophy has done much to prove the conception that hypertrophy occurs as the result of the muscle injury due to dilatation. He has found that there is always an initial dilatation which may disappear early and hypertrophy result; thus if the heart is examined at the end of the period of hypertrophy, the dilatation has disappeared and a histologic picture of simple pyhertrophy alone. He also concluded that prolonged overload is not essential to the development of hypertrophy, the prime factoe being the stratching of the heart muscle as a result of the overload, and that the hypertrophy

occurs after this stretching even though the overload is removed. Thus emphasis is placed on the injury to the heart muscle from stretching due to the overload.

An occasional observer as Christian does not accept the idea that hypertrophy is dependent, either directly or indirectly, on an increase in work, but he rather favors the view that enlargement is the result of disease of the heart muscle. Other investigators have ascribed the enlargement to alterations in the nutritional state of the heart. Post mortem examinations give the best evidence in favor of enlargement of the heart due to increased work, the clinical picture being correlated with the pathological findings. The basis for the conception of enlargement due to increased work is the fundamental physiological law established by Starling, which states that the strength of contraction of the muscle fibre is dependent on the initial length of the fiber. Thus it would make little difference whether greater strain is thrown on the individual muscle fiber, because of other fibers with consequent inability to carry their share of the load. Therefore, Harrison states "that cardiac hypertrophy seems to be a physiological response to prolonged and contiguous overwork of the organ and that the process is not a dystrophy as is implied by those who believe it to be a disease process in itself."

It is rather important to consider the relationship between hypertrophy and dilatation of the heart. The differentiation of these two states clinically is difficult, and depends upon inference from the patient's history and clinical state rather than upon actual objective

findings. Formerly it was believed that hypertrophy was a compensatory process, while dilatation was pathological and undesirable. This view is no longer held. T.R. Harrison and W. G. Harrison feel that dilatation does not follow hypertrophy, but preceeds and probably causes it. Thus they agree with Eyster that by hypertrophy is caused by dilatation, but they disagreee in that they believe that the overwork of the heart must be prolonged in order to produce the hypertrophy. They consider that dilatation is the normal immediate reastion to increased work; this, if prolonged, tends to produce hypertrophy after a time (the exact mechanism of which is not known). This hypertrophied muscle, being stronger, is able to do the work with shorter initial length; thus, Harrison feels that the dilatation disappears inna large measure. There are others who feel that increased load on a resting chamber produces primary dilatation, while increased load on a working chamber produces primary hypertrophy. Perhaps this latter group recognize the early initial dilatation which calls forth hypertrophy, but fails to give it importance in view of the prominence of the hypertrophy present.

Visscher stresses the importance of the dilatation of the heart, and states that the failing heart adapts itself to a new level of filling. He considers that "a small heart means a small systolic volume of residual blood, and that an enlarged heart is due physiologically to an increase in the residual blood after systole, which in turn, is due to the fact that the ventricular muscle in one chamber or another is

unable to do the work required to empty the chamber."
Thus, as already stated, the more the muscle fibers of the heart are stratched at the beginning of contraction, the more energy is liberated. It is then this property which allows the heart to adapt itself to the varying loads in the normal state and also permits the heart to function at all when it fails. Therefore, if the increase in residual blood did not give an increase in the amount of energy, the residual blood would progressively increase as soon as failure began, and soon the ventricle would dilate to a fatal limit. Thus in heart failure the heart may adapt itself to a new level of filling and be able to carry on. Therefore, from practically any viewpoint, it must be admitted that Starling's law of the heart seems to account for some of the important clinical aspects of the failing heart.

Harrison sums up the discussion of hypertrophy and dilatation as following: "Both of these processes are originally compensatory adjustments to an increase of the work of the heart in proportion to its strangth. Dilatation, by which we mean an increase in the length of the fibers relative to their width, is the immediate response and it offers a chemical advantage because of the greater surface and consequent opportunity for chemical interchange between the blood and its fibers. But dilatation puts the heart at a mechanical disadvantage because it increases the energy expenditure for a given amountof work. By some means, as yet unknown, this disproportion between the length and the diameter of the muscle fiber which has been produced by dilatation leads to hypertrophy, i.e., to increase in the width of the fibers,

and thereby the original relation of length to diameter tends to be restored. However, conditions are not the same as they were in the beginning because the mass of tissue to be nourished has increased as the square of the radius of the fiber, wehereas the surface of the fibers through which the nutrition processess must take place has only increased as the first power of the radius. The hypertrophic muscle fiber, while offering a mechanical advantage, suffers from a chemical disadvantage and its tendency will be to dilate further whenever conditions of stress arise. The vicious circle thus inaugurated from processes which were originally benign and compensatory adjustments tends eventually to produce congestive heart failure with its train of untoward phenomena."

As mentioned above, no one as yet has offered an entirely adequate account as to why or how the myocardium fails. The question of myocardial inefficiency has already been discussed. Hermann and Deckerd, Fishberg, and Harrison as well as many other investigators, have found that the anatomical findings in themselves often fail to show satisfactory correlation with the functional status of the heart. The term "fatigue" has been applied to this lack of knowledge, and Harrison believes that eventually the true physico-chemical processes which underlie fatigue of the heart will be understood. Fishberg has already pointed out the importance of inadequate blood flow, infection, and abnormal rhythm in the development of fatigue. "Fatigue" is used to describe the opposite of tone, which means the same as fitness.

The following is Starling's description of fatigue of the heart: "A heart in good condition, i.e., 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 fibers 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 diastolic volumes of the heart will be increases." Starling also stated: "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 occuring 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 fibers that the energy of the contraction becomes sufficent to drive on into the aorta during each systole the largely increased volume of blood

entering the heart from the veins during diastole.

"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 conditions 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 condition, 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 value even though it is doing increased work. It is only when the heart is fatigued or diseased that this secondary improvement fails to appear. When 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 than has to contract at such a mechanical disafvantage that the heart fails altogether. With the failure of the 'prime mover', all other mechanism of the body stops work, and the animal is dead."

From the above it is evident that Starling thought of cardiac fatigue as being manifested in the first place by dilatation of

increasing degree, the cardiac output remaining constant. The question of cardiac output and venous pressure in relation to the clinical phenomena of cardiac failure will be considered in a later chapter.

As already stated, Harrison feels that heart failure is a question of inefficiency and not insufficiency. He states that "in comparison with the normal heart the fatigued and dilated heart of a patient with congestive failure has to consume more oxygen in order to pump a given amount of blood against a given resistance. This inefficiency constitutes the cardinal physiological change associated with congestive heart failure."

Harrison also believes that there is a definite relation of cardiac fatigue to the heart rate. Patients with congestive failure often have increased pulse rates because of the Bainbridge reflex, which states that elevation of venous pressure results in increased rate of the heart. The advantage is that an increase in pulse rate makes it possible for the heart to pump a given amount of blood per minute with less dilatation and hence lower the venous pressure somewhat. The harmful effects of the tachycardia offset the above, in that the greater the rate the more frequently energy must be used in opening the semilunar valves, and this energy is not used in propelling blood. Thus a given minute output can be accomplished more efficiently with a slow than with a rapid heart rate. There is marked clinical evodence of the disastrous effects of tachycardia in persons with enlarged hearts.

Eyster has experimentally shown how tachycardia and abnormal cardiac rhythms decrease the efficiencymof the heart. Tachycardia, as well as increase in the work of the heart on a direct toxic action, may play an important part in producing congestive failure in cardiac patients when infections or severe emotional disturbances are present. Research shows that tachycardia is harmful because it increases the oxygen needed by the heart to do given work, it interferes with the blood supply of the heart, and it may not allow enough time for oxygen diffesion into the muscle fibers, especially if they are hypertrophic.

Most investigators will agree that there is a wide field for research along the line of chemical changes in the failing heart, and of what consequence these changes are. Wilkins and Cullen have studied chemical changes in fatigued hearts. They found decreased potassium, phosphorusa and magnesium, and an increase in sodium. Marked differences in calcium were not found. The total base was usually some less in cardiac patients. These fatigued hearts were richer in elements which are normally more abundant in tissue fluids. The interpretation of these changes in electrolyte content is as yet not cleare. Some differences are due in part to edema fluid. A change in permeability of the membranes of the muscle fiber may be increased. As far as we know these changes may tend toward producing further fatigue of the heart; then, on the other hand, any such trend may be compensated for by other chemical alterations as yet unknown.

Herrmann and Decherd have done work along the line of the chemical changes of heart failure. As stated, they also noted that anatomical findings often fail to show satisfactory correlation with the functional status of the failing heart. A derangement of the physio-chemical processes concerned in cardiac muscle contraction has long been suspected. Meakins directed attention to the newly established facts concerning phosphocreatine or phosphagan in skeletal muscle physiology, and commented upon a possible analogy in heart muscle functions. Meakins also stressed the importance of cardiac glycogen and lactic acid formation as affected by oxygen definiency and acidosis and other metabolic disturbances, and he related them to failure. Many have stressed the fact that the cardiac muscle fails to function properly when there is oxygen want, insulin deficiency, or a defect in cardiac glycogin metabolism. Thus oxygen, insulin and glycogen are essential to good cardiac contraction. After all the glycogen in the body is lostthere is still some in the heart muscle, because it can oxidize lactic acid and use it over and over. As soon as the oxygen supply is shut off the glycogen in the heart quickly disappears. It seems, therefore, logical to many that myocardial fatigue results by reason of its glycogen lack and anoxemia.

On data collected by Herrmann and Decherd it was apparent that some conditions which may contribute to heart failure may play a role in changing the creatinine and phosphorus content of the heart muscle. They found subnormal myocardial total creatinine in hearts from patients who showed "striking anemia, conspicuous asphyxia as a

result of strangling, acute or chronic pulmonary disease, syphilitic aortitis or coronary aeterial disease". In their studies hypertrophied hearts, which had not failed, from hypertensive patients who died of cerebral hemorrhage, and from chronic valvular disease cases showed normal or high creatinine values. Experimentally produced hypertrophy was always accompanied in the early stages by a building up or retention of creatinine and always by an actual increase. Lowered total creatinine values were found in the pneumonia heart. They stressed the fact that the apparent tendency of digitalis to cause elevation of the total creatinine is significant of a chemical myocardial action. In failed hearts it seemed that the total creatinine and creatine, total phosphorus and acid soluble phosphorus were reduced. Whether these chemical changes are the cause or result of heart failure could not be answered. These authors considered the possibility that some conditions lead to creatine and phosporus losses from human hearts and this results in cardiac weakness. Thus they extended Harrison's physical theory of circulatory failure to possibly include inevitable biochemical changes in heart muscle to account for myocardial insufficiency (inefficiency).

Visscher has given an excellent account of the importance of the coronary circulation in making decompensation a progressive phenomenon. He believes that the progressive nature of heart failure is due to certain vicious cycles which are set up. To understand his explanation a few fundamental facts about the coronary circulation should be understood. Visscher sketches the coronary flow as below:

Partition of the Coronary Flow

Coronary arterial blood

Arteriols

Capillaries

Coronary sinus Thebesian veins

Right atrium Right and left heart

Fig.1

The importance of this divided path can be understood when it is realized that the flow in the coronary system depends upon pressure gradients, the magnitude of flow through each of the channels depending upon the pressure gradient in each situation. The greater share of blood supplying the left ventricle emerges through the coronary sinus, while the larger share supplying the right ventricle goes into the chambers of the right heart via the Thebesian veins. The pressure difference between the aorta in diastole (when the most flow occurs) and the coronary sinus is the pressure gradient of greater importance for the left heart. Therefore elevations in pressure in the coronary sinus impede the blood flow through the vessels of the left ventricle because they result in a decrease in the pressure gradient. The pressure gradient between the aorta and the right ventricle primarily determines the coronary flow through the right ventricle. Visscher gives the following table:

Factors Influencing Coronary Blood Flow

1. Aortic blood pressure (primarily diastolic because most of the flow through the left ventricle is during diastole).

2. Systemic venous pressure (controls the pressure in the coronary sinus).

3. Right intra-ventricular pressure (controls the flow from the right Thebesian veins).

4. Chemical and nervous factors influencing the bore of the coronary vessels.

Fig. 2

Visscher then carried out experiments with cannulae to control the above factors, the blood was collected from the coronary sinus and at the output of the right which receives only Thebesian vein blood. Thus he had control of all the gradients which determined the coronary flow. He found that, if he held the aortic and pulmonic pressures constant and raised the coronary sinus pressure, there resulted a decreased amount of blood from the coronary sinus (normally 50-60% of coronary blood reaches the coronary sinus). If, on the other hand, he held the aortic and coronary sinus pressures constant but raised the pulmonary arterial pressure, there resulted a progressive relative increase in the flow into the coronary sinus because the Thebesian flow into the right heart frll off; this latter resulted in impairment of the nutrition of the right ventricle (the oxygen in the Thebesian blood has been proportionally more removed, and the muscle is working under less favorable conditions). Visscher thus charted the changes seen in Fig.3. From his findings Visscher was able to realize the vicious cycle that takes place

to make chronic cardiac decompensation a progressive phenomena. In Fig. 4 he gives the progression of heart failure as influenced by coronary circulation factors in the case of primary left heart failure.

Physiological Properties of the Normal and Failing Heart

	Normal	Failing
Systolic volume residual blood	Small	Large
Atrial pressure	Low 6 cm.water	High 15 cm. water
Efficiency of doing work	High (20%)	Low (as low as 1%)

Fig. 3 (From Visscher)

Below is the visious cycle as seen by Visscher which tends to make cardiac decompensation a progressive phenomena.

Initial Stage
Increased residual blood in left ventricle (systolic volume increase)

Impaired function of left ventricle	Elevated left atrial pressure
Decreased coronary sinus blood flow	Increased pulmonary venous pressure
Increased right atrial pressure	Increased pulmonary arterial pressure
Impairment of function of right ventricle	Increased right intraventricular pressure

Decreased right Thebesian flow

Fig. 4

From these investigations Visscher was able to draw certain important clinical conclusions. He concludes that the left ventricle can carry increased loads for long periods of time without serious embarrassment as long as pressure changes in the other chambers do not occue. However, mitral valve disease has a more serious prognosis even when its effect on the work of the left ventricle is a lot less. Arterial hypertension can be carried by the left ventricle without serious physiological consequences, because of the above described arrangements of its coronary flow (only a small fraction by Thebesian channels in the left heart). As long as no pulmonary engorgement occurs the left intra-ventricular pressure in diastole is not a determining factor in the regulation of the coronary flow in the left ventricle. The case of the right ventricle is very different because venous pressure elevation or increase in the pulmonary arterial pressure tend to restrict the coronary flow. Pulmonary hypertension is usually associated with general venous pressure elevation and both ventricles are functionally impaired.

Thus the function of the heart depends on its oxygen supply which can be diminished by altering the pressure factors or the oxygen carrying power of the blood. Anginal symptoms do not always occur in cardiac anoxia, and they rarely occur if the decrease in oxygen is gradual. From much of the above discussion it can be understood how the general signs of heart failure are more common with a reduction in the hypertension.

From his investigation Visscher concludes: "It will be seen that the failing heart is a muscular machine in which the amount of energy needed to do its work has increased and that its ability to liberate energy depends upon its oxygen supply. Oxygen supply is in turn determined by the coronary flow which again depends upon pressure factors. It happens that the pressure elevations which occur in heart failure are those which tend in themselves to diminish coronary flow, and therefore the nutrition of the heart. Thus these factors arrange themselves in a vicious cycle, and therefore cardiac decompensation tends to be a progressive phenomena.

With these changes in physiology in the heart itself in mind, we may outline, in the chapters to come, some of the important physiological changes which play a major part in the pathogenesis of the symptoms and signs of heart failure.

LEFT AND RIGHT HEART FAILURE

Before progressing into a consideration of the pathogenesis of the signs and symptoms of congestive heart failure, it may be wise to review briefly a few facts concerning primary right or left heart failure. It is generally accepted that there is an interdependence of the cardiac chambers in the maintenance of efficient circulatory function. But there are clinical manifestations which tend to indicate whether the right or left ventricle is mainly involved. It is naturally clear that, depending mainly on etiology, either the right or the left side of the heart is predominantly involved. Clinically one-sided failure may exist alone for some time, but eventually in chronic cardiac failure the whole heart usually fails. Thus, on a theoretical basis, for explaining signs and symptoms, the failure of each side may be considered separately; However, on a practical basis, the progressive nature of failure (as discussed in the last chapter) and the interdependence of the chambers must not be forgotten.

Korns feels that by studying the right and left heart failure separately the entire problem is reduced to its simplest terms and the everyday case of bilateral congestive failure can be apprehended more clearly. Primary left ventricular failure is more common since the left ventricle is more often subject to strain, particularily as the result of hypertension, aortic stenosis or regurgitation and occlusion of the descending branches of the left coronary. The right ventricle is affected mainly by mitral disease, chronic pulmonary disease, congenital pulmonic

stenosis, and as a result of progessive failure of the left ventricle.

In clinical terms, left heart failure implies pulmonary engorgement behind weakened left ventricle, without systemic venous congestion and its consequences, and with a normal venous pressure. Harrison defined left heart failure as a failure of the left ventricle to maintain a normal output in the presence of a normal filling pressure. The dominant clinical manifestation is pulmonary congestion and edema, which may be observed in all degrees. The symptoms may be noctural cough, slight wheezing, expectoration and hemoptysis on up to severe hypernea, dyspnea, and air hunger. One may class the manifestations as paroxysmal pulmonary congestion, pulmonary congestion of effort, or chronic pulmonary congestion. Basal rales are usually present. The congestion may even involve the pleura and hydrothorax result. Cheyne-Stokes breathing is sometimes a manifestation, as also is angina. Cardiac manifestations are varied, tachycardia being the rule, with gallop rhythm, pulsus alternans and auricular fibrillation sometimes noted. At first there is a hypertension in the lungs which enables the inefficient left ventricle to maintain its output for a time; next there is stasis and edema of the lungs against which the right ventricle struggles awhile, though eventually its yields, affording some relief for the congested lungs. Thus the pulmonary hypertension is looked upon as a compensatory adjustment by which the diastolic filling and hence the output of the left ventricle is maintained.

Right heart failure is much less dramatic symptomatically than is left heart failure. If long standing, however, it may result in severe

digestive symptoms as loss of appetite, persistent nausea, vomiting or even pain in the region of the stomach and liver. Shortness of breath may be enough to tire the patient, but it usually lacks the strangling element of true dyspnea. On the other hand the objective manifestations are very apparent, and may include odema, venous distention, visceral congestion with palpable enlargement and tenderness of the liver, transudation into serious cavities, oliguria with albuminuria, cyanosis and increased cerebro-spinal fluid pressure. If tricuspid insufficiency develops the signs become more pronounced, and there may be marked centrifugal pulse into the cervical veins and the liver.

Brill has considered cor pulmonale from the clinical aspect. He interprets it in a broad sense as including all types of cardiac strain and failure in which the right side of the heart is importantly involved, either as the initial circulatory disorder (primary cor pulmonale) or as consequence of an antecedent failure of the left side of the heart (secondary cor pulmonale). In most cases the immediate cause is an obstruction or increased resistance to blood flow within the pulmonary circulation at any point between the pulmonary conus and the mitral valve. In a few cases as in congenital septal defects and in organic tricuspid regurgitation, right sided strain and failure may result in the absence of the above. The ratio of primary and secondary cor pulmonale is one to five. The most common type of right sided heart failure thus, is the advanced stage of general heart failure (secondary cor

pulmonale). The immediate cause of secondary cor pulmonale is the pulmonary congestion and the consequent increased resistance to the pulmonary circulation resulting from the antecedent failure of the left ventricle. The remote causes of secondary cor pulmonale are naturally conditions which cause failure of the left side.

We have thus quickly reviewed the signs and symptoms most commonly the result of failure of one side or the other. We may now, in the chapters to come, consider the many controversal physiological changes in the body, and how different investigators derive the pathogenesis of the clinical manifestations of heart failure from these changes.

MAJOR PHYSIOLOGICAL CONSIDERATIONS

We will now attempt to review some of the proposed alterations in physiology as such, and then, in the following chapters, we will link these changes up in the pathogenesis of the primary signs and symptoms of chronic cardiac failure. As will be easily seen, there is great controversy concerning many of these alterations in physiology, and many of the points are undecided and have insufficient evidence as yet for their support.

A. The Cardiac Output

By far one of the most controversal and important subjects in congestive heart failure is the question of cardiac output. It is on the basis of changes in cardiac output that the entire theory of "forward-failure" is founded; this theory assumes that the cardiac output per minute is subnormal in persons with cardiac decompensation, that improvement in the clinical features is associated with an increase in the output of the heart, and that procedures which cause diminution in cardiac output in proportion to the metabolic needs necessarily result in an increase in the severity of congestive failure.

Harrison believed the majority of methods for determining cardiac output were inaccurate. He considered the Grollman acetylene method one of the most accurate, and using this method he studied cardiac output in numerous subjects. In general his conclusions were that the above assumptions of the "forward-failure" theory based on

decreased cardiac output were not carried out. He found that the output per minute of the heart, in relation to the metabolic needs, is usually subnormal in cardiac patients, that in certain cases it was within normal range and rarely in the upper limits of the normal range. The stroke volume was nearly always subnormal in patients with symptoms, the accelerated heart rate playing an important role here. He found that patients without heart disease have normal cardiac outputs, with the occasional exception of one who had an output as low or lower than the majority of those patients with cardiac disorders. Likewise, patients with congestive failure were found, in general, to have outputs within the same range as those of patients with cardiac disease but without congestive phenomena. Clinical improvements with the disappearance of congestive manifestations showed an associated increase, a decrease, or no change in cardiac output per minute. Harrison's conclusion was that various therapeutic measures which produce benefit in persons with congestive failure do not ordinarily produce an increase in cardiac output, and that inconstant effects are found from digitalis and diuretics, while rest and bleeding decrease the output. He also produced logical arguments in that, according to the "diminished output" theory, any measure which increases the output of the heart in relation to the metabolic needs should be beneficial. He then pointed out that there is such an increase in recumbency as compared with the sitting position, and a similar increase with psychic disturbances and with the use of alcohol and tobacco; but those conditions do not produce improvement, but

rather have deleterious effects on the congestive manifestations.

Since he concluded that the above arguments put the "forward-failure" theory on rather shaky ground, Harrison took up his defense of the "back-pressure" theory. According to him this hypothesis does not imply that the output of the heart is subnormal continuously throughout the duration of congestive failure, but rather implied that there is a reduction in the output for a few seconds or minutes at a time. An example given in Harrison's own words can best explain this: "Let us take a case of hypertension and assume that the left ventricle is hypertrophied and dilated hut has not yet 'failed', i.e., the pressure in the left auricle is normal. The output of each ventricle is, let us assume, 40 cc. per beat, and the minute volume 3.2 liters, the pulse rate being 80. Now if the left ventricle becomes a little more fatigued it may expel only 39 cc. per beat. For a short period of time, however, the inflow into the left ventricle will continue to be 40 cc. per beat and hence after ten beats it contains 10 cc. more blood at the end than it did heretofore. As the left ventricle becomes more dilated the pressure in it rises a little toward the latter end of diastole. Hence, the left auricle, which still has an unaltered pressure curve, now expels only 39 cc. per beat into the left ventricle-- the rate of clow being obviously affected by the difference in pressure in the two chambers. But the left auricle is still receiving 40 cc. of blood at each heart beat. If it is expelling only

39 cc. it is retaining 1 cc. at each beat. Since the left auricle is very distensible it may ratain considerable blood without a rise in pressure, but eventually its pressure will rise. Let us assume that the time required is that of thirty heart beats. The difference in pressure between the two chambers is now the same as it was in the beginning, and hence not 39 but 40 cc. of blood passes from the left auricle to the left ventricle during each diastole. But the latter chamber is now able to beat a little more powerfully because of its diastolic length, i.e., dilatation. Hence it again expels 40 cc. per beat.

"The conditions in the pulmonary circuit undergo change however. As soon as the pressure in the left auricle rises, less blood enters the left auricle than formerly. But since the right ventricle is still expelling 40 cc. of blood at each heart beat, the pressure in the lesser circuit rises as blood accumulates in the lungs. Because of their sponge-like consistency, and also because their cappillaries are unique in being surrounded by air, it probably takes a relatively large volume of blood to cause a small rise in the pulmonary vascular pressure. Let us assume that 200 cc. of blood would suffice. (This value is purely arbitrary but seems of reasonable magnitude).

"This rise in pressure now corresponds in degree to the increase in the pressure in the left auricle. As a result 40 cc. of blood again enter the left auricle at each beat. So far as volume flow is concerned the conditions are now exactly the same as they were in the be-

ginning; each ventricle is now expelling 40 cc. per beat, and, if we assume the pulse rate has remained constant, the cardiac output per minute is exactly what it was in the beginning. In order that this could occur, however, the following changes have taken place:

1. A temporary decrease in the output of the left ventricle.

2. An increase in the degree of dilation of the left ventricle.

3. An increase in the size of the left auricular cavity and in the left auricular pressure.

4. An increase in the pulmonary vascular pressure and in the volume of blood in the lungs.

5. A diminution of vital capacity because of (a) the greater content of blood in the lungs and (b) the resulting increase in rigidity (for the lungs can be regarded as erectile tissue).

6. A slowing of the average velocity of blood flow in the lungs- for the size of the stream has increased but the volume flow has not changed.

7. An increase in the work of the right ventricle because of the rise in pulmonary pressure. The ventricle consequently dilates and, after a time, may become hypertrophied.

8. A loss of 240 cc. of blood from the peripheral circulation (10 cc. into the left ventricle, 30 cc. into the left auricle, and 200 cc. into the lungs). Hence, if the amount of blood in the peripheral circulatory system is to be as great as before the total blood volume must increase by 240 cc."

From the above it can be seen that even a very mild degree of cardiac failure leads to rather complex changes in the various circulatory functions. Also it is seen that a temporary and small reduction in cardiac output, without significance from the standpoint of tissue blood supply, may have an important and very lasting effect on other circulatory functions. Thus Harrison concludes that "if the 'back-

pressure' theory is correct it would seem that the explanation of the clinical manifestations of congestive heart failure should not be sought in the cardiac output but rather in other functions, such as the venous pressure, the blood volume, and the velocity as distinguished from the volume of blood flow."

W. G. Harrison agrees that in general there may be a slight decrease in cardiac output during heart failure. He also feels that this change is not constant, does not go parallel with the severity of the disease, and does not show a parallel relation with the clinical improvement of the patient under drug therapy. Thus he does not feelthat the decreased output is the major cause of the signs and symptoms of heart failure.

Altschule also feels that in general it must be concluded that a diminution in the cardiac output relative to the metabolic requirements of the body is the rule in congestive failure, and that the accelerated heart rate accounts for the increased diminution in output per beat as compared with the decrease per minute. He suggests that in cardiac decompensation the output of the heart does not increase normally in response to work, since it is will known that in normal individuals a small increase in venous pressure gives a marked increase in cardiac output, but such is not the case in congestive failure.

Altschule then considers that the decreased output in failure may b e due to three things, these being either rapid heart action,

auricular fibrillation or weakness of the myocardium (the latter being the most common). He also concludes that there is a decrease in cardiac work in heart failure, since the work of the heart is directly proportional to the cardiac output. He disagrees with Harrison, and does not believe that diminished cardiac efficiency rather than low output determines the pressence or absence of congestive failure. The following statement is a summary of Altschule's ideas: "Changes in cardiac dynamics can influence tissues only through cardiac output and venous pressure. Cardiac efficiency is interesting and important, but is not directly responsible for the development of the signs and symptoms of congestive failure." However, in stressing the importance of lowered cardiac output in the pathogenesis of the clinical phenomena of heart failure, Altschule would seem to contradict himself to some degree when he states that the severity of the signs and symptoms does not parallel the decrease in the output of the heart.

McGuire and his assistants have done some concentrated studies on cardiac output. He recognizes the controversy between Harrison on one side and his opponents on the other. He considers the normal output of the heart to be 2.2 liters per minute per square meter of body surface. He explains the occasional normal or super-normal output found, in that certain factors known to elevate the output of normal hearts are usually present during decompensation, as exercise associated with hyperpnea, elevated venous pressure, increased metabolism, anxiety and apprehension, and low grade fever. Thus he

believes that the disease of the myocardium diminishes the systolic discharge of the ventricle (invariable decreased in relation to the accelerated physiological activities of the decompensated patient), which is the initial factor responsible for cardiac failure. This decreased output produces increased intra-venous pressure (back-pressure) and diminished peripheral flow (forward-failure) simultaneously.

McGuire at al. also did studies on the cardiac output in compensation and decompensation in the same individual, and studies on the influence of exercise on cardiac output in congestive heart failure. In the latter studies it was found that normal subjects on the average increased their output 2.07 liters per minute, patients with compensated cardiac disease increased cardiac output on the average 1.21 liters per minute, while patients with congestive heart failure averaged .75 liters per minute increase in output following exercise.

McGuire felt that Harrison's studies had convincingly demonstrated that back-pressure is the principle factor responsible for the cardinal manifestations of congestive heart failure; however, he considered that the simultaneous reduction of forward flow with the frequent decrease in oxygen saturation of arterial blood and the reduction of the volume of blood supplied to the tissues are probably contributory factors (these will be discussed in the next chapter). He

concludes that back-pressure is the principle mechanism responsible for the symptoms, but that the "forward-failure" and "back-pressure" factors cannot be divorced and that they develop simultaneously as the result of decreased cardiac output and operate conjointly to produce the clinicel manifestations of cardiac decompensation.

Thus the controversy concerning the place of cardiac output progresses, with each and every investigator, even though finding in main the same changes in cardiac output, giving a different interpretation to the importance of the cardiac output in the pathogenesis of the clinical features of congestive failure. To this writer it seems that Harrison, as a whole, gives the most thorough and convincing argument.

B. The Circulation Time

Practically all investigators agree that the velocity of the blood flow is reduced in congestive heart failure. W. G. Harrison has even gone so far as to say that the circulation time is of greater significance in prognosis than the venous pressure. Bedford states that the arm to tongue circulation time is always increased in left-sided failure; if the arm to lung time is substracted from the arm to tongue time, an index of the pulmonary circulation time (normally 4.5 to 10 seconds) is obtained, and this is always increased in left heart failure.

T. R. Harrison also notes a reduced velocity of blood flow,

but he does not believe that this should be interpreted as indicating that the volume flow, i.e., the cardiac output, is likewise diminished. Altschule on the other hand, believes that the slowing of the pulmonary circulation time is due to lowered cardiac output and engorgement of the pulmonary vessels; and he also states that, since slowing of the pulmonary circulation time is frequently associated with dyspnea in patients with congestive failure, measurement of this time is of use in telling between dyspnea due to cardiac decompensation and that due to pulmonary disease.

C. The Blood Volume

In the view of most investigators there is an increase in the blood volume in patients with congestive heart failure. Numerous experiments, which will not be mentioned here, have proven this view. Harrison feels that the failure of patients with cardiac decompensation to exhibit marked weakness early is probably due to their compensatory increase in blood volume. He illustrates by comparing a person with shock, who not only has a subnormal cardiac output but also relatively empty capillaries, with a patient in decompensation who may have equally low cardiac output, but has a greater number of open capillaries because of the increased blood volume. The exchange of substances between the tissues and the blood is dependent on the number of open capillaries as well as on the rate of blood flow. The origin and the fate of this increased amount of blood is as yet unknown.

Altschule feels there is a high degree of correlation between

the severity of the signs and symptoms of cardiac failure and the increase in blood volume. He believes that the increased blood volume is responsible for only a small part of the venoue pressure rise since diuresis causes marked decrease in volume and only small changes in the venous pressure. General vasodilatation, as suggested by the increase in the number of capillaries visible in the skin is probably related to the abnormally large volume. The increased volume may represent an attempt to compensate for the low cardiac output; this is understood if one considers that anoxemia results if the blood flow through a unit volume of tissue is low, and that larger volume of blood kept in contact with a unit volume of tissue helps remedy the anoxemia. It has been noted that the signs and symptoms of surgical shock can be caused by the rapid dehydration of a decompensated patient. Altschule noted that the red blood cell count and the hemoglobin value show no consistent change, and are near the normal values. Thus there must be an increased number of red blood cells in total since there is an increased blood volume. Sometimes there is a tendency toward increased corpuscular volume, and anoxemia, which is known to stimulate the formation of red blook cells, is probably the cause of this increase.

Gibson and Evans found that there is a progressive increase in the volume of plasma and red blood cells in the change from the state of compensation to decompensation in a cardiac patient. They state that the increase is sharedto a slightly less extent by the plasma than by

the corpuscles, thus resulting in a slight concentration of the blood. These investigators found that the average degree of increase in blood volume above normal parallels the average degree of elevation of the venoue pressure and the slowing of the circulation time, but they don't state whether they interpret the increased blood volume as responsible for the venous pressure rise or not. During recovery there was found to be a diminution in both plasma and cell volume, the decrease in the former being the more rapid and thus giving varying degrees of blood concentration.

Wood and Janeway agree that there is an increased blood plasma in congestive failure. Chronic passive congestion of the lungs was considered as associated with an increase in the volume of blood in the pulmonary vascular bed, as evidenced by a decrease in the vital capacity of the cardiac patient. They also state that if the right ventricle as well as the left has failed, the volume of blood in the systemic venous bed is likewise increased, as evidenced by engorgement of the superficial veins, increased venous pressure, and enlargement of the liver and sometimes the spleen. These investigators indicate that this large volume of blood transferred to the pulmonary vessels and to the systemic circulation is lost to the arterial circulation, and that, if the arterial circulation were not able to compensate for the blood loss, the patient would go into shock. They state that "the blood pressure is maintained temporarily by a decrease in the

volume of the arterial vascular bed, brought about by a local vasoconstriction, and more permanently by an increase in the total volume of blood resulting from the retention of water in the plasma. They stressed the increase in plasma in congestive heart failure with practically no mention of change in the red blood cell count, apparently believing that the red blood cells do not have an associated increase in number.

Starr did a study of the non-cardiac blood pressure in congestive failure. He found that after death in the dog there was a non-cardiac blood pressure, and that this increased in congestive failure. He considers three possible sources for this increased pressure after the heart has stopped, there being increased blood volume, compression of blood vessels by pressure from outside tham without compensatory reduction of blood volume (as fluid accumulation within the body) or constriction of the vessel walls(unlikely).

D. The Venous Pressure

Investigators are in agreement that outright congestive heart failure is invariably associated with a rise in venous pressure. There is no direct measure of the venous pressure of the lesser circulation, but we cannot doubt that it is present because such an increase must be present to bring about the congestion.

The importance attached to the venous pressure in the pathogenesis of the clinical phenomena varies with each investigator. W.G.

Harrison pronounces the venous pressure as the "common denominator" of congestive heart failure, and states that one must understand venous pressure in order to appreciate the physiology of heart d failure. He finds that the venous pressure runs parallel to the degree of congestive failure, and decreases as the heart decreases in size on therapy, and as odema disappears. Thus he concludes that the venous pressure in a patient with congestive heart failure under conditions of exertion, cough, straining, and excitement behaves very differently from that in normal people, and that it is this increase in venous pressure which is responsible for the manifestations of failure.

Altschule states that the rise in venous pressure is due mainly to the inability of the heart to take up and propel forward all of the blood brought to it, and that this view is supported by the fact that the rise which follows exercise is greater and more prolonged in cardiacs than in normal subjects. He also considers hyperpnea as another contributory factor in increased venous pressure, since the increased respiratory activity raises the intrapleural pressure and thus impedes the entrance of blood into the thorax. Pulmonary congestion must also be considered to have a similar effect since it raises the intrapleural pressure.

E. The Cerebrospinal Fluid Pressure

It is generally accepted that the cerebrospinal fluid pressure

parallels the venous pressure as in normal physiology, thus it is increased in congestive heart failure as is the venous pressure. Patients suffer none of the symptoms usually associated with similarily increased intra-cranial pressure due to primary intra-cranial disease such as headache, coma, vomiting, slow pulse or papilledema. Venesection lowers the cerebrospinal fluid pressure. Some investigators have noted the disappearance of orthopnea after venesection. W. G. Harrison did not note this, but he did see the disappearance of orthopnea after a spinal puncture. These observations would at first seem to be in accord with the hypothesis of diminished cerebral blood flow as the cause of orthopnea. However, W. G. Harrison also noted that the spinal puncture caused a decrease in venous pressure, and thus the relief of the dyspnea is to be attributed to diminished reflex respiratory stimulation as a consequence to the reduced venous pressure.

Altschule points out that patients with increased intra-cranial pressure due to local cerebral causes do not have orthopnez, and therefore concludes that no relation between increased spinal fluid pressure and orthopnea in heart failure can be demonstrated. As stated above, W. G. Harrison does not speak of a relation between these two, but rather that the spinal puncture relieved the orthopnea indirectly by way of reducing the venous pressure and thus diminishing reflex respiratory stimulation. The reason for the decrease in venous pressure following a spinal puncture is obscure.

F. The Pulmonary Physiology

The heart and lungs are intimately related, and thus some of the earlist evidences of congestive failures are usually manifestations of altered pulmonary physiology. Most investigators will agree that pulmonary engorgement is responsible for most of the changes in the pulmonary physiology. Unlike the systemic circulation, the chemical and nervous control of the calibre of small pulmonary vessels is of secondary importance in regulating the volume of flow through the lungs; thus numerous investigators have established that the volume of blood flow through the lungs is determined primarily by the activity of the heart, and that, in health, variations in the resistance in the lungs are of little moment. It is considered by many that the calibre of the arterioles in the lung is greater than that of those in the systemic circuit, and thus the blood encounters little resistance and flows rapidly through the lungs despite the fact that pulmonary arterial pressure is much lower than systemic arterial pressure. Therefore, in health, in most conditions of increased blood flow the depth of respiration is increased with resultant increase in the average cross-section of the pulmonary capillary bed due to distension of the lungs. Theresult of these arrangements is that, in health, any volume of blood returned to the right heart is readily pumped through the lungs, apparently with comparatively little rise of pressure in the pulmonary artery.

In review of the above facts, Fishberg states that there are

two conditions which are required for the production of passive pulmonary engorgement, namely: (1) Insufficiency of the left side of the heart, and (2) an adequate output of the right heart. The former is the prime cause of pulmonary engorgement. By means of the regulatory mechanisms described above, the blood content and pressure within the pulmonary circuit are maintained at levels inversely proportional to the functional efficiency of the left heart. Much like Harrison, Fishberg explains this as follows: "When the left heart weakens, its failure to empty completely, while the right ventricle continues to discharge its previous quantum of blood, results in accumulation of blood and rise in pressure in the pulmonary veins. This entails an increase in the pressure at which the left heart is filled during diastole. According to Starling's law of the heart, this invokes more powerful contraction of the left heart. The result is that the output of the left heart is once more equal to that of the right, and the circulation is again in equilibrium, albeit only at the expense of higher pressure and engorgement in the pulmonary circuit." Thus inefficiency of the left heart results in increase in the volume of blood contained in the pulmonary vessels, increase in the pressure within the pulmonary vessels, and decrease in the velocity of blood flow along the pulmonary circuit. These would not be present if the right heart did not maintain an adequate output for a time at least.

The pulmonary engorgement must be of great importance in the alteration of the mechanics of ventilation and of the air content of

the lungs; this cannot help but be of great clinical significance. The total capacity or total lung volume is decreased in pulmonary engorgement, due to the diminution in the capacity of the alveolar spaces. The minute volume of ventilation is increased above the normal, the increased rate more than making up for the decrease in tidal air. The vital capacity is decreased, thus the great significance of increased minute volume of respiration for the production of dyspnea becomes more evident in the light of the fact that the greater air exchange is accomplished in the face of decreased vital capacity. Even the strongest respiratory stimuli fail to increase ventilation (vital capacity) to the same extent as in health. There is always a relative or absolute increase in the residual air in pulmonary engorgement. There is increased pulmonary rigidity (decreased elasticity and distensibility) due to pulmonary engorgement. The lessened elasticity of the lung predisposes to dyspnea through decreasing the amplitude and increasing the work of respiratory movement. Thus the pulmonary rigidity is also a primary cause of the increased residual air and decreaded vital capacity of the engorged lung. There is shallow breathing and thus it is obvious that the dead space constitutes a larger portion of the total respiratory volume and thus lowers the efficiency of ventilation in cardiac dyspnea.

It is almost universally agreed that the exchange of gases between the alveolar air and the blood occurs by diffusion. Carbon dioxide normally diffuses 30 times more rapidly than oxygen, and this

may account for the fact that carbon dioxide tension in the arterial blood and alveolar air is almost identical, while there is a partial pressure of oxygen from 19 to 62 mm. of mercury lower in arterial blood than in alveolar air. In cardiac disease the difference between the partial pressures of the respiratory gases in the alveolar air and the arterial blood may be very much greater than in healthy persons. Arterial oxygen saturation is lowered in some, but not all, patients with cardiac dyspnea, while the oxygen content of the alveolar air is apt to be elevated. Carbon dioxide, which diffuses so rapidly, tends to show a much less difference in arterio-alveolar tension, and is only significant when pulmonary engorgement is severe. Fishberg summarizes such considerations as follows: "Probably, several factors are summated in bringing about the abnormally great oxygen and carbon dioxide arterio-alveolar tension differences present in some instances of cardiac failure. As a result of pulmonary rigidity and unequal ventilation of different parts of the lungs, aeration of the blood passing the poorly ventilated alveoli is correspondingly impaired and contaminated that from the well-ventilated alveoli when mixed with it in the pulmonary artery. But in addition it seems probably that the alveolar walls in passive congestion offer greater resistance to the diffusion of the respiratory gases than in health, although it is difficult to evaluate this factor quantitatively. The thickening and other change observed histologically in the alveolar walls of the engorged lung suggest decrease in their permeability. Certainly the

presence of transudate must interfere with the diffusion of gases. Another fact that suggests decreased permeability is the increase in oxygen saturation of the arterial blood that may follow the inhalation of high concentrations of oxygen. Finally the much greater increase in the arterio-alveolar oxygen difference than in that of the much more highly diffusible carbon dioxide is in accord with the conception of decreased permeability of the alveolar walls."

Increased minute volume of ventilation and decreased carbon dioxide and increased oxygen concentrations in the expired air show that the efficiency of ventilation is decreased in cardiac dyspnea, less aeration of the blood being affected by each liter of air breathed than in health. Exertional dyspnea in pulmonary engorgement and in health are fundamentally similar, but in the cardiac patient dyspnea appears with less activity because his respiratory factor of safety is dimished by the factors described above. Because of decreased efficiency of ventilation, the patient with pulmonary engorgement breaths a larger minute volume of air for a given exertion than in health. This is accomplished in the face of limitation in the maximum volume of ventilation of which he is capable. Thus the respiratory factor of safety, being the difference between the volume of air breathed per minute and the maximum minute volume of ventilation that the patient can possibly attain, is encroached upon at both ends, by increase of the former and decrease of the latter. Thus Fishberg states that as this gap narrows the patient experiences dyspnea

(the consciousness of the necessity for increased respiratory effort). Harrison and his associates have found that the severity of cardiac dyspnea roughly parallels increase in volume of ventilation and decrease in vital capacity, but that it more closely parallels the quotient: Ventilation vital capacity. They call this ratio the ventilation index.

It can be seen from the above discussion that pulmonary engorgement contributes most to these changes in lung physiology. Many arguments naturally arise as to which of these factors play the most important part in the pathogenesis of cardian dyspnea. These and other factors will be considered in this light in the following chapter. It may be mentioned that Altschule feels that it is impossible to correlate the subject dyspnea and objective changes in pulmonary function in a patient with heart disease.

G. Reflexes From The Lung

Drink, Peabody and Blumgart showed that when congestion of the lungs was produced by clamping of the pulmonary veins an increase in the respiratory rate occured. Many other experiments have followed that show that reflexes do arise in the lung which will cause increased respiratory activity. Fishberg believes that "while the total volume of ventilation is largely regulated by chemical mechanisms, reflex influences are of greater significance in determining the form of breathing, i.e., the frequency and amplitude of the individal respirations."

Hering-Breuer suggested a theory of autoregulation of respiration, that stated, when the alveoli were distended to a certain degree, inspiration is reflexly terminated by impulses along the vagus; while when the alveoli have been adequately deflated, other vagal impulses start inspiration. It does seem probable that the mechanical factor of alveolar distention plays a part in determining the depth and frequency of respiration.

There is evidence that this reflex is involved in the production of cardiac dyspnea. Appreciation of the importance of reflexes from the engorged lung in the production of cardiac dyspnea is almost entirely due to the work of Harrison and his associated. They found in dogs that reduction of the vital capacity of the lungs by pneumothorax, distension of the capillaries of one lung with blood, or introducing fluid into the lungs accelerated the respiration, provided the vagus nerves were intact. This work indicates that the tachypnea resulting from the decrease in vital capacity is produced by a vagal reflex, and since decreased vital capacity is characteristic of cardiac dyspnea, they attribute such reflex factors important roles in the production of this dyspnea. This reflex acceleration of breathing in pulmonary engorgement is doubtless to be considered a compensatory and beneficient factor.

H. Changes in the Chemical Composition of the Blood

Until the more recent years it was considered that cardiac

dyspnea was due to stimulation of respiratory center by changes in the chemical composition of the blood. There is still some controversy on the subject, but many of the investigators have swung away from that view. No one denies that there may be chemical changes in the blood, but the controversy concerns the amount of importance which should be placed on these changes. The old idea was that inadequate pulmonary ventilation caused an excess of carbon dioxide or an oxygen deficit which stimulated the respiratory center. Others said the stimulation was due to an increase in the hydrogen-ion concentration of the blood due either to carbon dioxide retention or to increase in the lactic acid content of the blood. The majority of these theories were based on analyses of venous blood, which is obviously inadequate because the arterial blood irrigates the respiratory center. Recent investigations on arterial blood have shown that changes in the chemical composition of the blood play a much smaller part in the genesis of dyspnea than formerly believed. This controversy will be considered more carefully in the chapters to follow. At present we must consider the actual chemical changes present.

Thearteriovenous oxygen difference has proved of some value in studying cardiac failure. One would anticipate that the decrease in cardiac output would be manifested by an increase in the difference between the oxygen contents of the arterial and the mixed venous blood entering the right heart. Altschule has noted that the low oxygen

content of venous blood is striking, and that low oxygen content and saturation of the arterial blood is a frequent finding but less constant and to a less degree than that of the venous blood. In very severe heart disease Harrison and his associates have found that the arteriovenous oxygen difference may be more than twice the normal proportion of the oxygen of the arterial blood. Harrison and his school have shown that there is no close proportionality between the severity of heart failure and the arteriovenous difference at rest, and that the former may be accompanied by a normal arteriovenous difference, which may not change during improvement. When present, the greater arteriovenous oxygen (and carbon dioxide) difference presents a compensatory function in at least partially atoning for the decrease in volume of blood flow. The difference must usually be even greater than would correspond to the decreased output, due to the fact that the basal metabolism is usually increased in heart failure (according to Altschule). With a decreased minute volume of the heart, the arteriovenous differences other than those of oxygen and carbon dioxide must also be increased; these will be discussed later.

There is wide difference in opinion among investigators as to the presence of low arterial blood oxygen saturation in cardiac failure. Well marked arterial anoxemia is common in longstanding heart disease with considerable pulmonary changes, while it is uncommon in early cerdiac insufficiency through dyspnea is severe. Altschule, who insists that the importance of the chemical changes in cardiac failure

be noted, states that the low arterial blood oxygen saturation is due to inadequate mixing of air in the lungs, to organic changes in the alveolaw walls, and to tachypnea itself. He also states that, since tissue oxygen tension cannot be greater than that of the venous blood, the former must be lower than normal in patients with cardiac decompensation, and he gives the cause of the low tissue oxygen tension as being slowing of blood flow, diminished arterial blood oxygen saturation, and increased metabolic rate in cardiac failure.

The question of carbon dioxide tension increase in the blood is also controversal. Fishberg feels that in severe pulmonary congestion or in other widespread lesions of the lung, the arterial carbon dioxide content may be elevated definitely above the normal values of between 40 and 55 volumes percent. This accompanies well marked anoxemia and is to be attributed to impairment of gas exchange in the lungs. Because of the greater diffusibility of carbon dioxide much more pronounced impairment of pulmonary gas diffusion is required to produce retention of carbon dioxide then depression of the oxygen saturation of the arterial blood. Fishberg further states that in cardiac dyspnea, not accompanied by extreme pulmonary changes, the carbon dioxide tension of the arterial blood is below normal, and at times is strikingly so. At the same time this low carbon dioxide content of the arterial blood may be accompanied by an abnormally high concentration of carbon dioxide in the venous blood; this is due to the fact that increase in respiration (hyperventilation) decreases the alveolar

air carbon dioxide content and tension, and that free carbonic acid in the arterial blood varies as alveolar carbon dioxide. In most instances a fall in carbon dioxide content of the arterial blood is not accompanied by a drop in alkali reserve, so that arterial alkalosis results. However, in some cases of very severe failure and with systemic venous engorgement there is often a depression of the bicarbonate and acidosis in the arterial blood is associated with the lowering of arterial carbon dioxide. In these latter cases a rise in the lactic and perhaps other fixed acids of the blood plays a substantial part in reducing the alkali reserve.

Altschule agrees with Fishberg that most of the patients at rest have a pH value of the arterial blood within normal limits or slightly increased, that with severe dyspnea some patients show the tendency toward an alkalosis of the arterial blood (marked lowering of alveolar carbon dioxide tension with subsequent fall in carbonic acid content of the arterial blood), that more patients with dyspnea do not manifest this trend toward alkalosis due to increase in blood lactic acid, and that a small group with organic pulmonary disease show carbon dioxide retention with a consequent lowering of arterial pH. Thus they admit that the carbon dioxide changes in arterial blood are usually the effect rather than the cause of dyspnea in patients with uncomplicated failure.

The consideration of changes in venous blood is also of

importance. Low venous oxygen tension has already been discussed, thus resulting in an increased arteriovenous oxygen difference. Thus similarily, when cardiac output is decreased, it is obvious that the normal carbon dioxide content difference between the arterial and the mixed venous blood is accentuated. Also one would expect the arteriovenous differences other than those of oxygen and carbon dioxide to be increased. Some investigators have found that venous stasis increases the transit of water, chloride, and bicarbonate to the tissues, and they believe that this transit of bicarbonate from the blood to the tissues is the principle factor producing the lowered alkali reserve of venous blood in some patients with cardiac dyspnea. The net result of these changes (increased carbondioxide tension, decreased alkali reserve and increased lactic acid) is shown to be a relative increase in the acidity of the venous as compared with arterial blood. Thus in cardiac failure a venous acidosis may accompany arterial alkalosis, the former being a manifestation of slowing of the blood flow in the tissues, the latter a manifestation of hyperventilation.

Altschule has found that the carbon dioxide carrying power of arterial and venous blood not infrequently is dimished in congestive failure, as manifested by lowering of the carbon dioxide dissociation curve. Some authors feel the carbon dioxide dissociation curve is normal in the arterial but lowered in the venous blood, while others say both are lowered but more in the venous blood. Logically the changes

in carbon dioxide carrying power of arterial and venous blood would depend on what one of the conditions mentioned above existed, i.e., on what factors were acting in each case in tending to cause alkalosis or acidosis of the respective arterial or venous blood. Thus in each case the carbon dioxide carrying power could be easily figured if the factors discussed above were known. Whatever the cause of the lowering of the dissociation curves in decompensation, they tend to return to normal on recovery. Altschule feels that after exercise the carbon dioxide combining power of the blood is markedly reduced in cardiac patients, due to the shift toward acidosis from the abnormal accumulation of lactic acid in the blood.

Altschule also states that deviations from normal in arterial or venous serum bicarbonate (usually normal or low) are associated with changes in the serum chloride level. On this basis he divides cardiac patients into three groups, namely: (1) Patients with low bicarbonate and high chloride levels; (2) Patients with high bicarbonate and low chloride levels (usually have some associated pulmonary disease); and (3) Patients with low bicarbonate and chloride levels (small group and there is probably an element of renal insufficiency accounting for the loss of serum base. In regard to the first group it has been noted that a rise in bicarbonate during recovery was followed by a fall in serum chloride and a transient increase in urinary excretion of chloride.

Thus, although Altschule realizes that the changes in arterial blood carbon dioxide and pH are, as far as can be ascertained, more the effect than the cause of increased activity, he states that this does not rule out acidosis of the respiratory center, since the reaction of the latter may become more acid than normal in spite of changes in the direction of alkalinity in the arterial blood delivered to the center.

It is known that lactic acid is produced in a working muscle, and that ordinarily about one-fifth of this is burned and the remainder is resynthesized into glycogen. The amount of oxygen needed, above the resting intake, for a given exercise depends on the amount of lactic acid produced. In exercise not all the required oxygen is taken in during the exercise, a portion being supplied after work has ceased. This latter amount is known as the "oxygen debt"; It is true in general, that patients with cardiac disease have a greater oxygen debt than does the normal person aster performing the same exercise. Harrison believes that this greater oxygen debt is probably due to the diminished ability (as compared with normal subjects) to increase their cardiac outputs, but that this difference, being small and inconstant, cannot be regarded as the essential factor in producing dyspnea.

Altschule states there is an increase in the resting blood lactic acid in heart failure, and that there is a general correspondence between this increase and the degree of decompensation. He has found that there is an abnormally large and prolonged rise in blood lactic acid after exercise in cardiacs. Other investigators have found that

there is an increase in the lactic acid output in the urine after exercise in cardiac patients. A few have felt that the disturbed lactic acid metabolism was due to liver damage alone, since there are similar changes in primary liver injury. However, others have pointed out by means of dynamometer experiments that the metabolism of the peripheral tissues is defective in congestive failure but not in liver disease. Altschule considers that the oxygen debt in cardiacs is abnormally large and prolonged, those performing light work taking up normal or slightly reduced amounts of oxygen during work, while those who work to the point of exhaustion absorb distinctly subnormal amounts of oxygen. Naturally in decompensation where the heart disease is more manifest, the increase in oxygen debt for a given amount of exercise will be correspondingly greater. Altschule feels that the beneficial response to oxygen therapy in some is confirmatory of the existence of a state of continuous oxygen debt. He states that elevated resting blood lactic acid can sometimes be abolished by the inhalation of high concentrations of oxygen, and that the oxygen debt may be cut to 75% in some by breathing high concentrations of oxygen while exercising. He considers the oxygen debt as a result of tissue anoxemia due to low cardiac output together with peripheral stasis, insufficient oxygenation of the blood in the lungs, and increased basal metabolic rate.

Harrison has considered oxygen debt from a different angle, in which he compares persons with cardiac failure with normal subjects

when both groups are performing the severest exercise of which they are capable. He then takes note of the fact that for oxygen to be absorbed at an unusually rapid rate it is necessary for the cardiac output to be large. This comparison might best be given in Harrison's own words: "The maximal rate of oxygen intake is in some measure related to the maximal cardiac output. However, the ability to acquire an oxygen debt has nothing to do with the cardiac output but is related to the power of the tissues to buffer lactic acid. Hence, if, a patient's exercise is limited because of inadequate cardiac output and because of this factor alone, he should have a relatively low intake of oxygen during the exercise but he should have a very great oxygen debt at the end of the exercise, provided it is maximal. If such a patient and a normal person both undertake the severest exercise of which they are capable and continue as long as they can, one would expect to find a lower oxygen intake during the exercise in patient--- because of limited cardiac output--- but at the end of exercise, the oxygen debt should be approximately the same amount in the two subjects. Actually, the first expectation is fulfilled but the second is not for 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 their maximum exercise. It is therefore evident that the chief factor which limits muscular exercise in patients with cardiac failure is not oxygen debt, and it is likewise evident that the important limiting factor is not inability

to increase the cardiac output, which would act by causing a large oxygen debt. Actually, they are checked by their dyspnea long before the exercise has become sufficiently severe to produce a large oxygen debt."

In the following chapter we will elaborate on the above physiological changes and show how they do or do not play a part in the pathogenesis of the important clinical features of heart failure.

1. Plasma and Edema Fluid Proteins

Most investigators have noted a low serum protein level often, though by no means always, in patients with cardiac insufficiency. The diminution affects the albumin fraction either exclusively or much more than the globulin fraction. These lowered levels are noted especially when the heart failure is of protracted duration, while when edema appears soon after the onset of heart failure sometimes normal concentrations of plasma proteins are observed. A number of investigators agree that a high degree of correlation between the presence of edema and a decrease in the serum protein level does not exist, and that the same degree of lowering in non-cardiac subjects gave no edema. Many suggestions have been made as to the cause of diminished plasma proteins, among these being malnutrition, albuminuria, loss of protein through repeated paracentesis, loss of some protein into the interstitial tissues with the edema, and dilution of blood plasma consequent to the increase in the blood volume which

occurs. Fishberg feels that the albuminuria is an important cause for loss of plasma proteins, especially if albuminuria is present over long periods of time and if the liver engorgement interferes with the regeneration of lost protein (there is some evidence that plasma proteins are produced in the liver). Thus this hypoproteinemia may play some part in the formation of edema in cerdiac patients, the exact importance of which will be discussed later. In conjunction with this finding of reduced plasma proteins it is well to mention that Altschule found that the subcutaneous fluid in failure has increased protein (especially albumin), and is 2 to 7 times as rich in proteins as similar fluid in nephrotic patients. Many others deny this latter finding and state that there is no or slight increase in the edema fluid protein.

J. Peripheral Capillaries

Altschule has noted engorgement of the tissue capillaries, often to the point where hemorrhage is noted on post mortem. He feels that the visible capillaries are increased in number with dilatation of the venoue group while the arterial loop may show narrowing. He observed that the blood in these capillaries is dark and moves slowly or may be motionless at times. Altschule states that anoxemia is the cause of capillary vasodilatation and thus the venous end is most greatly dilated. Most other investigators feel that the increased venous pressure is the prime factor in causing capillary dilatation.

K. Lymphatics

McMaster found dilatation and valvular incompetence of the lymphatic channels and complete absence of flow in the edematous patient. He found that diuretics caused no change in this condition, thatelevation of the limb caused a small increase in flow, and that he couldnt reproduce the stasis by tourniquets, so he ruled out increased venous pressure as the cause. Altschule feels that anoxemia may be important in the decreased lymphatic flow, or that increased venous pressure may be important since this pressure is transmitted to larger lymphatic vessels. Harrison considers that lympathic flow is increased early to compensate for the beginning of edema formation. He concedes that when venous pressure becomes high it interferes with the emptying of the thoracic duct, and thus is a factor.

In this chapter an attempt has been made to review some of the physiological changes of major importance in considering the pathogenesis of the clinical manifestations of cardiac failure. Naturally many of the physiological changes have not been disscussed here, some of which will be brought up later in reference to the pathogenesis of a specific sign or symptom in which they play a part. Some of the points of controversy have been pointed out. In the following pages there will naturally be some repetition of the points mentioned in this chapter in order to give a complete picture of the importance of these in causing various clinical phenomena.

THE MAJOR PHENOMENA OF CONGESTIVE HEART FAILURE

The preceding chapter contains a summary of much of the data now available on the physiology and chemistry of cardiac decompensation. In the following pages we will correlate this data in the pathogenesis of the signs and symptoms of that disorder. Some of the major phenomena as dilatation and hypertrophy of the heart have already been considered. One must remember that symptoms which might be of major importance in one patient may be of no significance in another.

A. Dyspnea -- General Consideration

Dyspnea has been defined by some as the consciousness of the necessity for increased respiratory effort. Ordinarily dyspnea is the first and often the last subjective manifestation of heart failure. Most clinicians feel that the first indication of failure is dimished tolerance to exercise with associated dyspnea. Harrison states that dyspnea usually causes the patient more distress than all other symptoms combined, and that the degree of dyspnea is by and large the best index to prognosis and the most reliable guide to treatment.

Altschule speaks of dyspnea as a sensation and as such is not amendabled to objective measurement. He states that marked difference in degree of dyspnea due to changes in subjective sensitivity can occur in different patients in whom all physiological measurements

are the same, or even in the same patient with relative constancy of the physical status. It must be realized that there is a definite correlation between the symptom dyspnea and the sign hyperpnea. McMichael states that dyspnea is the resultant of hyperpnea and pulmonary congestion. Back expresses the opinion that dyspnea is not to be graded by the degree of distress (subjective), but by the amount of effort that brings it on.

Altschule has made no attempt to differentiate the mechanism of dyspnea at rest from that of dyspnea on exertion, since he feels that similar factors are responsible for both, with the reservation that the various mechanisms may be relatively more or less important, in each type. On the other hand, Fishberg and Harrison have divided dyspnea into different clinical types, and then have considered the pathogenesis of each of these types. Harrison's classification of dyspnea on a clinical basis is as follows:

I. Dyspnea due to cardiac disease per se.
   A. Dyspnea on exertion
   B. Dyspnea at rest
      1. Nocturnal dyspnea
         a. Occuring before the onset of sleep
            (1) Orthopnea
            (2) Evening dyspnea
         b. Occuring after the onset of sleep
            (1) Cardiac asthma) Paroxysmal
            (2) Stokes respiration (Cheyne-Stokes respiration)) dyspnea
II. Continuous dyspnea

We will consider the different views concerning the mechanism of these various types of dyspnea.

B. Exertional Dyspnea

Normal persons may perform numerous strenuous activities without noticing their respiration. The cardiac patient has the sensation of dyspnea upon much less activity than the normal person. The theory of the pathogenesis of dyspnea has changed numerous times. Oxygen want, carbon dioxide excess, reflexstimulation from the lungs, and the effect of hydrogen in concentration have all been given as the possible cause of dyspnea through their action on the respiratory center. These theories have all had their era of popularity. Harrison's work on dyspnea has done much to clarify many points, but there are still those who disagree bitterly with his views.

Before Harrison's work the generally accepted view for the mechanism of exertional dyspnea was that the overstrained heart is unable to increase its output, the tissues are poorly supplied with blood, unoxidized lectic acid accumulates in them, and, pouring out into the blood stream, raises the hydrogen ion concentration of the blood with a resulting stimulation of the respiratory center. Present day investigators are arranged in two groups, those who think that dyspnea on exertion is due mainly to changes in blood chemistry and those who believe it is due mainly to changed pulmonary physiology with resultant reflexes to the respiratory center.

Altschule, who stresses the chemical changes in the blood,

states that there is proof of the anoxemia of tissues in cardiac failure by the low tissue oxygen since there is low venous blood oxygen, by the increased blood lactic acid content at rest and after exercise, by prolonged oxygen debt after exercise, and by low arterial blood oxygen. Of course the question of oxygen debt importance depends on how we look at it: Harrison's new conception has been reviewed in the preceding chapter in which he compares the oxygen debt of the cardiac patient and the normal person after the maximum exercise of which they are capable. He found the oxygen debt at maximum exercise to be smaller in cardiac patients, thus he concluded that the important limiting factor is not the inability to increase cardiac output which would act by causing a large oxygen debt. Actually the patient's exercise is checked by dyspnea long before the exercise has become suffieiently severe to produce a large oxygen debt.

Altschule believes that the two main factors in causing tissue anoxemia in decompensation are decreased delivery of blood to the tissues (forward-failure), and the effects of pulmonary congestion which acts to cause a lowering of the arterial oxygen saturation by edema in the alveolar walls and by impairment of the bellows function of the lungs. He also brings lactic acid metabolism into the picture and places importance on it. He follows Gesell's conception that the brain produces lactic acid and that interference with the normal rapid oxydation of that substance at the respiratory center causes dyspnea.

He also mentions that probably the high concentration of lactic acid that occurs in the blood after exercise may cause diffusion of that substance into the respiratory center and thus produce dyspnea and hyperpnea. He states that hyperpnea is a response to certain abnormalities in the physical or chemical status of the patient and that the hyperpnea may cause compensatory changes in the opposite direction so that deviations from the normal observed, for instance in the blood, may be negligible. The latter refers to the fact that when hyperpnea exists in cardiac patients without extreme pulmonary changes the arterial blood has a carbon dioxide tension below normal -- this reduction is a result of the hyperpnea.

McMichael has considered hyperpnea in heart failure. He concludes that there is a close relationship between the depression of cardiac output and hyperpnea (due to diminished cerebral blood flow). He states that cardiac output at rest is not very greatly lowered until later stages of the disease in which hyperpnea is found to be pronounced. He believes that there is no close relationship between the vital capacity and pulmonary ventilation, and thus the reflex explanation (to be considered) is unlikely to be valid. To him such an explanation would necessitate the assumption of a reflexly maintained alteration in the sensitivity of the respiratory center to carbon dioxide; and since there is no evidence this takes place, the chemical explanation of hyperpnea seems more likely to him. Even those investigators who oppose the chemical theory of dyspnea and

hyperpnea admit that in severe exercise the blood undergoes chemical changes which may play an important role in altering the respiration. Thus McMichael is basing his explanation of hyperpnea on the "forward-failure" theory, and believes there is no correlation between byperpnea and vital capacity, but that there is a close correlation between cardiac output and hyperpnea. He contends that cerebral blood flow is subnormal in hyperpneic cardiac subjects, but he offers little except the sensitivity of the respiratory center to carbon dioxide as an explanation of how the reduced cerebral flow produces hyperpnea. Since he considers dyspnea on exertion as the resultant of hyperpnea and pulmonary congestion, he thus places much importance on reduced cerebral flow as a cause for dyspnea.

Harrison in his experiments found that the chemical theory of dyspnea is inadequate, and that dyspnea produced by exertion in persons with cardiac disease is not primarily a matter of blood flow or blood gases. He found that dyspnea on mild exertion in patients with congestive failure cannot be due to the inability to increase the cardiac output since the oxygen debt is on the average only slightly greater in these patients than in normal subjects performing the same exercise, and since neither during nor after mild exertion do changes in the direction of greater acidity occur in the venous or in the arterial blood. He found dyspnea on mild exertion could not be due to dimished cerebral blood flow because the gaseous composition

of the internal jugular vein is not altered by mild exercise. He concluded that it was evident that dyspnea on mild exertion is not related to alterations in the oxygen, carbon dioxide or reaction of the blood, either arterial or venous.

With dyspnea produced by moderate exertion in patients with lowered cardiac reserves but without frank congestive failure Harrison found that the inability to increase the cardiac output sufficiently is one factor because the grestest oxygen intake is less than in normal persons. However, he did not believe this to be sole factor since the maximum oxygendebt is less than normal, and since maximal exertion produces dyspnea of comparable degree in patients and in normal persons but the patients show much less marked acidosis than the latter.

Fishberg agrees with Harrison's conception that cardiac dyspnea on exertion is fundamentally not an "acidotic dyspnea", for most often the arterial blood is alkalotic. He also feels that in instances in which severe pulmonary lesions result in carbon dioxide retention with gaseous acidosis, or in which there is great elevation of lactic or other fixed acid in the blood, the increased hydrogen ion concentration of the blood doubtless plays a part in producing dyspnea.

It is interesting to notice how inadequate the idea of diminution of cardiac output and of lowered blood flow through the respiratory center is at times. For example many patients with left heart failure resulting from hypertension, or mitral or aortic disease have severe

pulmonary engorgement with dyspnea on slight exertion or even at rest, although there is no cyanosis and the extremities are warm (bespeaks very little slowing of systemis blood flow). However, when the right ventricle fails in such individuals, the systemic blood flow is further retarded, yet dyspnea often becomes less severe. This observation naturally leads one to correlate the reduction of pulmonary congestion following right ventricle failure and the reduction of the dyspnea. Thus it would seem from clinical observations that dyspnea is much more closely linked to the severity of the pulmonary congestion than to the slowing of systemic blood flow.

If the above factors do not sufficiently explain dyspnea on exertion, what changes in physiology do adequately explain dyspnea? Pulmonary congestion causes a diminution in the vital capacity, which indicates that for a given level of ventilation the cardiac patient is more likely to feel respiratory distress than he would if his vital capacity were normal. Also the efficiency of ventilation is decreases in cardiac dyspnea, less airation of the blood being affected by each liter of air breathed than in health. Because of his decreased efficiency of ventilation, the person with pulmonary engorgement breathes a larger minute volume of air for a given exertion than in health. This is done in the face of limitation, as a result of the decreased vital capacity, in the maximum volume of ventilation of which he is capable. Thus the respiratory factor

of safety -- the difference between the volume of air breathed per minute and the maximum minute volume of ventilation that the patient can possibly attain -- is encroached upon from both ends, by increase of the former and decrease of the latter. When the gap is sufficiently narrowed, the patient experiences dyspnea. Harrison and others have found that while the severity of cardiac dyspnea roughly parallels increase in volume of ventilation and decrease in vital capacity, it is much more closely proportional to the quotient; ventilation/vital capacity. They call this ratio, determined with a correction for body weight, the ventilation index, and find that it is of practical value in patients with evidence of heart disease in determining whether the subjective symptoms of dyspnea is actually due to heart failure or is neurotic in origin.

Besides the above factors there are also vagal reflexes from the lungs which cause some increase in ventilation even at rest. Altschule admits that such a factor exists, and that abnormal rigidity of the lungs and simple congestion activate reflexes which travel to the brain and evoke a motor response, hyperpnea. Perception of this increased motor respiratory activity may result in the sensation of dyspnea. However, he states that the role of reflexes in the genesis of dyspnea is secondary to that of the pathological congestion in the lungs, and the importance in causing the sensation is still a matter for investigation.

Harrison concludes that when muscular exercise is performed there is an immediate reflex increase in the ventilation of the normal subject and of the cardiac patient, due to afferent impulses from the moving muscles. Harrison and his associates also found that ventilation increased when they elevated the pressure in the venae cavae, either by intravenous infusion or by the inflation of a ballon in the right auricle -- this no longer occured after the vagi were cut. Since the venous pressure does not rise immediately but gradually, the ventilation is less during the first than during subsequent minutes of exercise. The cardiac patient has a greater increase in venous pressure and thus a greater increase in ventilation than does the normal person. Since the rise in venous pressure persists longer in the cardiac patient than in the normal subject, the dyspnea of the cardiac patient lasts longer after exercise is stopped; thus the ventilation returns to the resting level more slowly. This greater increase in breathing is sufficient to cause ventilation to exceed the threshold of dyspnea, which is lower than in normal subjects because of the diminished vital capacity.

Fishberg also gives notice to another type of reflex which may be concerned in the production of hyperpnea and consequent dyspnea in circulatory failure, that being one that is initiated in the sensitive zones of the carotid sinus and the root of the aorta. Thus the part that anoxemia plays in producing hyperpnea may act through the sensitive areas in the arteries, while carbon dioxide excess may act both on the sensory zones in the arteries and on the respiratory center.

It has also been found that fall in pressure within the aorta and carotid sinus reflexly stimulates ventilation, and this too might play a part especially in hyperpnea of shock.

W.G.Harrison, Jr., feels that dyspnea on exertion is most likely due not to chemical changes in the blood, but to reflexes arising from the moving muscles stimulating respiration, and also to a reflex stimulation of respiration from an increase in the systemic as well as pulmonary venous pressure. Bedford considers that cardiac dyspnea is due to a direct nervous reflex originating in the congested lungs and transmitted to the respiratory center through the vagus.

Altschule considers that the factor of impaired heat dispersion is a much neglected mechanism in causing hyperpnea. He feels that there is an alteration of the heat dispersal mechanism due to a decrease of flow of blood to the periphery -- low skin temperature in spite of high rectal temperature, and low insensible perspiration strongly indicate the existence of this factor. He concludes that hyperpnea which is a response to the inability to disperse normal amount of heat via the skin in the cardiav patient must contribute to the dyspnea they experience. He upholds this clinically by the observation that many patients indicate relief of dyspnea if the bed clothes are removed and he is placed in front of an open window.

Thus no matter what mechanism one considers for the pathogenesis

of dyspnea there are in operation a multiplicity of factors, and the importance of these various factors in the production of dyspnea varies from patient to patient.

A brief survey of Altschule's conception of the mechanism of dyspnea in congestive heart failure is shown by his own diagram below:

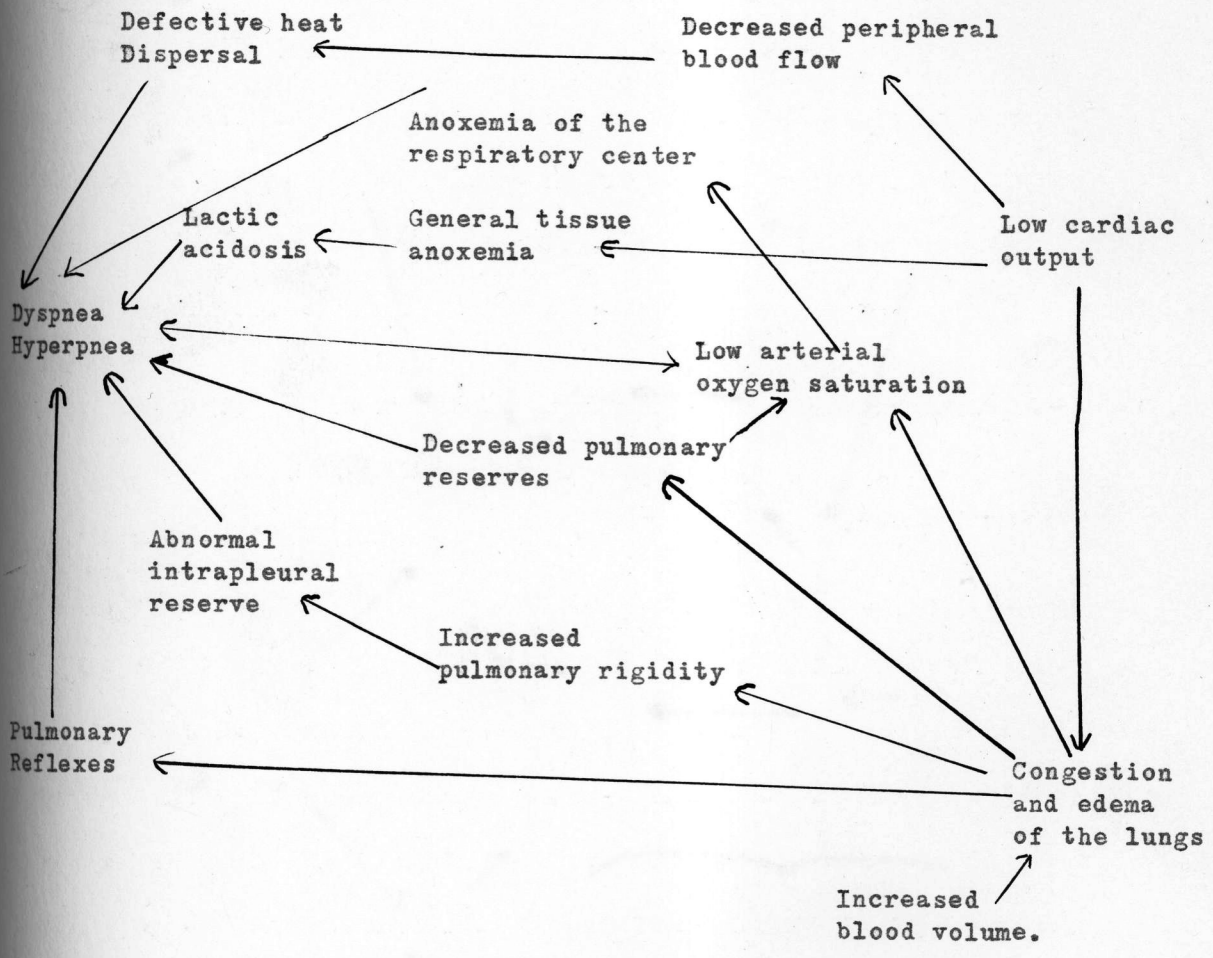


FIG. 5 - MECHANISM OF DYSPNEA IN CONGESTIVE HEART FAILURE

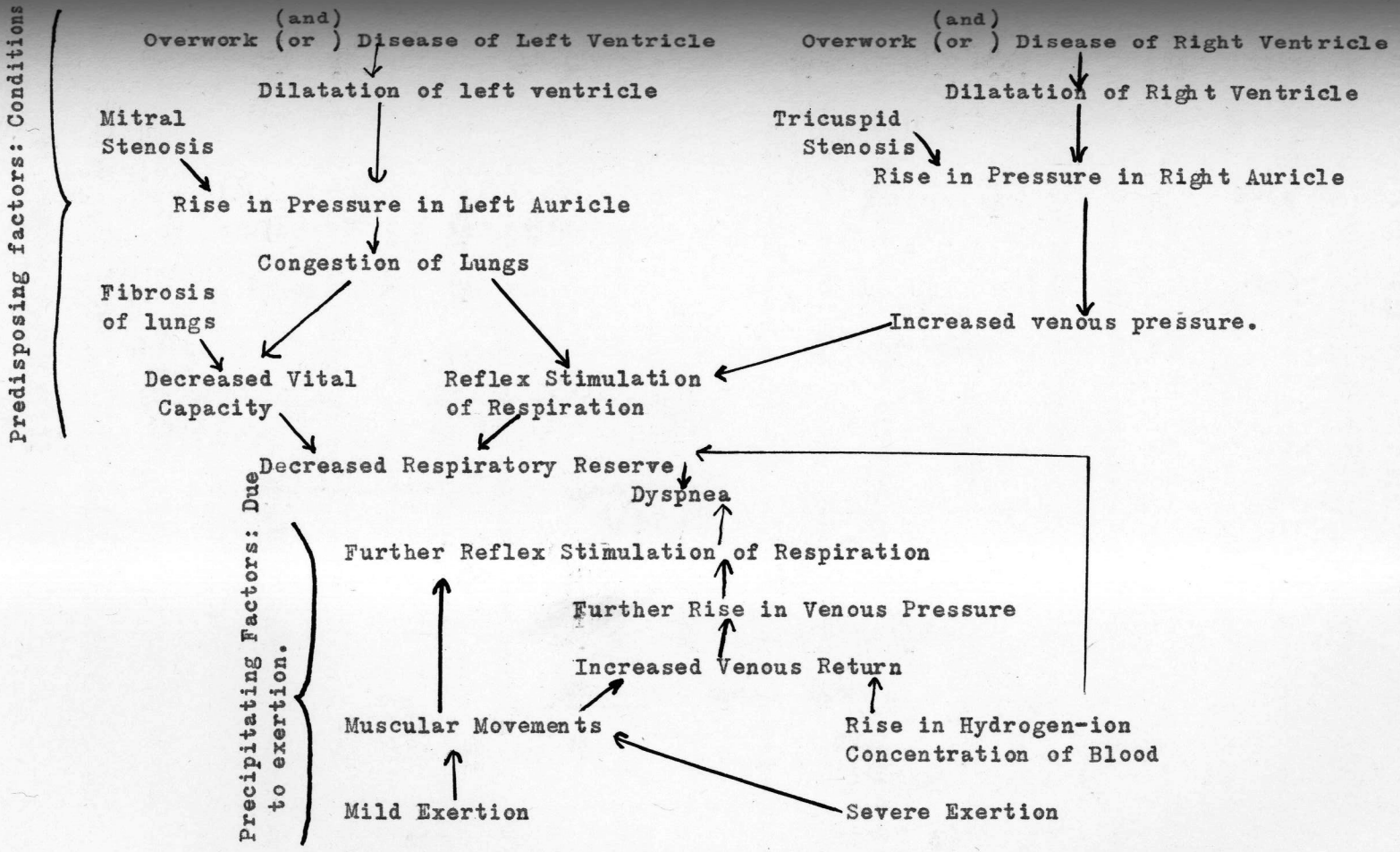


FIG. 6 - DIAGRAM OF THE MECHANISM OF DYSPNEA PRODUCED BY EXERTION (Harrison)

On the whole it seems to this writer that Harrison's views are the most logical and most well-founded. Fishberg agrees for the most part with Harrison, but has presented a few divergent ideas. Altschule presents many good points, and is in opposition to Harrison on many factors. Altschule, on the whole, does not have such well founded experiments to back his ideas as Harrison does, but many of his theories may in time become widely accepted.

C. Orthopnea

Orthopnea is that type of distress which is produced by assuming the recumbent position. It may coexist with all other forms of dyspnea. There have been a great number of theories presented as an explanation.

One of the theories proposed was that deficient aeration of the blood in the lungs in the recumbent posture was the cause of orthopnea. Altschule states that whatever the mechanism of pulmonary and intrapleural changes, they serve to explain the decreased arterial blood oxygen saturation which occurs, even in normals, while lying flat, and that this change in arterial oxygen saturation is a factor in the genesis of orthopnea. On the other hand, Harrison, on studies in arterial oxygen saturation could find only slightly diminished values in some of the persons in the recumbent as compaired with the upright position. He felt that this change was too small to be more than a slight factor.

Another hypothesis has been that of alteration in the blood flow through the lungs. Many investigators feel that there is a decrease in the venous return to the right heart when the patient is erect. Fishberg feels that the weight of evidence strongly indicates a greater venous return to the heart in the recumbent than in the erect posture, and that such increased venous return when recumbent would obviously augment pulmonary engorgement in the reclining patient and thus favor dyspnea. Harrison disagrees in part with this view, but grants that there is, on the moment of assuming the recumbent posture, a shift of blood from the abdomen to the thorax accompanied by temporary increase in the output of the right ventricle. He does not consider that this has lasting significance in increasing the output of the right heart.

Dock has given an interesting anatomical and hydrostatic basis for orthopnea. He claims that "when an adult of average size is recumbent, the blood flowing from the pulmonary venous bed must be lifted from 4 to 7 cm. against the force of gravity in order to fill the left ventricle. Thus the pulmonary venous pressure which is adequate in the erect position to maintain a given level of left ventricle filling and cardiac output is lower than that needed to maintain the same level of cardiac output, when the individual is recumbent, by the pressure represented by a column of blood 7.5 to 10 cm. high." Thus he concludes that this may to some degree help explain orthopnea. At the least it is a very interesting consideration.

Another theory which has been proposed is diminished cerebral blood flow (venous stasis) in the recumbent position. This hypothesis assumes that cardiac failure tends to cause an inadequate gaseous interchange between the blood and the respiratory center. Studies on blood taken from an artery and the internal jugular vein showed no increased arterio venous difference in the recumbent over the erect positions. Also application of a blood pressure cuff about the neck, thus increasing the intracranial venous pressure, did not produce dyspnea. Harrison, Fishberg, and Kirk are opposed to this theory. Altschule believes that this increased venous pressure in the center plays an important part in causing orthopnea (certain investigators have found relief from orthopnea was obtained by flexing the head while the patient was in a recumbent position). This theory of diminished blood flow is not supported by clinical evidence, as orthopnea is common in isolated left heart failure with normal venous pressure, and is often relieved when the right heart fails with the development of high systemic venous pressure. Also it is very striking in the rare cases of primary right heart failure due to such causes as pulmonary or tricuspid valvular defects, that orthopnea may be absent despite extreme cyanosis and enormously engorged veins.

Another hypothesis seeks to explain orthopnes on the mechanical changes in the lungs. Most investigators will agree that the vital capacity of the lungs is decreased in the recumbent position, this

diminution being greater in cardiac cases. As a rule clinical observation reveals a striking parallelism between orthopnea and pulmonary engorgement. Even in the upright position the patient with some pulmonary engorgement has congested lungs with a diminished respiratory reserve (vital capacity). This causes the patient to approach the threshold of dyspnea. The congested lungs also become the site of origin of a reflex through the vagus nerve to the respiratory center, which causes rapid breathing and greater ventilation and encroaches further on the respiratory reserve by increasing the quotient: Ventilation/vital capacity. When the above patient lies down there is a shift of blood from the abdomen and other parts of the body to the chest, this being due to gravity and a short period of increase in the output of the right ventricle. This with the mechanical effect of a high diaphram decreased the vital capacity and further causes reflex stimulation of respiration. The quotient, ventilation/vital capacity, undergoes a further rise, which now crosses the treshold and the patient becomes short of breath. On sitting up the reverse occurs and he gets relief.

W. G. Harrison, Jr., has stressed the importance of increased cisternal pressure in the region of the medulla in the recumbent as compaired with the upright posture in a patient with systemic congestion. If systemic congestion also appears in addition to pulmonary congestion, the increased venous pressure causes an increased

filtration of spinal fluid with a subsequent rise in intra-cranial pressure. Possibly by a reflex mechanism this rise in intra-cranial pressure may lead to further increase in the venous pressure. Assumption of the upright position leads to reduced intra-cranial pressure with a consequent decline in venous pressure and diminished reflex respiratory stimulation. Thus orthopnea is in main due to pulmonary congestion, but is aggravated by systemic congestion.

Altschule has mentioned the effect of pressure of abdominal viscera or ascites on the diaphragm and thus interfering with the free movement to some degree (based on frequent occurrence of orthopnea in patients with ascites due to other causes, such as cirrhosis or neoplasms). He also considers that the greater ease of thoracic movement in the upright position may be a contributory factor. On the whole Altschule seems rather hesitant in giving the exact mechanism of orthopnea, but his views are presented in diagram form in Fig.7 below.

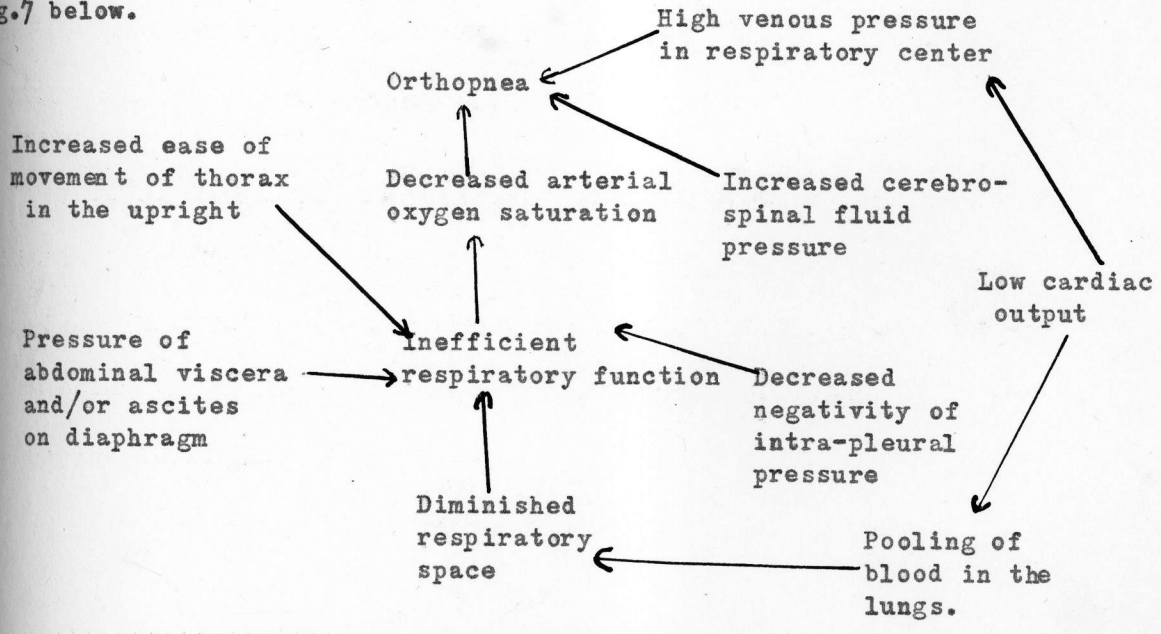


FIG. 7 - MECHANISM OF ORTHOPNEA IN CONGESTIVE HEART FAILURE

Harrison, Kirk, Fishberg and many others agree quite well as to the mechanism of orthopnea. These views have been mentioned above. Then, too, Dock's experimental evidence of the anatomical and hydrostatic factors cannot be ignored. Harrison's conception of the mechanism of orthopnea is shown in Fig. 8 below. In this diagram he gives no mention to the part that systemis congestion may play by increasing the intra-cranial pressure as described above, although he recognizes that this may be of some importance.

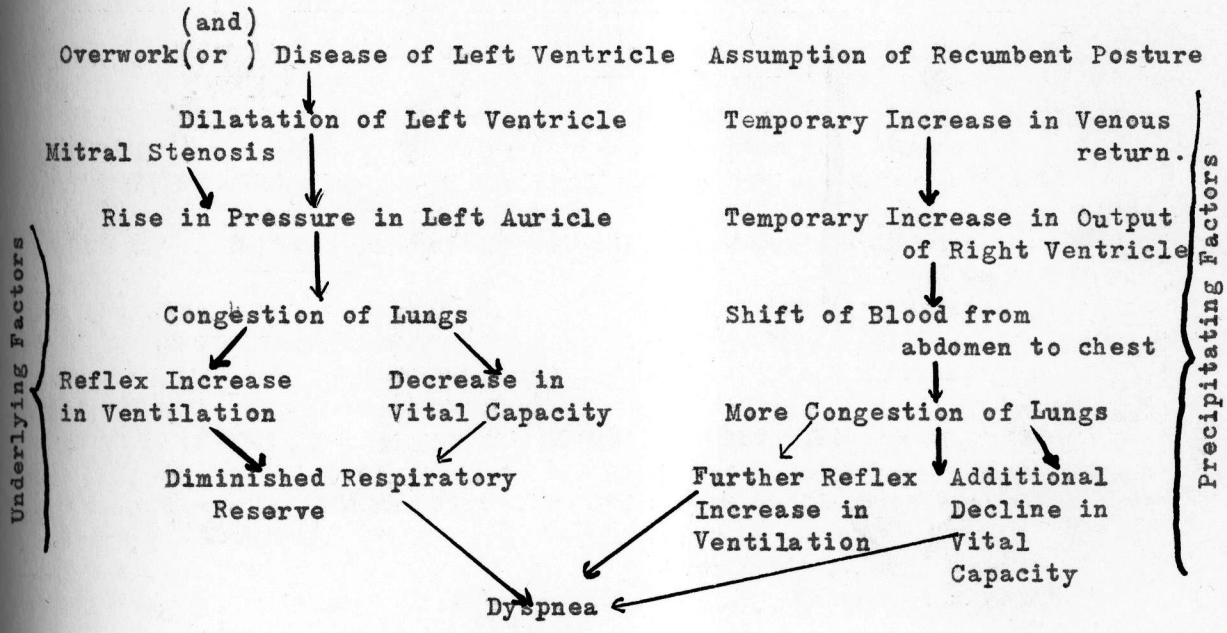


FIG. 8 - DIAGRAM OF THE MECHANISM OF ORTHOPNEA (Harrison)

D. Evening Dyspnea

The term, evening dyspnea, according to Harrison applies to that "type of respiratory discomfort which developes gradually in the course of the waking hours, reaches its maximum before bedtime, and may prevent the unfortunate sufferer from going to sleep." It differs from orthopnea in that it occurs even though the patient remains in bed and in the same position all day long, and it differs from paroxysmal dyspnea in that its onset is during the waking hours, and that it has a gradual onset rather than a sudden onset. This symptom is most marked in those patients who have initial strain on the left ventricle.

Arterial blood samples taken at intervals throughout the day showed that the blood toward evening is slightly more alkaline and had a little lower average carbon dioxide tension, and the oxygen saturation tended to be a little greater in the evening (Harrison). Thus Harrison concluded that a gradual shift of reaction of the blood to the acid side was not the cause of evening dyspnea.

Harrison did find that the respiratory rate was slightly increased toward evening and the ventilation was increased. Normally the ventilation ratio, ventilation/vital capacity, is 1.5 to 2.0. Patients with evening dyspnea had resting ratios of 3.3 in the morning and 4.2 in the evening. Subjective respiratory distress usually begins when the resting ratio is 3.5 to 4.0, thus patients with evening dyspnea are close to the threshold of dyspnea in the morning,

and that during the day they have a slight decrease in vital capacity and a moderate increase in ventilation, which causes the ventilation ratio to increase and cross the threshold of dyspnea.

The oxygen consumption in Harrison's cardiac patients was on the average 10% higher in the evening than in the morning. This increased metabolic rate could not be the direct cause of greater respiration as normal persons have a metabolic increase of 15% in the evening with no increase in ventilation.

It has been shown that only a small decline in vital capacity can be responsible for an increased ventilation. In the morning the body functions are low but as the day goes on the increase in activity of the organs tend to be associated with increase in their blood supply. Thus the venous return to the heart is greater at the end of the day and the output of the right ventricle tends to increase. If the left ventricle has less reserve than the right ventricle it will be less able to expel the oncoming blood, and congestion of the lungs results. This sequence of events is not in accord with the "diminished-output" theory of dyspnea. There is a relative diminution of the output of the left ventricle as compared with the right, the difference being very small -- 100 or 200 cc. out of a total cardiac output of at least 1000 liters in 12 hours -- as to be without significance when viewed as a decrease in the blood supply to the tissues. Thus evening dyspnea. like the other forms of dyspnea discussed above is

reflex in origin, and is due to "back-pressure".

The more active the patient during the day the more likely he is to have evening dyspnea. Orthopnea often accompanies evening dysynea. Harrison's diagram of the mechanism of evening dyspnea is shown in Fig. 9 below.

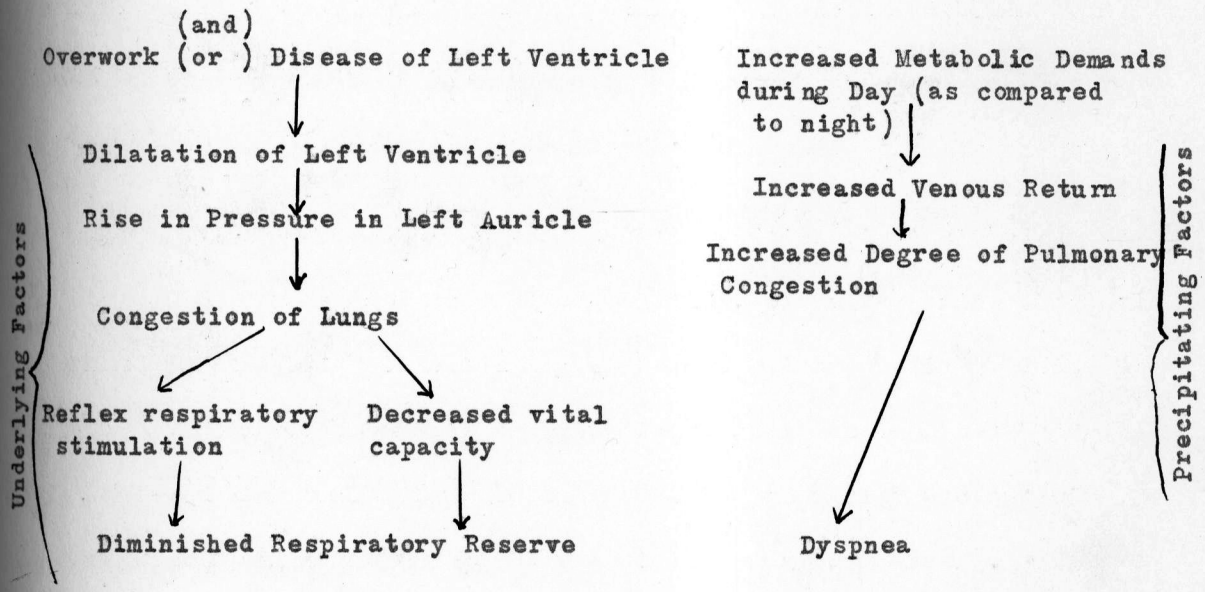


FIG. 9 - THE MECHANISM OF EVENING DYSPNEA (From Harrison)

E. Cardiac Asthma

The dramatic and terrifying attack of cardiac asthma is a well knownclinical picture. Numerous theories have been proposed to explain the pathogenesis of this condition. It is a phenomenon clearly associated with left ventricular failure. Cardiac asthma is not immediately incited by obvious physical exertion; in fact it occurs most often when the metabolic demands on the circulation seems to be at a minimum, namely, during the early hours of sleep. These facts indicate that there are factors in the pathogenesis of cardiac asthma which do not participate in the production of exertional dyspnea; there are, of course, pathogenetic factors common to both forms of dyspnea, and the underlying basis of both is largely identical.

The "insufficient aeration" hypothesis first considered paroxysmal dyspnea as being due to congestion ot the lungs, which caused the capillaries to encroach on the air spaces thereby interfering with the ventilation of the lungs and causing defective aeration of the blood. Another investigator considered that the decreased aeration was due to the rigidity of the lungs. Other modifications of this theory resulted, but the end result is thal all of these theories of diminished aeration of the arterial blood as the cause of cardiac dyspnea have been discredited by recent investigators. Their studies also agree that a mild alkalosis rather than an acidosis of the arterial blood occurs except in cases of extreme pulmonary disease. Thus the "diminished cardiac output" theory (accumulation of

acid metabolites in the respiratory center dependent on diminished cerebral blood flow due in turn to decrease in cardiac output) was shown to be incorrect by the fact that arterial blood and blood obtained from the internal jugular vein of patients with dyspnea failed to show any alteration in hydrogen ion concentration, carbon dioxide content or oxygen content.

Some authors believed in the "nervous" hypothesis, which held the syndrome had its genesis in the nervous system. Brunn and others believed that cardiac asthma was due to a nocturnal passage of water from the tissues into the blood stream, and that this led to pulmonary congestion which resulted in decrease in the residual aie, which in turn caused reflex stimulation of breathing. Basis for the latter theory was placed in the fact that the use of diuretics may prevent attacks of paroxysmal dyspnea. Harrison reasoned that if there was nocturnal passage of water into the blood stream the hemoglobin concentration of the blood of these patients should be lower in the morning than in the evening. He found the reverse to be true, and used this as strong evidence against the "water-shift" hypothesis. Many other theories have been proposed but have been found inadequate.

Then what is the mechanism of cardiac asthma? It has been shown by many and most investigators that disturbances in the lesser circulation play the predominant role in causing this phenomenon. Pulmonary engorgement has been found to be of prime importance in cardiac

asthma. The pulmonary circulation time (arm to tongue) is always prolonged during the attack, which, in view of the frequently normal venous pressure, is to be attributed to slowing of blood flow through the lungs. X-ray changes show definite increase in pulmonary engorgement during the attacks.

Some of the most important evidence of the fundamental significance of pulmonary engorgement in the pathogenesis of at least many instances of cardiac asthma is afforded by the clinical course. Often previously severe and frequent attacks of paroxysmal dyspnea disappear when the right heart fails, as shown by peripheral edema. Patients often volunteer the fact that when their legs became swollen the nocturnal paroxysms disappeared.

Weiss and Robb have done much to prove the predominant role played by pulmonary engorgement in the pathogenesis of cardiac asthma. They find that in many patients with this type of difficulty the systemic circulation is hardly impaired, as shown by normal cardiac output, arteriovenous oxygen difference and venous pressure. On the other hand, they found conculsive evidences of passive engorgement of the pulmonary circuit, namely, increased in the blood content of the lungs, slowing of pulmonary circulation time, decreased vital capacity, and hypertension of the lesser circulation. All of these as well as the clinical manifestations of pulmonary engorgement are greatly intensified during the actual attack. Thus it is established,

as Fishberg states that "cardiac asthma develops on the terrain of pulmonary engorgement and the actual paroxysm accompanies an intensification of the engorgement." Thus both exertional and paroxysmal dyspnea are fundamentally of similar pathogenesis, resulting primarily because of passive congestion of the lungs.

Harrison has generally found that changes in the blood gases are not of a nature to be a very great factor in the genesis of cardiac asthma. He also observes that patients who are subject to attacks of paroxysmal dyspnea have, in the intervals between seizures, abnormally great ventilation and abnormally low vital capacity. During the seizure the vital capacity becomes still lower and the ventilation increases. Thus the resting ventilation is increased. This change in a person already close to the threshold of dyspnea will be associated with respiratory distress.

Bedford feels that the most obvious solution is a sudden disproportion between the two ventricles, and this might result either from increased output of the right ventricle or from a diminished output of the left. Tachycardia and the unfilled veins suggest increased cardiac activity in which the left ventricle is outstripped by the right. Bedford states that without accepting this view entirely there is no doubt that once a patient is awakened by pulmonary congestion the venous return will be increased by muscular movements and by the struggling for air. Thus Bedford feels that the fact that

the paroxysm ceases with the onset of right-sided failure points to the importance of a powerful and efficient right ventricle. Thus he concludes that the essential condition of paroxysmal pulmonary congestion is a disproportion between the two ventricles, and that in different circumstances an increased output from the right ventricle, a sudden failure of the left ventricle, and the recumbent posture may all play some part in the causation of cardiac asthma.

Harrison then considers that certain precipitating factors must be present, as cough, unpleasant dreams, abdominal distension, constipation, desire for urination, hunger, heat, amount of activity during the day and the position of the body. All of these precipitating causes are things that patients themselves propose as associated with the paroxysm.

The importance of the recumbent position can easily be understood after studying the above consideration of orthopnea. Possibly the patient falls asleep in the semi-orthopnea position and then slides down in bed and blood is displaced to the pulmonary circuit which results in further decrease in vital capacity and increase in ventilation, which finally become so great that the dyspnea awakens the patient. This does not explain nearly all cases of cardiac asthma, so other factors must play a part.

Sleep may be of great importance in that it lessens the sensitivity of the central nervous system, and this may allow pulmonary engorgement resulting from other factors (as assumption of the recumbent

position) to attain a mush higher degree before reflexly inciting an increase in ventilation than is the case when awake. This role has not as yet been proven, but it seems probable.

Such precipitating factors as dreams are difficult to evaluate objectively, but it would seem plausible that fear or other emotion accompanying a dream may increase venous return to the heart and thus promote pulmonary engorgement in the presence of a weak left ventricle. Harrison showed that sudden fear increases ventilation.

The resorption of edema or nocturnal "water-shift has been discussed above and was sgown to be of little consequence by Harrison, since the oxygen capacity of the blood was found higher in the morning than in the evening and thus probably no resorption of fluid and dilution of the blood takes place at night. Fishberg, in spite of this, feels that, in individuals who are up and around during the day,nocturnal resorption of fluid may sometimes be an accessory factor in overloading the heart at night.

Harrison stresses the importance of cough as a precipitating factor in cardiac asthma. He also believes that cough may help maintain the attack. He bases these conclusions on experiments in which he found that coughing caused reflex stimulation of respiration from the muscular movements involved, caused an increase in the metabolism because of the muscular work involved, caused reflex respiratory stimulation by increasing the venous pressure, and initiated a vicious cycle, the forced breathing resulting from coughing and producing

further cough. He explained the fact that the cough is more likely to cause a paroxysm at night since, because of the decreased nervous irritability during sleep, the increased bronchial secretion often present in pulmonary engorgement accumulates until it produces a violent paroxysm of cough which wakes the patient and there is thus an immediate increase in reflex irritability. Thus the cough becomes severe and causes more dyspnea because of the associated increase in ventilation in a person whose respiratory reserve is already low. Kirk and Fishberg agree in main with mechanism of cardian asthma as proposed by Harrison. In Fig. 10 below in diagram form is the mechanism of cardiac asthma as suggested by Harrison.

Relief of the attack isusually obtained by getting rid of the stimulus plus the assumption of the sitting position. Also the loss of carbon dioxide due to increased ventilation may cause sufficient respiratory depression to end the seizure. The patient may rid himself of the stimulus by expectoration, by casting off the bedclothes, by belching, or by urination, etc.

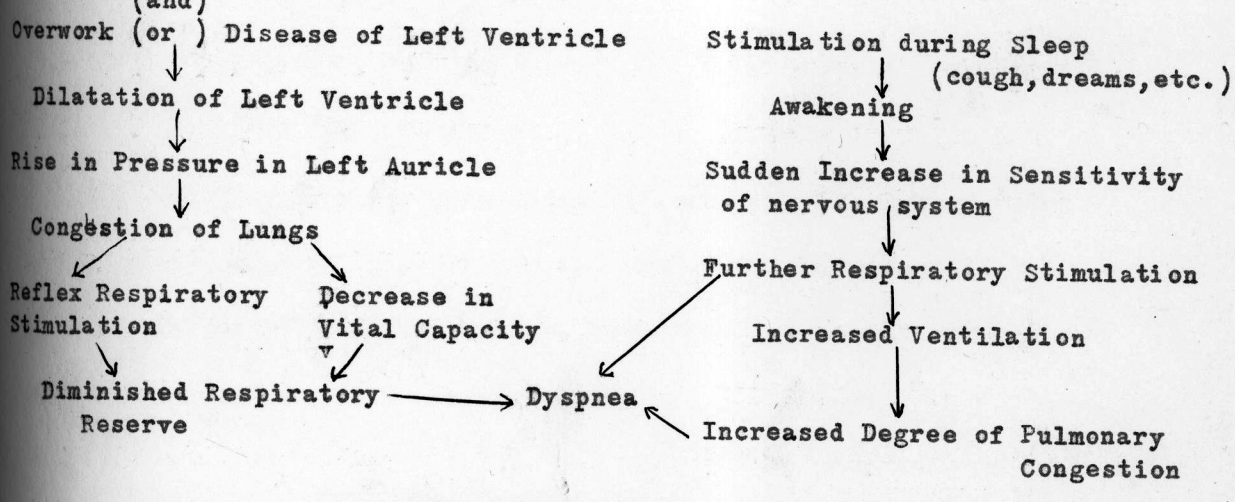


FIG. 10 - THE MECHANISM OF CARDIAC ASTHMA (Harrison)

Thus Harrison feels the most common stimulus is the tencency to cough, caused by musus in the respiratory tract, but other factors may play a role. This stimulus finally wakes the patient and the ventilation is suddenly increased because of the effect of a strong respiratory stimulus acting on a suddenly more excitable nervous system. The factors mentioned above tend to relieve the attack. The vicious cycle already mentioned tends to make the paroxysm worse. The increased respiratory movements favor a greater return to the heart and -- since the reserve power of the left ventricle is less than that of the right -- tend to produce an increased degree of pulmonary congestion, which will cause further reflex respiratory stimulation. This cycle may more than offset the factors which tend to relieve the paroxysm, and the seizure becomes progressively worse. Morphine is of value here because it diminishes the sensitivity of the respiratory center to reflex stimulation and thus breaks the cycle. If morphine therapy is not instituted in such a case, acute pulmonary edema sets in, and an oxemia results which causes chemical stimulation of respiration and may increase venous return, thereby causing pulmonary congestion to increase still more.

Bedford and Harrison both recognize the disproportion between the two ventricles. To this writer this disproportion seems of extreme importance in the pathogenesis of all forms of dyspnea (since dyspnea is mainly a result of left heart failure).

Harrison has shown that certain patients with cardiac disease

have a rather marked decline in blood pressure during sleep. He feels that "the decline in the aortic pressure may cause diminution in the coronary blood flow and thereby lead to further dilatation of an already dilated left ventricle, with a consequent rise in the left auricular pressure resulting in a still greater degree of pulmonary congestion. Once the seizure sets in the blood pressure is usually elevated". Direct evidence is lacking as yet concerning this latter possibility.

Fishberg brings up the problem as to why paroxysms of cardiac asthma are so much rarer in the pulmonary engorgement of mitral stenosis than in that of left ventricular failure. This remains to be explained, but Bedford has suggested that the acute pulmonary edema of mitral stenosis does not develope when the left auricle is grossly dilated, or is fibrillating (thus the left auricle may act as a cushion to the lung).

F. Cheyne-Stokes Respiration

This is also a type of paroxysmal dyspnea. It usually occurs in older patients than cardiac asthma; the seizures are most marked just at the onset of sleep; the condition is rarely complicated byacute pulmonary edema; and the type of dyspnea is periodic. In these ways Cheyne-Stokes respiration differs from cardiac dyspnea.

Cheyne-Stokes respiration usually infers a rhythmical waxing and waning of the depth of the respiration, usually having an associated

period of apnea between the periods of hyperpnea. As stated, this phenomena may occur at the onset of sleep, or may occur during the day and be more pronounced toward the sleeping period.

There is good evidence that oxygen deficiency is concerned in the genesis of at least some forms of Cheyne-Stokes breathing. Some authors go so far as to even consider it the whole cause. However Harrison feels that anoxemia cannot be the sole cause or even the chief cause of periodic breathing. Fishberg considers oxygen deficiency is of importance only under certain conditions and in association with other factors. Although periodic breathing cannot usually be abolished by breathing oxygen it can be modified by the administration of this gas -- the phase of hyperpnea being prolonged and less stormy, and the period of apnea shorter. Clinical observation shows that oxygen deficiency per se does not suffice to cause Cheyne-Stokes breathing. For patients with right ventricular failure secondary to pulmonary lesions and those with congenital heart disease, who may be cyanotic for years, rarely develop periodic respiration. Thus the conclusion drawn is that anoxemia may be important in the pathogenesis of periodic breathing but only in association with other factors.

Depression of the carbon dioxide tension of the arterial blood favors the development of Cheyne-Stokes respiration. However,Fishberg feels that low carbon dioxide pressure in the arterial blood is not a necessary condition for the occurrence of Cheyne-Stokes breathing. He cites morphine poisoning as an example where there may be periodic

respiration despite very high carbon dioxide tension in the arterial blood; however, the inhalation of carbon dioxide abolishes the periodicity of the breathing, showing that the latter is conditioned by carbon dioxide pressure which is relatively low in comparison to other factors in the regulation of respiration, especially the sensitivity of the respiratory center. The general conclusion by most investigators is that lack of carbon dioxide is an important factor in the production of Cheyne-Stokes respiration. This substaniated by the facts that periodic breathing can be produced in normal man by loss of carbon dioxide due to over ventilation, that the same procedure is ineffective if the alveolar carbon dioxide is maintained at a normal level, and that periodic breathing is usually stopped by breathing air with high concentrations of carbon dioxide.

Harrison from observation or recordings, gives the following explanation: "It can be seen that during apnea the oxygen saturation diminishes at first slowly and then-when the alveolar oxygen tension has decreased to a point corresponding to the steep part of the oxygen dissociation curve--more rapidly. This decline continues until just after the beginning of breathing and then the oxygen saturation abruptly rises to a normal or a supernormal level and remains throughout the remainder of the hyperpneic phase.

"The behavior of carbon dioxide is rather different. Shortly after apnea begins this gas accumulates in the blood, at first rapidly and then more slowly. Soon after the onset of breathing the carbon

dioxide content begins to decrease. During the crescendo phase of hypernea the rate of carbon dioxide loss increases and then the excretion becomes slow as the breathing becomes diminuendo.

"These differences between the behavior of the two gases are in accord with what one would expect from the differences in their physiological properties, the changes in carbon dioxide being more gradual because its dissociation curve approaches a straight line. Oxygen on the other hand exhibits little change so long as oxygen tension is in the normal region because at this point its dissociation curve is almost flat. However, when oxygen pressure is low its dissociation curve is more nearlu ventricle and hence, once this point has been reached, the decreased in the amount of oxygen in the blood at the end of apnea, and the increase shortly after the onset of breathing occur with great abruptness.

"The pH curve is of especial interest. At the beginning of apneathe blood becomes rapidly more acid, but toward the end of apnea there is either no further change or a slight increase in alkalinity. The latter phenomenon is to be attributed to the rapid conversion of oxyhemoglobin into the less acid reduced hemoglobin. At the onset of breathing there is a very slight initial rise in pH because the carbon dioxide begins to decrease immediately. However, this is followed by a second acid peak which occurs at the same time as, and is due to, the sudden oxygenation of the hemoglobin. Consequently, since the most acid point in the cycle occurs several seconds after the onset of

breathing, the respiration is crescendo in type. After the blood has become oxygenated the further effect of breathing is to cause the blood to become more alkaline from loss of carbon dioxide and the result is the second or diminuendo portion of the hyperpneic phase. Then apnea occurs and the cycle repeats itself."

Thus both oxygen and carbon dioxide are considered important in the production of Cheyne-Stokes breathing. Lack of either gas tends to produce it. However there are other factors which play a part, as periodic breathing may exist in patients whose blood is normal in respect to oxygen and carbon dioxide.

Diminished irritability of the respiratory center is considered to be a factor of importance in the genesis of some forms of Cheyne-Stokes respiration. It seems likely that both sleep and morphine lead to Cheyne-Stokes respiration through this mechanism which elevates the threshold of carbon dioxide in the respiratory center, which in the end is similar to decrease in the carbon dioxide tension in the blood due to hyperventilation. Fishberg feels that this results in the transfer of the "lead" in the chemical regulation of respiration from carbon dioxide to oxygen.

The effect of the immediate onset of sleep has been mentioned. However after a patient has slept for a while the decreased ventilation is associated with a gradual rise in the carbon dioxide tension of the blood and this is likely to abolish periodic breathing. In cases of

severe respiratory or coma the duration os apnea may be so long as to allow marked arterial anoxemia, and then when breathing sets in there is an overshooting of hyperpnea because of the sudden increase in acidity due to the rapid oxygenation of hemoglobin.

Eyster and Cushing have shown that when spinal fluid pressure was increased artificially, alternating waves of respiration were produced. These were associated with alternating waves of arterial blood pressure and spinal fluid pressure, and Cheyne-Stokes respiration ensues. Such conditions are also seen in states of increased intra-cranial paressure as in brain tumors, cerebral hemorrhage and uremia. Thus it was felt that the respiratory periodicity was secondary to circulatory periodicity. T. R. Harrison feels that as a rule the blood pressure changes were the result rather than the cause of Cheyne-Stokes respiration. He admits that there is evidence that increased intra-cranial pressure may be important in certain instances because we can sometimes abolish Cheyne-Stokes respiration by a lumbar puncture and reduction of spinal fluid pressure. Fishberg also feels that this factor may be of importance in some cases. W. G. Harrison, Fr., has found an increased spinal fluid pressure in a large proportion of patients with cardiac failure, and he feels that the Cheyne-Stokes respirations may be initiated by alternating waves of arterial and increased spinal fluid pressure as a direct result of increased venoue pressure. He considers Cheyne-Stokes respiration as a compensatory phenomenon in which the individual unconsciously attempts to keep his arterial blood pressure ratio level above that of repidly rising spinal fluid pressure in order to keep the cerebral circulation intact and to prevent prolonged cerebral anemia.

Fishberg presents the point that decrease in circulation through the medulla may be a factor in the production of Cheyne-Stokes respiration. He states that this type of breathing is especially apt to ensue in hypertensive and arterio-sclerotic heart failure after the blood pressure has fallen somewhat, and that this factor may play a part in cutting down the blood flow through the brain.

Thus Fishberg considers that five factors might be of importance in causing Cheyne-Stokes respiration. The importance of any one of these vary in different cases. Below are listed these factors:

1. Oxygen deficiency.
2. Decrease in the carbon dioxide content of the arterial blood.
3. Diminution in the sensitivity of the respiratory center.
4. Increase in the intra-cranial tension, which produces respiratory periodicity indirectly through the intermediacy of cerebral periodicity.
5. Decrease in cerebral blood flow.

Harrison's conception of the mechanism of Cheyne-Stokes respiration is shown in the diagram in Fig. II.

According to Harrison two essential iniating factors are over-ventilation, and the onset of sleep with its consequent depression of the irritability of the respiratory center. In the end Cheyne-Stokes respiration in cardiac failure may be considered as being dependent on a lack of coordination between the various factors which control normal breathing. Pulmonary congestion causes reflex stimulation of breathing, which in turn causes a decrease in the carbon dioxide content of the blood and thus a depression of the chemical control by this gas. Thus the blood is too

much aerated as regards carbon dioxide and too little aerated as regards oxygen. The result is a waxing and waning of respiration, which produces the sensation of dyspnea in patients so predisposed by pulmonary congestion.

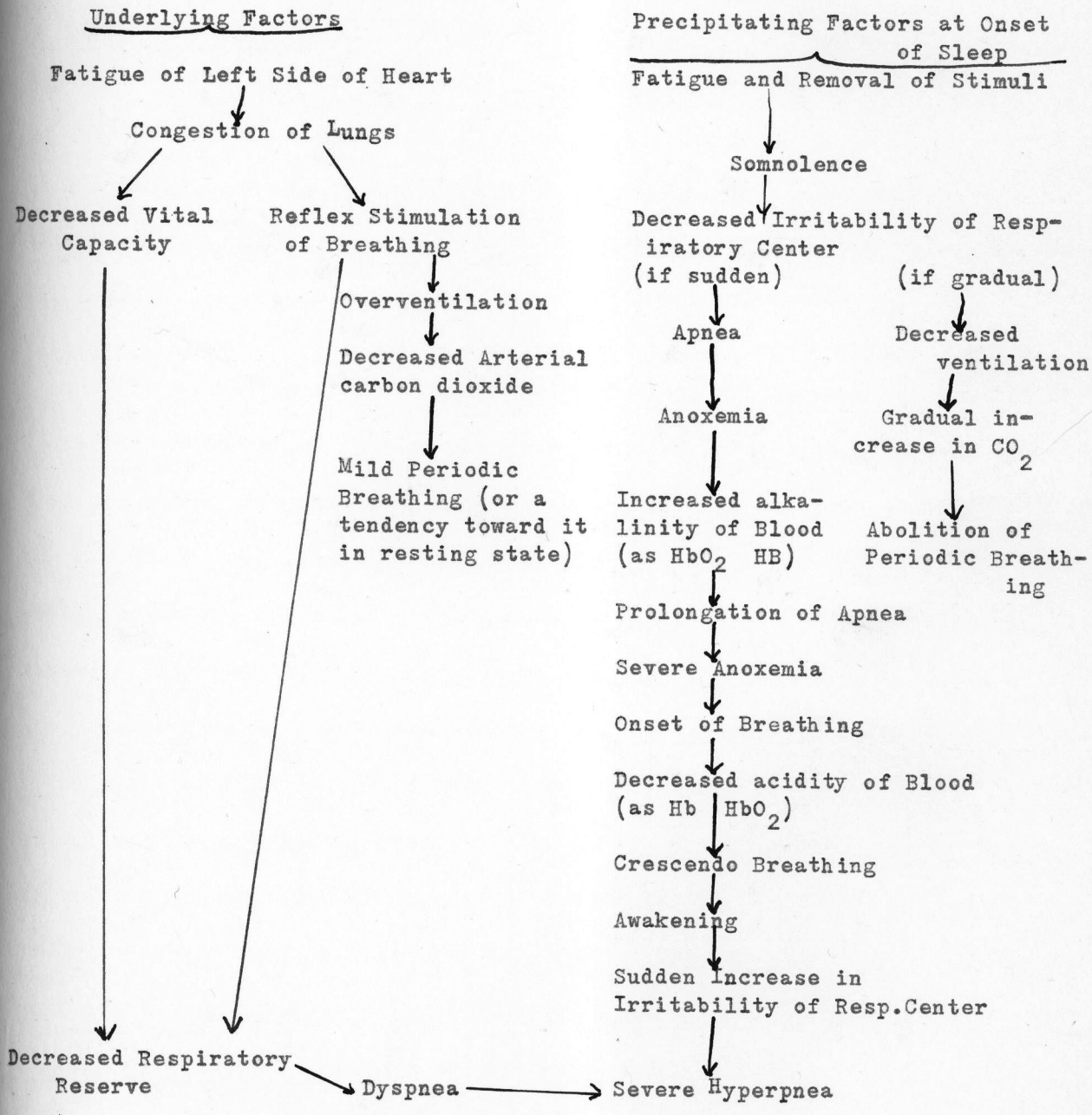


FIG. 11 - THE MECHANISM OF DYSPNEA OCCURRING AT THE ONSET OF SLEEP (from Harrison)

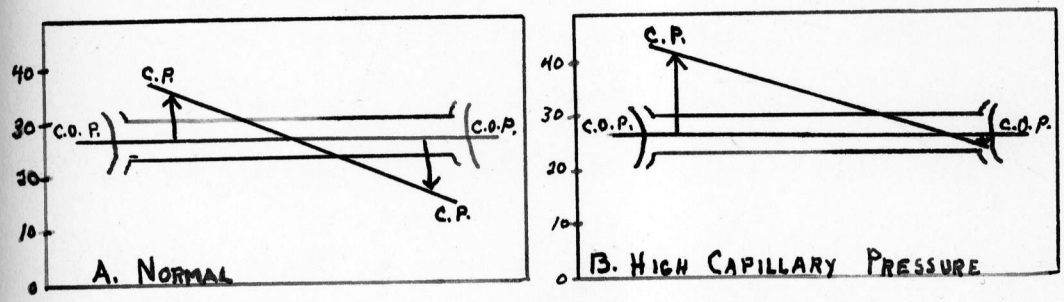
G. Edema

Even though the blood plasma and the tissue fluids have somewhat different compositions are in separate "compartments", they are essentially a uniform medium. In maintenance of normal blood volume the interstitial fluid is the first line of defense. Its usual volume represents a large margin of reserve. Loss of fluid, as in dehydration, is replaced quickly at the expense of the tissue fluid. On the other hand the tissue spaces can accomodate increased amounts of fluid filtered from the capillaries with little or no difficulty.

The mechanism of fluid equilibrium between the blood and tissue fluid is easily understood. The blood flows through the capillary network under pressure which, if unopposed, filters fluid from the blood plasma through the capillary wall into the tissue spaces. The capillary wall, though permeable to water, salts and simple organic compounds, is, in most tissues, relatively impermeable to plasma protein. Those substances (salts, urea, creatine, glucose, etc.) which pass easily, and are present in approximately equal concentration in the plasma and the tissue fluids, cannot exert a permanent osmotic pressure across the capillary wall and should not, therefore, affect the distribution of fluid except temporarily. Plasma proteins, by reason of their greater molecular dimensions, are retained by the capillary wall and thereby develop a small but physiologically important colloid osmotic (or oncotic) pressure which, if unopposed, leads to the absorption of fluid from the tissue spaces.

The capillary blood pressure at heart level is 32 mm. of mercury at the arterial capillary and 12 mm. of mercury at the venous capillary. The

average normal colloid osmotic pressure of blood plasma is about 24 mm. of mercury. Albumin is osmotically the more active because of the smaller molecule -- thus also more easily goes through the capillary wall. A schematic expression of this mechanism is shown in Fig. 12.



C.P. - Capillary Pressure C.O.P: Colloid Osmotic Pressure.

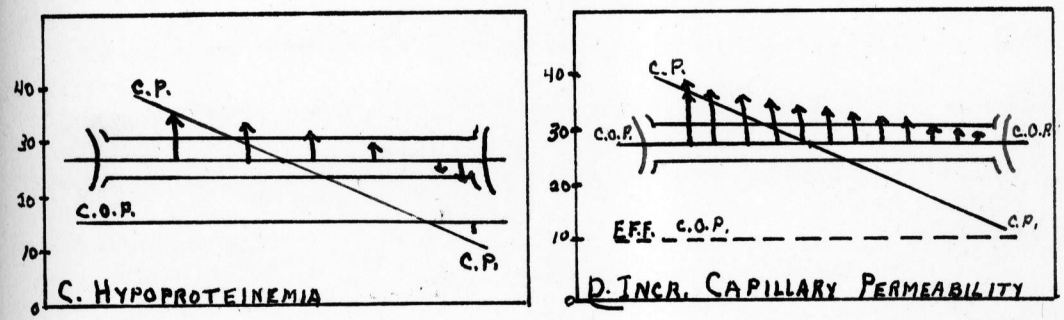


FIG. 12 - DIAGRAM ILLUSTRATING FILTRATION AND ABSORPTION THROUGH THE CAPILLARY WALL IN RELATION TO CAPILLARY BLOOD PRESSURE AND COLLOID OSMOTIC PRESSURE OF PLASMA PROTEINS (From Stroud and Vander Veer-45).

Edema may be defined as the abnormal accumulation of fluid in the interstitial compartments. Cardiac edema may apply to the lungs or to the general systemic circulation. This chapter will consider mainly systemic dropsy. Systemic dropsy is usually a late phenomenon of cardiac disease mainly because it is usually dependent on failure of the right ventricle which often takes place relatively late in the patient's course.

It is generally accepted by most investigators that the factor of prime importance in the formation of systemic cardiac edema is the increased venous pressure which in turn gives elevated capillary pressure (shown in Fig. 12B). There is no compensatory increase in the osmotic pressure of the blood and increased filtration of water to the tissues results. Harrison feels that at first there is increased lymphatic flow to try to compensate for the increased tissue fluid. As the venous pressure rises this compensatory mechanism is insufficient and edema results. Such processes are most marked at the dependent portions of the body due to the fact that gravity tends still further to impede the upward drainage of lymph and increased the venous pressure. Harrison states that when venous pressure becomes high it interferes with the emptying of the thoracic duct, and thus is a slight factor in edema formation. Altschule feels that the absence of normal lymph flow in cardian patients is an important factor in edema formation, but that the mechanism of the reduced lymphatic flow is obscure. Altschule believes that a moderate increase in venous pressure commonly found in congestive failure constitutes an important contributory factor, but does not result in edema formation

unless additional influences are operating at the same time (as low cardiac output, deficient oxygenation of the blood, low plasma protein). Most investigators agree that other factors may be of some significance, but they point out the prime importance of increased venous pressure in that patients may go for months to years with cardiac enlargement and dyspnea, and edema only sets in when the right heart finally fails.

Another factor that may play a part is lowered colloid osmotic pressure due to low plasma protein (as the result of albuminuria and ascites, inadequate protein intake, dietary restriction and impaired absorption, impaired synthesis of plasma proteins, rarely due to abdominal or pleural paracentesis, and increased plasma volume).

Another factor to be considered is damage to the capillary wall as the result of anoxemia. Altschule, who favors the "forward-failure" theory in part, again puts more than the usual importance on this factor. He believes that anoxemia causes vasodilatation and increases the permeability of the capillaries. He bases this conception on the work of Smirk who raises the venous pressure to the same level above oncotic pressure of normal and cardiac patients with the result that much larger amounts of tissue developed in the latter, and he also showed that edema increased in patients even when the pressure of the edema fluid already present was greater than the venous pressure. Harrison dosn't share this view; he feels that anoxemia plays very little part since edema fluid as a rule does not have high protein value. The absence of peripheral edema in left heart failure and in the peripheral circulatory

failure of shock shows that diminution of blood flow per se, and without increased capillary pressure, does not produce edema.

Lymphatic obstruction due to increased venous pressure effects, decreased physical activity and poor muscle tone has already been mentioned as a factor. Capillary dilatation, giving increased filtering surface, might be factor especially since there is increased venous pressure.

Low tissue pressure may be a rather important factor at times, especially in cachetic patients with lax subcutaneous tissues. Loss of weight and poor muscle tone tend to give diminished tissue pressure. Tissues stretched by previous edema usually leave tissues without elasticity, and thus edema easily reforms.

Given the tendency to edema formation, a high salt intake if water is available will increase the edema, and conversely high fluid intake if salt is available will increase the edema. Warm environment tends to increase all types of edema. Other factors not usually important in cardiac failure are disturbed innervation (increased edema of paralysed extremities), mixed edema, and hormonal abnormalities.

Altschule feels that edema of congestive failure is usually not due to the operation of any one factor, but the result of a combined of sub-maximal or even minimal changes in many factors.

In Fig. 13 below is Altschule's complex mechanism of cardiac edema formation: Note the importance he places on low cardiac output (since he favors the "forward-failure" theory in part.

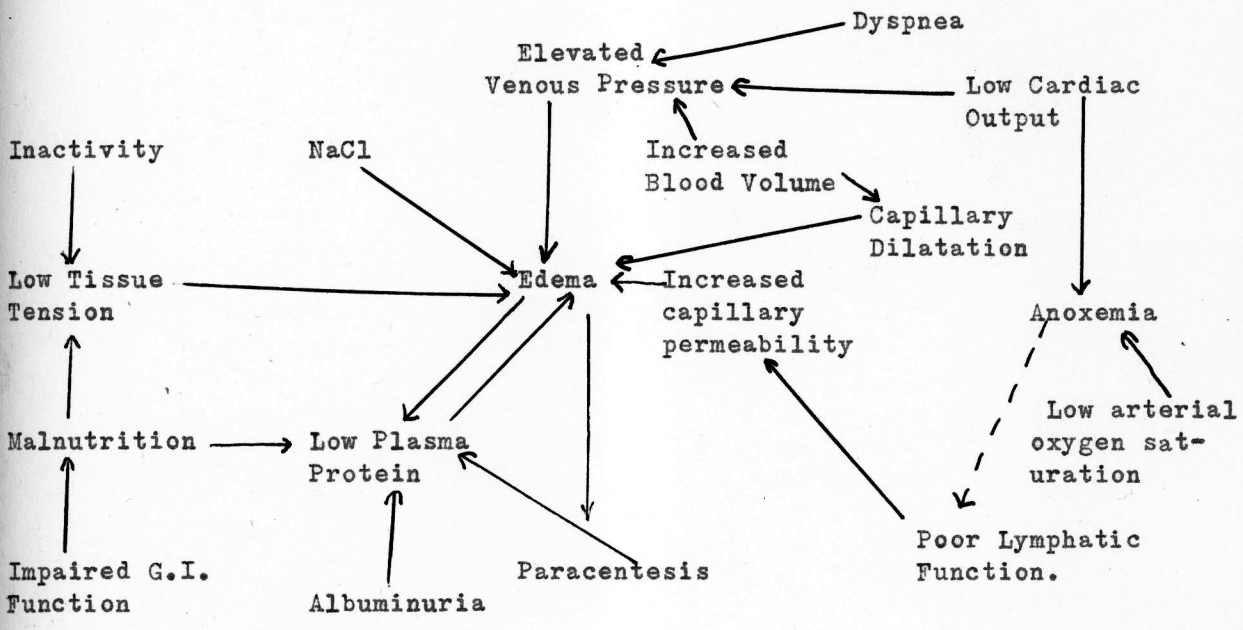


FIG. 13 - MECHANISM OF EDEMA FORMATION IN CONGESTIVE HEART FAILURE (from Altschule).

The points on which Harrison and others disagree with the above have already been discussed. It seems to this writer that Altschule summarizes all the possible factors involved in cardian edema formation, but that he tends to put too little importance on the really big factors, and too much importance on the insignificant ones. Stroud and Vander Veer give the following list of possible factors in the pathogenesis of cardiac edema in the usual order of their importance:

1. Elevated capillary pressure (increased venoue pressure, increased blood volume, increased intra-pleural pressure).
2. Lowered colloid osmotic pressure (albuminuria, etc.).
3. Damage to capillary wall (anoxemia).
4. Lymphatic obstruction.
5. Capillary dilatation.
6. Low tissue pressure.
7. High salt intake (with available water).
8. High fluid intake (with available salt).
9. Warm environment.
10. Disturbed innervation.
11. Miscellaneous - - Vitamin deficiency, hormonal abnormalities, etc.
12. Other diseases -- edema of mixed etiology.

It may be of interest to consider for a moment why there is a preponderance of right hydrothorax in patients with heart failure. Dock's anatomical studies of the chest may be of importance here. He has found that the pulmonary venous outflow from the right lung of an adult in the right lateral recumbent position must be lifted 10 cm. or more to reach the left ventricle, and that from the left lung, when in the left lateral position need be lifted only 5 cm. Thus the average venous pressure needed to maintain the flow of blood will be much higher in the right lung than in the left, even if the individual spends equal

periods lying on the two sides. In patients, like cardiacs, who favor right lateral decubitus, this difference in average pressure between the venous beds in the lungs will be increased. This might be of great importance in explaining the preponderance of right hydrothorax over left hydrothorax.

THE MINOR PHENOMENA OF CONGESTIVE HEART FAILURE

Our discussion of the following signs and symptoms will be brief, since our knowledge is limited and these phenomena are usually of less importance than those discussed above. It may be mentioned that in certain individual cases one or more of the following manifestations may be of major significance to that patient. There is a wide field for further study along these lines.

A. Cyanosis

Altschule considers cyanosis a common finding in cardiac decompensation, and that the onset frequently precedes that of edema and orthopnea, but rarely, except in patients with congenital heart disease, that of dyspnea. Harrison states that cyanosis is most likely observed in elderly patients with emphysema or other chromin pulmonary disease, in patients with rheumatic disease of one or both of the auriculo-ventricular valves, and in persons with congenital malformations of the heart. If acute pulmonary edema is present cyanosis is likely to appear. It is not common in hypertensive or syphilitic heart disease. Many consider that cyanosis tends to predominate over dyspnea in right heart failure and dyspnea over cyanosis in left heart failure.

"We speak of cyanosis when the contribution of the reduced hemoglobin of the skin becomes marked enough to influence it discernibly in the direction of blue"-- Fishberg. According to this quotation the

primary condition for the production of cyanosis is probably an increase in the concentration of reduced hempglobin in the blood of the venules and capillaries. It has been shown that the presence of unsatured hemoglobin in a concentration of at least 5 grams % is necessary for the production of cyanosis.

The ashen gray cyanosis of acute heart failure, as after coronary thrombosis, is due to the diminished cardiac output and consequent increase in the amount of reduced hemoglobin. Decreased arterial blood oxygen saturation may be important in cyanosis formation, especially if such conditions as emphysema, pneumonia, large infaration, pleural effusion or severe pulmonary edema complicate heart failure. Decrease in blood flow through the tissues with a resulting increased capillary reduction of oxygen may be important in the formation of cyanosis (seen by the arteriovenous oxygen difference), and this factor is especially important in peripheral circulatory failure as shock.

However, Harrison and many others feel that the cyanosis in chronic cardiac failure is usually a rather faint reddish blue tint confined to the lips and finger nails, and is due primarily to increased venous pressure and consequent increase in the size of the venules and venous ends of the capillaries as compared to the size of the arterial capillaries. Altschule dosn't feel that this is of such great importance, but that it merely exaggerates the degree of blueness already present. Thus right heart failure with increase in the venous pressure results in distention of the venules and venous ends of the capillaries (subpapillary venous

and capillary networks).

Thus cyanosis may result from changes in the blood present in the skin (includes lowering of the arterial oxygen saturation before the blood reaches the tissues, and extraction of abnormally large amounts from each unit volume of blood in the tissues), or from the increased amount of blood in the skin (increased venous pressure resulting in greater capillary and venule dilatation). Congenital heart disease where there is a direct shunt falls into the former group. However in the majority of cardiac cases without pulmonary complications the cyanosis is due to increased venous pressure and thus dilatation of venules and venous ends of the capillaries. It may be mentioned that patients with very high hemoglobin may be cyanotic and anoxic (polycythemia), or that patients with very low hemoglobin may be anoxic and not cyanotic (anemia).

B. Tachycardia

The advantage of tachycardia is that the more rapid rate enables the heart to accomplish a given output with a smaller diastolic volume than is the case with slower rates. Thus it tends to diminish the venous pressure and to prevent further dilatation of an already dilated heart. Harrison feels that this advantage is more than offset by the disadvantages. A fast heart has less mechanical efficiency, since excess energy is used in opening the semilunar valves more frequently, the circulation of the myocardium may be impeded, and the shortened recovery period may be inadequate for oxygenation of the fibers.

It is generally felt that the tachycardia is of reflec origin, and is due to rise in venous pressure (Bainbridge reflex). The efferent path lies in the vagus, and part of the efferent path is in the vagus (diminution in vagus tone), and part in the sympathetic system(accelorator tone increased). Fishberg states that the carotid sinus and aortic reflexes may play a part in the tachycardia, especially in advanced heart disease where the cardiac output is diminshed and the blood pressure is low.

C. Gallop Rhythm

This phenomenon is charterized by the occurrance of three hearts sounds during each cardiac cycle. The extra sound is actually inpependent and not merely a splitting or reduplication of the normal two sounds. Fishberg has divided gallop rhythm into two types, auricular gallop rhythm and gallop rhythm due to an accentuated third heart sound.

It has been conclusively shown that the adventitious sound in auricular gallop rhythm appears at the time of auricular systole. Fishberg considers that the extra sound in this type of gallop rhythm results from auricular systole, else it would not disappear during auricular fibrillation. He feels there is an abnormally powerful contraction of the auricle as revealed by the large auricular excursion in the cardiogram. He thus considers that auricular gallpp rhythm is the result of an exaggeration of the sound normally produced by auricular systole due to more forceful contraction of the auricle. Harrison

considers gallop rhythm as due to an almost taut ventricle which does not dampen the auricular sound, and that there is also usually a more marked auricular pressure with possibly a stronger auricular contraction. Fishberg also recognizes the importance of the taut ventricle. According to Fishberg, this auricular gallop rhythm is usually considered to be presystolic in time, but the time in the cycle may change due to tachycardia or partial heart block.

Harrison does not divide gallop rhythm into two varieties. He feels that the protodiastolic type is due to the taut ventricle and inrushing blood from the auricle (the same mechanism as he upholds for the presystolic type). Fishberg feels that there is definite proof that the protodiastolic sound is due usually to the accentuation of the third heart sound, since the physiological third heart sound occurs at the end of the protodiastolic period of rapid ventricular filling and seems to be in some way produced by this filling. There is an exaggerated protodiastolic wave in the cardiogram of those with this form of gallop rhythm, which would indicate that the accentuation of the third heart sound is due to an increase in the pressure at which early diastolic filling occurs, thus being indicative of increased venous pressure (pulmonary venous pressure in the usual left-sided gallop). Thus the only differentiation that Fishberg makes is that in the presystolic gallop rhythm third sound is produced in part by auricular contraction, and in the protodiastolic gallop there is no element of auricular contraction. In reality, then, Harrison and Fishberg agree on the mechanism of gallop rhythm, but Fishberg has considered the subject a little more deeplu.

Harrison states that auricular pressure is higher and there is dilatation of one ventricle at least causing it to be taut, then "at the beginning of diastole the blood rushes more suddenly than normal into a ventricle that is already almost taut. The sudden increase in tension may produce a lew pitched sound, which is the 'ectopic' sound of the gallop. Likewise at the end of diastole the auricular contraction causes a second sudden increase in the intra-ventricular tension which may produce a sound."

Thus gallop rhythm indicates that one or both of the ventricles is dilated. It is usually considered a relatively early sign of dilatation and hence of impending congestive failure. It is of grave prognostic significance, and indicates an urgent need for therapy.

D. Functional Regurgitation

Without going into this condition in detail it may be mentioned that the mechanism of functional regurgitation is not entirely clear. However, two factors seem to be of most importance in the pathogenesis of this condition. The first is weakness of the myocardium surrounding the valve ring. The other is displacement of the attachment of the papillary muscles. In reference to the latter, this factor only takes place when there is broadening of the ventricle and not simply from lengthening.

E. Cardiac Pain

Everyday clinical observation show there is no direct correlation

between cardiac pain and heart failure. Some of the most severe forms of heart failure run their course without any pain. Thus a full discussion of cardiac pain would be more appropriate in a consideration of coronary occlusion, syphilitic, aoritis, aneurysm, pericarditis or cardiac neurosis, besides other factors of pleurisy and arthritis of the spine.

We will limit our discussion to saying that, while the cause of cardiac pain is still controversal, the essential pathological physiology underlying pain in the heart is believed to be anoxemia of the myocardium, which may be brought about by obstruction of blood channels (coronary disease), by deficiency in the quantity or quality of the blood (anemia), or by impairment of the mechanism or pressure gradient by means of which blood is propelled into and through the coronary circulation (aortic valvular disease, paroxysmal tachycardia, etc.).

F. Basal Metabolism

It is generally accepted that the basal metabolism is increased in cardiac failure. Many investigators have concluded that the greater oxygen consumption in heart failure is due primarily to the increased work of the muscles of respiration. The latter results from pulmonary engorgement in two ways: (1) Pulmonary engorgement entails an increase in the minute volume of ventilation, and (2) there is greater rigidity of the lungs and thus more muscular work is necessary for a given volume of respiration. Thus the increased metabolic rate would appear to be due primarily to pulmonary engorgement and consequently to failure of the

the left side of the heart. Resnik and Friedman observed rates below zero in 3 cases of constrictive pericarditis with marked systemic venous engorgement but not severe pulmonary engorgement, since dyspnea at rest was not present. The increased oxygen consumption of the hypertrophied and dilated heart may also add to the increased metabolism in some cases.

Altschule considers that the elevated basal metabolism might be due to rise in temperature and to severe dyspnea. He also feels that the value obtained may be too high since sick patients can't assume a basal state, and also patients may take up excessive amounts of oxygen in an attempt to discharge their oxygen debt.

G. Body Temperature

Fever in some degree is considered to occur in a large proportion of patients with congestive heart failure. Cohn and Steele found that 153 of 172 persons with heart failure exhibited a rectal temperature of at least 100F on two or more occasions, and in 49 of these no cause for the fever other than heart failure was discovered. They found that both the fever and the heart failure disappeared simultaneously. Kinsey and White found fever in most of their cases, but found that the fever was related to a complication rather than to the heart failure. Complications as pulmonary infarction, broncho-pneumonia, active rheumatic fever, acute coronary thrombosis and others -- respiratory infections were important. Kinsey and White did feel that congestive failure alone may possibly explain up to one degree of fever.

Harrison considers that a slight increase in temperature may be dependent on the increased metabolic rate. Fishberg points out that in heart failure oxygen consumption and consequently heat production is generally increased, while at the same time the mechanism for heat dissipation may be impaired. Both Fishberg and Altschule explain the latter on the fact that, when cardiac output is diminished, the blood flow through the skin and periphery, which plays so important a part in the dissipation of body heat, is decreased. Steele has found that the difference between skin and rectal temperature is abnormally great in heart failure as compared with unimpaired circulation, and that three times as much heat is eliminated via the lungs in heart failure. Steele also suggests that the rise in temperature might be one cause of hyperpnea since some patients with congestive failure claim increased dyspnea when wrapped warmly or in a stuffy room.

H. Fatigue

Harrison considers that muscular weakness is not as a rule an important symptom of congestive heart failure. In acute cardiac collapse, as with coronary thrombosis, weakness may be marked. It is admitted that patients who have been in bed a long time have asthenia, especially persons with cardiac cachexia.

Oshlag feels that the sensation of fatigue and exhaustion may be prominent in heart disease and indicates the presence of oxygen debt and of accumulation of the by-products of muscle activity. He states that in the normal individual an augmentation in minute output compen-

sates for the production of fatigue bodies up to a certain point and there is no sensation of fatigue. Thus he considers that the absence of notable diminution of this reserve power must be considered as a failure of the left ventricle and in the case of fatigue as a "forward-failure". Altschule feels that generalized muscular weakness may be related to abnormal creatine metabolism.

I. Gastro-intestinal Function

Loss of appetite, nausea, distention, gaseous eructation and flatulence are frequently complaints in moderate or severe cardiac failure. Anorexia is often due to digitalis or morphine. Some investigators say that gastric tonus is decreased, peristalic and hunger contractions diminished and emptying time of stomach prolonged in the presence of anoxemia. Once compensation is restored the appetite should return, but if it does not cardiac cachexia must be feared.

Loss of weight may or may not occue. It is more frequently associated with rheumatic heart disease or bacterial endocarditis. Cardiac cachexia may develop following prolonged decompensation, and it is characterized by anorexia, anemia, marked undernutrition, and asthenia. Gastro-intestinal impairment is in part responsible for the loss of weight.

Abdominal pain is most commonly due to liver engorgement. Nausea and vomiting are most commonly due to digitalis, morphine and ammonium chloride. Cardiac or abdominal infarction may also cause nausea and

vomiting. Constipation is often a serious symptom because of the muscular effort required to pass the stool and because of increased intrathoracic pressure. Mineral oil should be used freely.

J. Cough

Cough is a frequent symptom in patients with pulmonary congestion due to left ventricular failure or to mitral disease. It may be due to the congestion or to secondary low-grade infection. Coughing throws a strain on the whole heart and also causes a rise in pulmonary pressure.

Hemoptysis occurs under certain conditions. Brownish rusty sputum is most common in mitral valve disease since there is often an indurated lung of long standing congestion and hemosiderin deposits are present in the cells. In patients with pulmonary congestion due to left ventricular failure frothy blood stained sputum is more common because the congestion is apt to come on suddenly and in severe form. Infarction of the lungs is the most serious and one of the most common causes of gross hemoptysis in patients with congestive failure.

K. Liver Function

Swelling of the liver is one of the common manifestations of heart failure, and failure of the right heart is by far the most common cause of this passive engorgement. From the pathological anatomical findings it cannot be doubted that liver function is diminished. However, the factor of safety is so great that fatal hepatic insufficiency

apparently does not occur as a result of uncomplicated heart failure. The hyperbilirubinemia that is the rule, and the jaundice that occasionally occurs in severe heart failure are believed by most investigators to be due primarily to impaired hepatic function. Liver function tests are less likely to show abnormalities than is serum bilirubin determinations. The degree of hyperbilirubinemia is considered as not necessarily related to the size of the liver.

Jaundice is not so uncommon in association with congestive heart failure. The factor of prime importance in this is generally considered to be impairment of liver function which is a result of mechanical compression of liver sells due to congestion and of anoxemia. Another factor which plays a part is increase in the production of bilirubin, which is evidenced by the increased urobilin in the stools and increased urobilinogen in the urine. Probably the greatest amount of blood destruction takes place in the lung. Fishberg feels that a third factor of diminution in blood flow through the liver plays a part in jaundice formation by causing the retention of bilirubin in the blood. Some investigators say there is bilirubin in edematous fluid, while others say there is not. Andrews,who is of the former view, found that the protein content in the edematous fluid influenced the bilirubin content.

Meakins related the degree of hepatic engorgement and central necrosis to the increased venous pressure. Other investigators produced the typical pathological changes in the liver by obstruction of the inferior vena cava in animals. Harrison is inclined to agree with this idea

that jaundice is due primarily to the mechanical compression of the liver cells by the dilated capillaries (increased venous pressure). However, Mallory pointed out that if back pressure were the cause of necrosis in the liver it should involve the entire lobule, since pressure is everywhere and is actually higher in the periphery of the lobule to maintain a gradient of pressure; thus he concluded that some toxin was responsible for liver cell damage. Many authors, including Altschule and Fishberg, consider anoxemia as the factor of prime importance in the altered histology and physiology of the liver. The fact that jaundice of heart failure is especially apt to develop in the wake of pulmonary infarction supports this latter idea, and some investigators have found most patients with jaundice of heart disease have pulmonary infarction. It cannot be denied, however, that increased venous pressure plays a large part in many cases of liver damage in congestive failure, and that in some cases no degree of anoxemia can be shown.

At this point a few views on "cardiac cirrhosis" of the liver may be mentioned. It has long been debated whether cirrhosis of the liver is ever an outcome of long standing passive congestion of that organ due to heart failure. Altschule feels that diminished liver functions in itself is rarely severe enough to be of clinical importance. He states there is indicated the presence of damage which may lead to cirrhosis, but that few live long enough for this to take place. He further states that often on post mortem examination there is evidence of Laennec's cirrhosis rather than "cardiac" or central cirrhosis.

Some authors feel that chronic passive congestion never leads to the development of cirrhosis of the usual portal type. Bolton produced passive venous congestion experimentally and observed not only widespread degeneration of liver cells about the central hepatic veins, but an inflammatory infiltration of the portal canals leading to some degree of cirrhosis. Katzin, Waller and Blumgart had a large series of cases with 286 deaths due to congestive heart failure. In these 286 hepatic fibrosis was found in 95 (being three times as common as cirrhosis found in 1714 control necropsies). They found the worst cirrhosis in cases of the longest duration of failure. Central fibrosis was found as peculiar to the group of cardiac decompensation cases. In 7 of the cardiac cases the severe form of Lannec's portal cirrhosis was present. They considered central cirrhosis as resulting from growth of fibrous tissue about the central vein, due to the organization of hemorrhage or to metabolic changes occurring as a result of repeated or prolonged anoxemea. These investigators concluded as follows: "Cardiac cirrhosis signifying morphologic increase in connective tissue in the liver consequent to congestive failure is present in the majority of patients who have suffered from even mild congestive failure for 9 months or more; fibrosis may be central or portal or both. Clinical cardiac cirrhosis, signifying extreme fibrosis which clearly results from chronic passive congestion and which causes evidence of portal obstruction, does occur, but is rare. The clinical diagnosis of cardiac cirrhosis can be made only rarely, since it must be based on the findings of preponderant ascites, a small liver in spite of elevation of the venous pressure, and part-

icularily the presence of a palpable spleen. Not infrequently, however, the liver may be enlarged. In such cases, although increased fibrosis tissue is present and the surface of the liver is generally non-tender and sometimes irregular, the dilatation of the sinusoids leads to an increase in the size of the liver."

Boland and Willius also have published examples of "true cirrhosis" but they admit it is rare. Day and Armstrong summarize fibrosis in heart failure as being a "fibrosis affecting both the central and peripheral parts of the lobule, having its maximal incidence beneath the capsule and around the branches of the hepatic vein and accompanied by parenchymatous atrophy. Cellular increase either in the form of parenchymatous regeneration or interstitial inflammatory infiltration is remarkedly slight. There is always evidence of edema." From the above findings the latter investigators figured that edema may cause fibrosis by the direct production of connective tissue cells extracellularily out of an amphorous substrate. They suggested that fibrosis without cellular proliferation occurs when edema distends the tissue spaces and that mesenchymal cells are necessary only as a "diffusible stimulus" to evoke the formation of fibrils in the edema. Thus they explain the fibrotic changes on a purely mechanical basis.

At least it may be concluded that the majority of the investigators feel that there is such a thing as "cardiac cirrhosis", and more important that this may at times be a form of portal cirrhosis.

L. Renal Function

Fishberg states that impairment of renal function is evidenced by a diminution in the ability to form urine of high concentration, and that the high specific gravity of the urine that is produced by kidneys that are the seat of passive congestion is evidence that renal function is unimpaired. However Harrison feels that the slight elevation in the urea and non-protein nitrogen of the blood indicates a diminution of renal function. Fishberg and Altschule state that in the majority of cases the non-protein nitrogen and urea concentration of the blood are not elevated, and that the urea concentration test shows unimpaired kidney function in the high concentration of urea in the urine. Harrison does admit that in heart failure not complicated by renal disease there is only very slight functional impairment of the kidneys.

The urinary volume is diminished in passive congestion of the kidneys, and oliguria is a very early sign of cardiac decompensation. While the patient is up and about he passes little urine, but when he goes to bed at night he eliminates a correspondingly larger volume of urine, and consequently has to get up once or twice to pass urine. Fishberg explains this in part by the fact that there is dependent edema and thus during the day less water reaches the kidney for elimination, but at night when the patient is recumbent the venous engorgement of the lower extremities is reabsorbed into the blood stream and is eliminated as urine. Harrison states that nocturia may be due to diuretics, sleeplessness, or to irritation of the bladder by concentrated urine.

Another manifestation of oliguria in heart failure is the delay in the urinary elimination of ingested water. Thus one of the most valuable signs of improvement in a patient with heart failure is increased in the volume of urine. Fishberg found that the amount of urine eliminated in a given time by a subject who sits up is much less for a given amount of intake than by a patient who is recumbent.

Fishberg considers two factors as operating in the pathogenesis of cardiac oliguria. The first and most important is the extra-renal retention of water in the tissues so less is available to the kidneys for excretion. The second relatively unimportant factor is the renal factor of decrease in the capacity of the engorged kidney to excrete water (unimportant since the engorged kidneys are able to increase their output considerably as correspondingly more water is mobilized into the blood stream.

The urobilinogen content of the urine depends on the liver function and is increased when there is liver damage. Albumin and casts are common constituents in the urine in congestive failure. Urea and uric acid concentrations are found to be high. The acidity of the urine is usually high. Hematuria of a microscopic degree occurs whenever the kidneys are engorged. Gross blood usually signifies infarction of the kidney.

M. Mental Manifestations

Psychoneurotic symptoms concerning the heart are very common. It must not be forgotten that many patients have both organic cardiac

disease and cardiac neurosis. Fishberg states that transitory illusions and hallucinations are more common in heart failure than is generally thought. Insomnia and bad dreams often accompany cardiac failure. Syncope sometimes occurs.

On rare occasions severe psychoses result from heart failure. Worris states that the psychosis of heart failure is characterized by confusion, anxiety and delusions of persecution, and that the patients are often overtalkative and circumstantial, and that persecutory delusions are dependent on the degree of associated confusion. He feels that the fundamental cause is still unknown, but that the development of a psychosis in a cardiac patient is of grave prognostic significance.

Lewis considers that the mental reaction depends on the integration of the personality and constitutional factors other than and existing prior to, the cardiac disorder. Thus he feels that the serious physical illness of cardiac failure releases the mental expressions and disorganizes the previous integration of some cases, while in others it modifies the psychosis, if mental trouble is already in existence.

Michael also recognizes the rare incidence of psychoses in cardiac failure. In his series of cases reviewed (2293) he found that digitalis and other drugs were not found to cause psychoses, that syphilis accounted for some, that alcoholism accounted for some and arteriosclerosis for some. However he found no one series of causative factors which were not also observed in the 99% non-psychotic subjects treated

for cardiac failure.

Harrison believes cardiac psychosis is rare except in elderly arterio-sclerotic patients, or in subjects with extreme arterial anoxemia secondary to diseases of the lungs.

SUMMARY

We have considered in part, at least, the pathological physiology involved in chronic heart failure. A review of some of the prominent theories for the pathogenesis of the clinical manifestations of this condition has been presented. The "back-pressure" and "forward-failure" theories of heart failure have been compared to some degree. A consideration of experimental works in favor of various theories concerning the origin of the signs and symptoms of heart failure has not been presented in detail. Volumes have been written on this subject, and it has been our task to review rather briefly the literature stressing especially the Harrison's monograph edited in 1935 and the literature since that time.

The discussion has included physiological changes in other organs and tissues as well as the heart itself. Therapy, etiology, pathology, diagnosis and prognosis have not been discussed. The interdependence of the two ventricles of the heart has been noted, and the importance of ventricular imbalance has been mentioned. The idea of inefficiency of the heart rather than insufficiency of the heart is stressed.

CONCLUSIONS

Cardiac decompensation is associated with a large number of complexly interrelated bodily changes. There has been wide controversy as to the importance of these changes in the pathogenesis of the clinical manifestations of chronic cardiac failure. It would seem that due primarily to Harrison's brilliant work there is more proof in favor of the "back-pressure" theory than the "forward-failure" theory; the former is favored by most investigators and seems to be most closely confirmed by clinical findings. However it would seem that neither theory fits fully all the requirements needed in describing the phenomena of heart failure. Thus there is a wide field for further study and experimentation.

It appears that the understanding of heart failure is to a great degree a physiological problem, and that the understanding of the clinical phenomena constitutes a problem inseparable from the physiology of the heart and other organs. Thus a patient with congestive heart failure, when seen by the physician, is in a definite state not only of pathological but also of a profound and fluctuating physiological disturbance; it is only by a knowledge of the nature and course of these physiological phenomena that one is able to evalute the changing status of the patient.

It must be remembered that often the signs or symptoms of chronic congestive heart failure are due to a summation of the effect of submaximal changes in a multiplicity of complexly interrelated factors. The fact that each factor may vary greatly from patient to patient shows that

each patient is an individual problem and deserves consideration as such by the physician. When the clinician has reduced the problem which each case presents to its simplest terms, then he can synthesize the individual pathological physiological patterns and institute rational therapy aimed at correcting these changes. Often the basic pathology or etiology cannot be remedied, but the patient may be treated and helped by attacking the physiological problems present, as reducing the size and increasing the efficiency of the heart, lowering venous pressure, and controlling edema.

Thus life for the patient with chronic cardiac failure may become more enjoyable and useful because the physician understands the pathological physiology which such a case presents.

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