Cause and dynamics of heart failure in chronic valvular disease

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THE CAUSE AND DYNAMICS OF HEART FAILURE IN CHRONIC VALVULAR DISEASE

W. Harold Civin

Senior Thesis
Presented To
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Omaha 1940
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INTRODUCTION

The interest which one feels in a subject is heightened by his proximity to it. This nearness may be either as regards time or place. The subject of cardiac failure brings with it a peculiar fascination, in that the work on it is yet in its infancy. The mere fact that a subject is controversial shows that it is being developed. In the attempt to learn a little concerning this theme, I have gained a quick glance into the construction of the processes of scientific deduction. My presentation of this subject is, of course, colored by the views of those authors whose ideas seem to me to overbalance those of their opponents. I have attempted to be impartial and in most cases have tried to set down a little concerning all contentions. The last chapter in this topic of failure is a long way from being written. Nevertheless, the small peek which I have been afforded into the mechanism of decompensation will cause me to follow this with keen interest. As more and more of the maze is untangled, I shall be desirous of seeing how close the truths are to the theories of the pioneers in the field. For, at present to me, their work appears on the verge of solving the problem of cardiac fatigue. I also hope that if the situation arises, I may
HISTORY

Those episodes in the history of medicine which deal with the circulatory system to a great extent antedate the epochal work of Sir William Harvey, although it is generally agreed that it was his exposition of the manner of the circulation of the blood which gave work in this field its much needed impetus for advancement.

Prehistoric man knew of the spurting of cut arteries. There is proof in the Edwin Smith Surgical Papyrus (39) that Imhotep, possibly the first surgeon of history knew that the pulse is an index of the heart. In 250 B.C. Hemophilus, an Egyptian physician, counted the pulse and associated it with the action of the heart. Erasistratus, an Alexandrian contemporary of the above mentioned, is stated to have been on the brink of the discovery of the circulation. This remarkable individual studied the chordae tendinae, the auricles, and the valves of the heart, and even advanced the now widely accepted fact that the heart functions as a pump. He labored, however, under the misconception that the blood was conveyed to the heart by arteries and returned to the periphery by the veins.

The Greek physicians had a great number of misconceptions concerning the human vascular apparatus. From this realm of uncertainty and bad logic the world was to some
extent extricated by the work of Aristotle of Stagira, who described the gross anatomical relations of the heart and noted the movement of the fetal cardiac mechanism. Four hundred years following him came the most remarkable of all ancient physicians and physiologists, Galen. It was he who demonstrated the motor power of the heart by showing that blood pulsates between that organ and a ligated artery, but not beyond this. He also showed that an excised heart continued its beating after removal from the body and further demonstrated that the fluid contained in the arterial tree was blood. With all his remarkable work, Galen nevertheless foisted upon an unsuspecting world a series of misconceptions which he came about honestly. It must be remembered that his experiments were performed on dogs, monkeys, and pigs, and the fact that his edicts were so slavishly followed was no fault of his own.\(^{39}\), \(^{40}\).

Following Galen came that period which was free from any advance whatsoever in the field of medicine, the Dark Ages.

The Light of Medical Learning was once more uncovered and fittingly perhaps by Harvey's historic work. Preceding this, however, that versatile Italian, Leonardo da Vinci, in the late fifteenth and early sixteenth centuries developed a creditable concept of valvular action in the
heart, and he quite accurately reproduced the anatomy of this organ on paper. His work on the function of the valves was independently matched by Berengar of Carpi. Vesalius attacked many of the anatomical concepts of Galen, but was more hesitant about opposing any of his physiological usages. During the latter part of his career he did, however, disagree with the idea that blood passed from one ventricle to the other, one of Galen's statements, as he could find no channel to permit such a passage. Servetus (1509-1553) developed the course of the pulmonary circulation. In 1616 Sir William Harvey, in his Lumleian Lecture before the Royal College of Physicians, ventured to develop his views on the circulation of the blood. It was not until 1628 when he published his quarto volume of seventy-two pages entitled, "Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus", that first his ideas of circulation began to be of wide note. About one century later Stephen Hales first measured the blood pressure. (39), (40).

In the seventeenth and eighteenth centuries, pathological work came to the foreground. Giovanni Maria Lancisi noted hypertrophy and dilatation of the heart as causes of sudden death, first described valvular vegetations, and classified diseases of the heart. He was the first to describe luetic affection of the heart. Morgagni
described mitral disease, and Baille pointed out the relationship of rheumatic fever to heart disease. In 1806 Jean Nicholas Corvisart wrote "Essay on Diseases and Organic Lesions of the Heart and Great Vessels" in which he described active and passive heart enlargement. In 1810 Wells called attention to the cardiac complication of heart failure. In 1811 Bertin introduced the terms eccentric hypertrophy for hypertrophy without dilatation and concentric hypertrophy for the situation wherein dilatation was also present. In 1832 Hope first advanced the "Backward Pressure Theory of Cardiac Failure" and his work will be referred to later on in discussion of the dynamics of failure (65). Also in 1832 Corrigan described the pathology of Luetic Heart Disease with Aortic Regurgitation (20). He described many of the clinical manifestations. In 1839 Johannes Evangelista Purkinje demonstrated the fibres which bear his name. Robert Remak, some five years later discovered the intrinsic nerve ganglia of the heart. Some time after this Gaskell worked in the heart with ligatures, stimulated sectioned hearts, and developed many of the physiological conceptions of cardiology. He worked out the sinus origin of the beat and showed the effect of the nerves on the heart. The bundle of His was discovered in the latter part of the nineteenth century. Tawara
described the A-V node. Bouillard showed digitalis to be the opium of the heart (39), (40).

In 1906, Einthoven developed the principle of the electocardiograph. Since then work on the various phases of heart afflictions has progressed rapidly.

This will serve to lay the foundation for the rest of this paper. In the succeeding pages the recent work pertaining to the subject of this paper and limited by the scope of these pages will be alluded to.
DEFINITIONS

To make for clarity it will be necessary to define some of the terms in accordance with their use in this paper.

Congestive heart failure, heart failure, and cardiac decompensation are used synonymously. They denote the condition of passive engorgement, occurring as a result of cardiac disease. The engorgement may be in the systemic, the pulmonary, or both circulations.

Cardiac output designates the volume of blood expelled by either ventricle, in a unit time, through a complete cross-section of the vascular bed, i.e., either the pulmonary artery or the aorta proximal to the orifices of the coronary arteries. Fishberg uses the term "minute volume of the circulation" and states that in the absence of regurgitation the cardiac output equals the minute volume. In this paper we will use cardiac output and minute volume interchangeably; since while Fishberg has perhaps more exactness in his definition, Harrison uses cardiac output in the same sense and can claim priority in much of the work in this field.

The Fick principle points out that all the blood pumped by the right ventricle traverses the pulmonary capillaries where gaseous exchange occurs. If the amount of oxygen absorbed per minute be divided by the difference in oxygen
be able in some small way to contribute in this line.

The study in the work of cardiac failure originated in the realm of the pathologists. The tools of the pathological worker were the first to be developed to an extent wherein there could be any extensive searching done upon the heart. Just as pathological work reached an impasse; the physiologist came to the fore. When the physiological experimenters had carried the "torch of truth" forward for a great distance, the biological chemist took up his share of the burden and began seeking the unknown elements in the riddle of failure. Thus, with the cooperation of numerous workers in various fields, progress has been made to our present stage of knowledge of the subject.

This paper will first give a brief resume of the history concerning the heart and related factors. To establish a common meeting ground, there will next be a section of definitions. Following this will be presented some pertinent facts concerning chronic valvular disease. The pathological findings in failure will be given consideration. The conception of hypertrophy and dilatation is discussed. Then fatigue in enlarged hearts is elaborated upon. The altered dynamics in a fatigued heart is developed, and this is followed by a brief summary. The entire paper is an attempt to elucidate on what I have learned about cardiac failure.

With this brief prologue, the body of this paper is entered upon.
content between a liter of blood in the pulmonary artery and that in the pulmonary veins, the result will be the number of liters of blood passing through the lungs in that minute. Thus, if the arterial blood contains 200 c.c. of oxygen per liter, the mixed venous blood 150 c.c. per liter, and 250 c.c. of oxygen are absorbed in a minute; the volume of blood passing through the lungs is \( \frac{250 - 150}{200} \times 5 \) liters. Similar calculations can be made for carbon dioxide.

Circulation rate (circulatory rate) refers to the speed with which the blood travels through the vascular tree. In the body of this work, the circulation time as well as the rate will be mentioned. The time varies inversely with the rate.

Cardiac fatigue is the condition wherein the amount of work able to be done is lessened as a result of physico-chemical changes, and which ultimately produces the syndrome of failure.
General Considerations of Chronic Valvular Disease

It is perhaps best to classify chronic valvular disease under five headings as follows:

(1) Rheumatic Valvular Disease
(2) Luetic Valvular Disease
(3) Subacute or Chronic Bacterial Endocarditis
(4) Arteriosclerotic or Calcareous Valvular Disease
(5) Congenital Affections of the Valves

Although no generalizations can be made, there are certain periods of life wherein each of the above classes are predominantly found. The congenital type is present, of course, at birth. Most of the severer of the lesions are incompatible with existence. During childhood, adolescence, and early adulthood, the rheumatic variety of disease comes into ascendancy. Bacterial endocarditis, subacute or chronic in course, tends to parallel the age incidence of the rheumatic affliction and to extend a little beyond this period. Luetic heart disease is found in increased frequency in the forties and fifties. Arteriosclerotic heart disease tends toward the oldest age group.

It is not within the scope of this paper to discuss the pathology of the various types of cardiac valvular disease. Suffice it to say that in any of these, the
ultimate change as a result of valvular injury is a stenosis, an insufficiency, or both. It must be stated that although the results of the valve injuries are similar, the pathological pictures of these lesions differ.

Chronic valvular disease of congenital origin consists almost entirely of pulmonic stenosis. This is often associated with defects of other parts of the heart. Of exceedingly rare occurrence are congenital pulmonic regurgitation, and mitral, aortic, or tricuspid stenosis (1). A further congenital factor is evidenced in the fact that bicuspid aortic valves are peculiarly susceptible to subacute bacterial endocarditis.

Rheumatic heart disease is not merely a valvular affliction, but is in reality a pancarditis affecting all the fibrous tissue of the heart (7),(34). Therefore there is an added factor of injury to the heart aside from an inefficiency (stenosis or insufficiency) of the valve. This produces a less efficient heart, of course. As a result of this chronic inflammation, there may be a dilatation of the orificial ring which further increases any insufficiency (66). Mitral stenosis was generally believed to be the most common valvular lesion in rheumatic disease of the heart. A great many authorities now agree that there is a preceding and concomitant
regurgitation often accompanying this. The same sort of pathology which makes for a stenosis of the mitral valve, because of difference in structure, produces a regurgitation of the aortic valve. At times there is an accompanying stenosis which tends to be found more in individuals who have reached an older age group (13). Pure cases of tricuspid involvement are very rare, and these are exceeded in scarcity by rheumatic involvement of the pulmonic valve solely. The idea has been advanced that one always finds mitral involvement in rheumatic heart disease although clinically there may be no sign of this (7).

It is a clinical observation that patients with acute endocarditis seldom decompensate. This fact may be explained, in part, by the supposition that most of them do not live long enough to develop failure. This cannot be the only explanation for it has been found that in the stage of the disease wherein there are no bacteria in the blood, cardiac failure does develop (82).

Syphilitic disease of the valves really commences as an aortitis which ultimately extends to involve the aortic semilunars and may extend up as far as the anterior crisp of the mitral valve. This process produces a regurgitation (7), but not a stiffening of sufficient degree to bring about a stenosis of the aortic valve (13).
A most important complication of luetic aortitis is a narrowing of the mouths of the coronary arteries (7), (18), (34).

Arteriosclerotic valve disease is an almost constant accompaniment of arteriosclerosis of the aorta. This usually establishes itself as a regurgitation. Mitral valve affection in such a condition is a recognized entity (34). Hypertension is often an associated factor with arteriosclerosis.

One must admit that it is neither the valve lesion or the pathological process which is the sole determinant as to the duration of the condition before decompensation sets in, but these are factors. Christian (13) in an attempt to correlate the various factors in decompensation after valve disease states that important regulators are the physical activity of the patient, the degree of myocardial injury, and the mechanical effect of changes in the heart valve on the efficiency of the heart. If more than one valve is involved the progression of decompensation is more rapid. Diseased mitral valves seem to lead to decompensation more rapidly than abnormal aortics, and the insufficiency of the heart develops earlier in life. Aortic stenosis is a very slowly advancing lesion. Patients with this disease, however, die after the first period of marked decompensation. Pure aortic insufficiency of rheumatic
origin has a good prognosis even with the onset of failure. Myocardial involvement takes place to a greater extent in mitral than in aortic affection by the rheumatic virus. Pericarditis speeds up the process of decompensation and is found more often with mitral disease. In summary, the ascending order of functional defect is mitral stenosis, mitral insufficiency, aortic stenosis, mitral stenosis and mitral insufficiency, mitral and aortic stenosis and insufficiency. An interesting point is that aortic stenosis superimposed on mitral insufficiency is supposedly of benefit.

In a study of the mode of death in chronic valvular disease, Willius (125), in a study of ninety one cases of valvular disease, found that sixty eight died of cardiac failure. In general, this is the way a patient with valvular disease is apt to depart from this "vale of tears", if nothing else intervenes. (124).
Pathological Findings in Failure

Although in the minority of cases there are pathological changes which are adequate to explain failure, there are, nevertheless, a number of these. Von Haam (115) states that perhaps the heart is unable to withstand as much change as other organs. This, however, does not seem likely, as many hearts with more changes than those with congestive failure seem to have been capable.

Most cases of heart failure show histologically an acute or chronic myocarditis (34). There occur vacuolar, granular, fatty, or other regressive changes in the muscle fibres with parallel nuclear changes.

According to Fishberg (34) most investigators agree that the above changes are insufficient to explain failure.

Stokes (112) discusses the possibility of fatty change in the heart as one of the factors in cardiac failure. Recent investigators have demonstrated that even in health appropriate stains reveal the presence of finely divided fat in heart muscle. Fishberg (34) believes that the lipid bespeaks of changes in metabolism which are in themselves probably not deleterious. The droplets present between fibrillae wherein the contractile power of the heart resides. There appears to be no alteration in the nuclei and fibrillae. As proof of the proposition that
the above is not a sufficient factor to excite failure, is the finding that in metabolic disturbances, in anemia, and in intoxications, there is a greater amount of fat accumulation without any inadequacy of function. Steatosis of the myocardium is rarely if ever the primary cause of the failure. It is rather to be considered that lipoidal change is a result rather than an incitant of failure. The uneven fat distribution might be an expression of circulatory disturbance in the heart.

Cloudy swelling following deposition of albuminous granules is a common discovery in intoxications, such as bronchopneumonia, accompanying cardiac failure. The value of this finding is negated by the fact that severe cloudy swelling is found without failure, and contrariwise, the latter is present in absence of the former (34). Boyd (7) believes that cloudy swelling in many cases is a post mortem artefact.

The appearance of vacuoles containing fluid in the sarcoplasm is a rather constant finding, but their distributions is not extensive. Many authors regard them as a consequence of the venous stasis present, rather than an etiological factor of failure. Rarely one finds widespread necrosis of heart muscle but there is always an infection or intoxication underlying. In rheumatic fever there is present focal necrosis in heart muscle as a
result of minute thromboses. The necrotic areas are usually insufficient to account for failure.

Another curious pathological phenomenon found in examination of the heart is brown atrophy. With senility the heart becomes atrophic and of a dark brown coloration. In starvation or disease there is diminution in the weight of the cardiac musculature paralleling that occurring in the skeletal myotomes. Diminution in the work required of a chamber of the heart leads to selective atrophy of that chamber. Clawson (17) states, for example, that with overwork of the right ventricle as compared with the left, the latter is atrophic and undergoes an increased fibrosis. The atrophy of the heart is brought about by decrease in length and thickness of the individual muscle fibres. Karsner, Saphir, and Todd (68) state that the fibres tend to diminish to a uniform size. Pathological studies indicate that the fibres of the conduction system do not participate in the atrophic process. The pigmentation of the myocardium is the result of the microscopical deposition of pigment granules at the poles of the nuclei, and when marked tends to be interspersed among the fibrillae. The pigmentation is in itself merely an accentuation of the physiological appearance of pigment granules which commences in the first decade of life. The pigment is a lipochrome which fails to stain for iron.
It is said to result from deficient removal of the katabolic products of the cell. Atrophy of the heart is undoubtedly associated with a diminished capacity for functioning of the fiber, especially if one holds to the work theory of hypertrophy (48), for a basic governor of the contractile strength of a muscle fiber is its length and cross-sectional area (95). It is countered that often when one finds brown atrophy there is a diminished demand on the chamber. This does not alter the fact that apparently the functional capacity is lessened.

The most common form of myocarditis is the Aschoff nodule. This may appear as a tiny white speck under the endocardium. Microscopically there is a center of necrotic material, then a layer of large multinucleated basophilic epithelioid cells (Aschoff cells), then a layer in which lymphocytes and plasma cells predominate, and externally a proliferation of fibroblasts with subsequent fibrosis. The lesions are those of rheumatic fever and are predominantly interstitial and perivascular. The healing of these areas result in numerous scars which rarely appear extensive enough so that cardiac failure may be directly assigned to them.

There is a condition of heart muscle fibres where they are found to be split. If the splitting is along the general course of the fiber, the condition is
designated as fragmentation. Segmentation is the appellation denoting the condition wherein the splitting is along the intercalated disks. Karsner, Saphir, and Todd (68) found no such a thing to occur in atrophic hearts, producing the atrophy. As a matter of fact it is now generally agreed that if such things occur, and segmentation is of questionable incidence, they are agonal phenomena (7) (34). The phenomena appear to be more extensive with advancing age.

In summary, let us consider the work of Clawson (17) in his study of 429 hearts at autopsy. He found that acute or chronic myocarditis, either localized or diffuse, is a common condition in the myocardium in acute and recurrent rheumatic endocarditis, in subacute bacterial endocarditis, and in old valvular defects. Proliferative or exudative affection of the myocardium is a rarity in luetic aortitis (18). Clawson also concluded that the extent of myocardial injury as shown by anatomical changes seldom appears sufficient to produce failure. So called myocarditis is usually a condition of the myocardium, probably fatigue, which is not anatomically manifest.
Although as has previously been mentioned the findings pathologically in heart failure are often variable and apparently inconsequential, there are two constant findings in a heart failing after a period of valvular disease. These findings are hypertrophy and dilatation. The significance of these findings is even at the present time one of the most debatable elements of this controversial subject.

Two chief schools of thought have grown up concerning these manifestations. One which had faded into obscurity is once more coming to the fore. This group holds that a dilated and hypertrophied heart is one which is not as efficient as normal, and which has undergone a change due to inclement factors acting upon the heart (13), (30), (32), (67), (103), (116), (118). Diametrically opposed to this theory are the members of the school who maintain that hypertrophy is a response to increased tension, work, or nourishment which allows the heart to accomplish more than it would otherwise be capable of doing (8), (29), (63), (77), (95), (123). There are some advocates who state that hypertrophy is of value but hold that dilatation is importune (80).
In general, however, it is believed that dilatation and hypertrophy are more or less parallel responses, and that the former is both a precursor and successor to the latter.

Those who support the first school includes, according to Krehl (78), Albrecht who held that a chronic myocarditis is the forerunner of all dilatation. He is supported in the injury theory by Eyster et al (30), (32), who reached this conclusion after producing experimental valvular lesions in dogs. They found that the first result of aortic regurgitation and stenosis was a dilatation of the heart which passed off by the tenth day after the production of the lesion. Then there was hypertrophy until the eightieth day. The size of the dogs' hearts were studied by x-ray until they were killed. Dogs killed during the stage of dilatation had hearts showing extensive change. There was stretching and thinning of the myocardial wall. Microscopically the heart showed hydropic degeneration. Dogs killed after hypertrophy took place showed no abnormal change except for increased fiber thickness. Eyster concludes that stretching of the heart following overload was the cause of hypertrophy and not work per se. He based his conclusion on the fact that when he removed the bands by which he produced stenosis after several days, the entire process
was gone through, although the work of the heart had been diminished. Lewis and Drury (81) suggest that the enlargement found in patients with arterio-venous fistulae (63) and aortic insufficiency might be due to deficient circulation as a consequence of reduced diastolic pressure which is a concomitant of these conditions.

Wiggers (118) believes that dilatation of the heart is the cause of insufficiency (94). He is uncertain as to whether or not hypertrophy is inauspicious. Christian (12), in a purely speculative article influenced by his years of experience, states that the normal response of muscle to work is hypertrophy. He ponders the possibility that a cavity surrounded by muscle may convert hypertrophy into a malicious condition. One of the most important arguments in favor of the above theory of the bad effects of hypertrophy is the work of Shipley, Shipley, and Wearn (103). They found that hypertrophy is associated with an increase in the cross-sectional area of the individual fibres in rabbit hearts. Previous work had proved that in the normal heart there is approximately one capillary per fibre. This relationship remained the same in the hypertrophic heart, but here the amount of fibre per capillary was increased; oxygen had farther to diffuse through the fiber, and this could affect the nourishment of the heart. Wearn (116) found the above relationships, as far as
capillaries and fibres were concerned, true for humans.

A small but important group of investigators are those who hold that increased work is a factor in hypertrophy of the heart, but that this must be accompanied by other factors in order for this to take place. Representative of this group is no less an authority than Lewis, who believes (80) that mechanical factors are not the only ones in hypertrophy. Davis and Blumgart (25) came to essentially the same conclusion. After experimentally producing aortic insufficiency in dogs, they discovered the hearts to be hypertrophied, but nowhere approximating the degree found clinically. Also they noticed no relationship between the degree of obstruction producing the stenosis and the amount of hypertrophy. They speculate that other factors contributing may be elevated metabolism, physical exertion, anemia, or defective nutrition of the heart. It is seen that the last two are in direct contradiction to increased nutrition which is given as a cause of hypertrophy (63), (81).

Among the initial proponents for the proposition that hypertrophy is the means by which the heart is able to accomplish greater work and is not dependent on injury were Krehl, Aschoff, and Martius. The latter two are quoted by Krehl (78). Starling in his famous "Law of
the Heart" discussed by Williams and Horner (123) and Patterson, Piper, and Starling (95) in the work which lead to the formulation of this noted precept, support the idea that dilatation and hypertrophy is an asset in the labor of the heart. The Broadbents (8) also concur. As has previously been stated the increased nourishment associated with increased work in arterio-venous fistulae is believed to be a determinant (63). Evans and Matsuoka (29) state that dilatation occurs from increased work. It may also follow exhaustion with decreased metabolism according to these workers. Nemet and Gross (93) believe that increased initial fiber tension rather than an elevated quota of work is the stimulus for cardiac hypertrophy. This is essentially what has been held in the previously mentioned "Law of the Heart (95) (123)". It is not the purpose of this paper to argue as to whether increased work per se or increased tension is the essential factor. Increased volume flow may be brought about through the medium of a raised tension. This does not deny the proposition that through hypertrophy increased work by the heart may be accomplished. Nemet and Gross (93) state further that a lowered blood supply and severe muscle damage produce a loss of
contractility, and this may lead to failure without hypertrophy. It would seem therefore that hypertrophy may be desirable in certain circumstances. The authors (93) do add that ultimately the hypertrophied fibres may lose their contractility, but this usually is a matter of time (34). Harrison (47), (48), (49) believes that hypertrophy is a response to increased work continuing over a period of time. He (48), (49) believes this since athletes apparently getting sufficient rest between strain are not found to get hypertrophy; according to his idea because then the physico-chemical factors tending to produce this are reversed. He (48), (49) quotes the work of Kulbs producing hypertrophy by increased continued work in dogs as an argument for the work hypothesis of hypertrophy. The idea is that hypertrophy is a response to increased work and may be of value if certain undesirable situations are not present. This will be discussed later under cardiac fatigue.

Perhaps it would not be amiss to treat somewhat with the relationship of dilatation and hypertrophy in chronic valvular disease. The development of insufficiency in a valve causes a reflux of blood into the chamber immediately behind the valve as that chamber goes into a state of relaxation and its pressure is exceeded by the column of blood ahead of it, with no barrier to the regurgitation (119), (120), (121). The largest amount of the research
work on the dynamics of regurgitation has been done on the aortic and mitral valves; those most frequently affected in the process of regurgitation (86), (120), (121).

Study on the aortic valve shows that after they should have approximated, in insufficiency, there is a regurgitation of blood which in small leaks is distributed throughout diastole, but in large leaks has most of the reflux occurring before the auriculo-ventricular valves open (121). Similar findings have been advanced for the mitral valve in regurgitation (70). In the aortic injury, Wiggers (119) found in dogs that the reflux amounts to 50-60% of the discharge. There is then added to the usual amount of flow from the auricle, the refluxed amount from the aorta. The fibres of the ventricle are stretched and a greater discharge of blood into the aorta is the result. This is aided by an increased ejection time (119), (70).

Ultimately there is established an equilibrium whereby the output is equal to that previously, in spite of the regurgitation. Wiggers holds (119) that about eighty per cent of the reflux after incompetency of the valves is established artificially is due to prevention of auricular filling. This is questioned by Fishberg (34) since patients show no evidence of pulmonary engorgement
which the rise in auricular pressure would necessitate. Furthermore Wiggers' work was on dogs, and there is no report on how long he followed them. The establishment of equilibrium might soon have taken place. The mechanics of dilatation in any regurgitation is essentially the same as above in all probability.

In stenosis the process is a little different, and most of the work has been done on mitral and aortic lesions of this sort (70), (73). As a result of an impediment to the flow in the form of a less resilient mitral valve, there is a damming back of blood in the left auricle and stretching of the muscle. There results a rise in the pressure head of this chamber. There is an increase in the magnitude of auricular activity due to stretching of the muscle. Prolongation of the time of diastolic filling is brought about as the heart slows by methods as yet undetermined. An increased aspirating action of the left ventricle is evidenced by the steeper rise of diastolic portion of the intraventricular pressure curve. These mechanisms serve to produce a normal output in spite of the increased resistance of the valve. There is therefore a dilatation of the
auricle, and if these mechanisms per se maintain the volume of ventricular filling, the effects of mitral stenosis are not great. Straub, quoted by Fishberg (34), has shown that in faultlessly compensated mitral stenosis, pulmonary engorgement is confined to the venous half of the pulmonary circuit, and there are no manifestations which are clinically recognized as failure.

The process of dilatation is probably very similar in all types of stenosis, and has been shown to be quite so in aortic stenosis. True the dynamics are a little different (119).

It is now with establishment of dilatation that the greatest gap in our knowledge occurs. Just what process converts dilatation into hypertrophy is not known, but a continuous dilatation over a long period brings about hypertrophy. According to Fishberg (34), most authors now believe that all hypertrophy is preceded by dilatation, even though it is not demonstrable clinically. After one chamber enlarges, the one immediately behind it tends to go through the same processes, if the single dilated and hypertrophied chamber is still unable to carry on the work. This may go on until the whole heart is hypertrophied (34), (94). When the entire heart becomes inefficient, it may dilate still further, and venous congestion ensues.
The Development of Fatigue in Enlarged Hearts

With the occurrence of failure unable to be accounted for by pathological findings, other mechanisms have been advanced to explain its occurrence.

Eppinger and his associates developed a theory of failure, according to Fishberg (34), based on the fact that metabolic changes produce failure. They believe that there is a deficient resynthesis of lactic acid to glycogen in the muscles of the body. In an attempt to compensate for this, the cardiac output is increased. As the work of the heart increases failure ensues. They believe it to be due to an actual increased output.

Fishberg (34) believes this theory to be invalid since the cardiac output in failure is seldom increased. Moreover the increase in lactic acid is more probably explained as a result of failure, than as its cause. Sudden excessive work may initiate failure, but the heart is unable to accomplish this work. It does not fail, as the above theory states, after elevating its output. We must, therefore, look along other lines for the cause of failure.

The dilated and hypertrophied heart must be furnished with a sufficient blood supply to maintain its nourishment. Fatigue of the myocardium and subsequent cardiac failure
may be precipitated either through an overload on the heart, or by the inability of the heart to perform its work properly, what Harrison calls heart inefficiency.

We therefore come to the consideration of the manner of deficient metabolism of the hypertrophied heart. Inadequate blood flow leading to insufficient nourishment with the development of fatigue is a phenomenon of all muscle. This may be brought about in two ways.

There is an absolute decrease in blood supply to the heart in arteriosclerosis of the coronary lumina. This latter is almost a constant accompaniment of arteriosclerotic valvular disease. This is also often the mechanism in syphilitic valvular disease since the mouths of the coronary vessels are often involved. It must be remembered that we are speaking of gradual failure in valvular disease and not of sudden occlusions. Diminution of the blood supply in luetic valvular disease and in aortic regurgitation of rheumatic origin is also effected by the diminution in diastolic pressure with inadequacy of coronary flow. This may account for the sudden deaths in aortic regurgitation (86).

Absolute inadequacy may not be the factor in most cases of decompensation following long standing valvular
lesions of the heart, but relative inadequacy of blood supply might exist. Let us discuss this further.

Patients with congestive failure often have an increased pulse rate. The obvious advantage of such an increase is that it permits the heart to pump a given amount of blood with a lesser degree of dilatation, and hence, to lower somewhat the venous pressure. There is a disadvantage to this, however, in that (48), (49) it means that more energy must be expanded per minute to open the valves, and this energy cannot be appropriated in propulsion of blood. Therefore, a given minute output can be accomplished more efficiently with a slow (91) than with a rapid rate. This has been demonstrated by Evans and Matsuoka (29) and Starling and Visscher (106). The latter investigators found in an isolated heart preparation that, at the same diastolic length of fibre, a heart uses more oxygen per unit time when contracting at a high rate, than at a low one.

Harrison, Ashman, Larsen (50) performed a remarkable series of observations on the connection between heart rate and the thickness of heart muscle fibres. In general, their findings with various species indicated that the thicker the normal fiber, the slower the optimum heart rate of the animal.

A. V. Hill (62) has demonstrated that the rate of oxygen diffusion varies as the square of the distance
diffused. This should be borne in mind as it plays a part in what is to be developed.

Clark et al (14), (15), (16) have demonstrated that the mammalian heart cannot operate in the face of any oxygen debt. There must therefore be available to the heart, a sufficient supply of oxygen. The restoration of the physico-chemical process needed to promote contraction takes place during diastole and necessitates oxygen (114). Therefore, the recovery time of the heart is related to the duration of diastole. When the heart speeds up moderately, the diastolic period is shortened, and in this way a sufficient time is allowed for expulsion during systole (49). As the rate further increases, however, systole is also curtailed. Thus, as diastole shortens, the recovery period may become insufficient, and failure may ensue.

The normal heart fiber of an adult averages 16.2 mm. according to Harrison, Ashman, and Lassen (50). There is according to Wearm (116), one capillary per fiber in the human heart. Each capillary supplies the adjacent halves of the two fibres on either side. As a fiber becomes thicker, the number of capillaries remain the same. The distance supplied by each capillary becomes greater. The mean head of pressure, the capillary oxygen tension, remains the same. As the oxygen diffuses through
the fiber, the head of pressure diminishes, and hence the oxygen diffuses more rapidly through the outermost than through the central portion of the fiber. One would expect an increased period necessitated for recovery. It follows then, that the thicker the fibers, apparently the slower the optimum rate. The average length of diastole in the normal heart is .56 second. If the thickness of fibres is 24.4 mm. (the average thickness for fibres in hearts with hypertrophy without failure), the time for recovery of the heart may be found by the formula

\[ \frac{0.56 \times \left(\frac{12.2}{8.1}\right)^2}{2} \]

The formula may be explained as follows. If we consider .56 second as the optimum time for diffusion through 8.1 mm. (since a fibre of 16.2 mm. is only half supplied by its capillary, and the adjacent halves of two fibres are supplied simultaneously), then by Hill's work (62), the greater duration for oxygen diffusion in a 24.4 mm. fiber is \( \frac{(12.2)^2}{(8.1)^2} \) of what is for a normal 8.1 mm. fiber. It would then take that much of .56 second for the oxygen to diffuse through the thicker fiber. The result is 1.26 second which gives a rate of thirty-eight per minute if we assume a constant systole time of .3 second. Using a similar calculation for fibres of 31.8 mm. thickness, which (30) has been found to be the average thickness of the heart in failure, we find the optimum rate to be twenty-three per minute. Thus, we may have an absolute or relative
The calculations tell of optimal rate of the heart, if we assume the average length of diastole to be optimal. Clinical experience presents evidence that even the normal heart will not tolerate extremely rapid rates for an extended period. Harrison (48), (49) believes it is safe to assume that decompensation will develop in a normal heart if it beats continuously at rates more than 150 for an indefinite period of time. At such rapid rates the duration of systole is lessened to .2 second, so diastole is also .2 second. Using calculations as we did previously, we can calculate that in moderately enlarged hearts, failure will develop when diastole equals $\frac{.2 \times (12.2)^2}{(8.1)^2}$ or .45 second. This amounts to a rate of eighty per minute. In still larger hearts, failure will develop at correspondingly lower rates.

Krogh (79) developed the work on oxygen diffusion from a capillary. Using this complicated formula, to which the reader is referred if he is interested, Harrison (48), (49) calculated the difference in tension between two points, necessary for oxygen diffusion. He found that the oxygen tension difference necessary to cause diffusion through a normal fiber is 1.2 mm. of mercury. In fibers of 24.2 mm. thickness, the tension difference should be 24 mm. of mercury. The oxygen tension of the venous blood is in the general region of 30 mm. of mercury. It can be
seen that this is far in excess of the tension difference necessary for diffusion through a normal fibre, but only slightly so for a fiber which is moderately hypertrophic. As the fiber becomes still larger, the normal oxygen tension is unable to supply it completely during recovery. These findings are calculated for a duration of diastole of .5 second with a rate of eighty per minute. If the rate varies, the tension differences vary, but the proposition holds that the greater the fiber and the faster the rate, the greater the tension difference must be to effect diffusion throughout the fiber. Therefore, we see that while hypertrophy may be a response to increased work; if it continues, it soon grows away from its blood supply, i.e. the heart is apparently unable to get sufficient oxygen as it hypertrophies, and its work increases. In this way we get a relative inadequacy. The fatigued heart is inefficient and produces failure.

In valvular disease the heart tends to do more work; it needs more nourishment. As failure comes on, it dilates still further, and its blood supply becomes yet more deficient since its oxygen consumption seems to depend on diastolic volume (15), (16). Starling and Visscher (106), on the heart lung preparation, found that the heart in failure necessitates more oxygen to
perform the same amount of work. Moe and Visscher (92), Peters and Visscher (96), and others (57) have verified these observations. An apparent controversy has arisen in that Katz and his co-workers (69), (71), (72) have stated that the mechanical efficiency of the heart is not diminished in failure. As far as the above ideology is concerned, it does not matter which investigators are correct. The reason is this: the latter also state that the oxygen consumption is lessened, as is the work done by the heart. Therefore, we still arrive at the same conclusion; more oxygen and consequently more blood is required by the failing heart. It is unable to get this (26).

The above explanations involve a great deal of theory, but Harrison (48), (49) and Fishberg (34) believe that clinical and pathological observations bear them out. Kountz (77) found a lowered coronary flow per gram of muscle in the hearts of individuals dying in failure. This certainly may be in favor of an inadequacy. Furthermore, we will now mention factors which may initiate decompensation. These are all such that increased work by the heart, would be demanded.

Precipitating Causes of Cardiac Failure

Harrison (48), (49) states that the various disease processes which constitute the underlying causes of cardiac disease will usually progress, and if left to their
The ultimate conclusion will terminate in cardiac failure, provided that no other condition intervenes. The rate of progression of the condition is ordinarily quite slow, and often there is able to found a precipitating factor.

Infection is one of the most important of the initiating causes of cardiac failure. Eighteen out of fifty-five patients in Sodeman and Burch's (108) series had an infectious basis for the initiation of cardiac decompensation, of these upper respiratory infections were found to be a factor in fifteen cases.

Harrison lists exertion as the factor bringing about the initial break in compensation, occasionally. Sodeman and Burch, on the other hand, found this to be the cause more often than any other single condition.

Pregnancy has been definitely related etiologically to the initial decompensation. Most agree (34), (108), (48), (49) that the work of the circulatory system is increased during pregnancy. Five cases were reported in Sodeman and Burch's series.

The role of obesity is much discussed, and it has been decided that an obese individual markedly increases his chance of cardiac inefficiency, if he has chronic valvular disease. An overweight patient has a greater oxygen consumption for a given amount of work, and this is more apt to tax the heart. It is said (87a) that an
increase of one pound of fat adds five-sixths of a mile of blood vessels. If this be true, the heart of an individual who is thirty pounds overweight must propel blood through twenty-five extra miles. The work of the heart is markedly raised. Clinicians believe that it is best to keep an individual somewhat under average weight.

It is difficult to evaluate the factor of anemia in the production of failure because of the fact that there is often a superposition of other things upon this. Cardiac output is increased in anemia (43).

The relationship of tachycardia to heart failure has already been discussed. Abnormal rhythms tend to initiate failure, either through increased rate or through a pulse deficit (48), (49), (3).

Emotional strain and psychic trauma may increase the cardiac output as has been demonstrated by Grollman (43). Surgical shock, coitus, sodden elevation of blood pressure, heavy meals, and alcoholism are also listed by Sodeman and Burch (105). Perhaps undernutrition may be an accessory factor if added to any of the above, by decreasing the nourishment of the heart. All the factors mentioned increase the work of the heart, and with decreased nourishment of the myocardium may bring on fatigue.

If we accept the theorem that possibly cardiac failure has its inception in deficiency of oxygen to the heart,
let us try to elicit some of the chemical changes which have their intimate workings bound up with fatigue.

Chemistry of Cardiac Fatigue

The work in this field has been sporadic and as yet disconnected in many ways. Chemistry, however, holds out a great deal for the unraveling of many of the mysteries of failure.

It has generally been agreed that phospho-creatine, lactic acid, glycogen, and adenosine pyrophosphate are closely bound up in the chemistry of muscle metabolism. The investigators in cardiac chemistry were soon to realize that cardiac and skeletal muscle metabolism bore a great number of resemblances (14).

Leakins (89) states that normal muscle metabolism is tied up with the breakdown of phospho-creatine and the complete oxidation of glycogen to carbon dioxide and water. Visscher (114) states that the chemical processes may be summarized in what follows. Contraction is associated with the breakdown and subsequent resynthesis of creatine phosphate and adenylic pyrophosphate with the formation of lactic acid from glycogen, through several intermediate steps. In the recovery period, the oxidation of lactic acid, and perhaps carbohydrate and fat releases energy for the restoration of the system.
The above system started work on the various components of heart muscle. The creatine content of eighty hearts was analyzed by Cowan (21). In forty-eight approximately normal human hearts, the creatine content was 194 mg. per one hundred grams of tissue. Seventeen decompensated hearts had significantly lower values. Fifteen abnormal but compensated hearts had values ranging between the two. The author concluded that the reserve of the heart closely parallels its creatine content. Herrman and Decherd (61), (62) state that in the light of chemical findings, it appears significant at least, that total creatine and creatinine loss accompany failure. These men propose the idea that in anoxemia, asphyxia, and aglycemia, there is an inability of resynthesis of creatine phosphate. These same conditions might conceivably lead to depletion of the phosphorus and creatine content with ultimate causation of myocardial fatigue.

That in severe failure an anoxemia and an aglycemia are present cannot be denied. Clark et al (13), (14), (15) have shown this experimentally on animals, and Meakins (89) states that three conditions produce a defect in glycogen metabolism in failure. These are always oxygen wants, occasional thyrotoxicosis, and at times insulin decrease. Resnik (88 I, II, III) found
that anoxemia brings about changes in the functioning of the heart grossly. Meakins and Long (90) have found an increase in the level of the resting level of lactic acid in the blood in severe failure. This is rather a result of failure, and not a concomitant finding. It can be seen that anoxemia is closely bound up in the intimate processes of failure.

Analysis of the mineral content of the heart soon convinced investigators that potassium was a key mineral in this picture. Harrison, Pilcher, and Ewing (55) decided that a lowered potassium content could be a factor in muscle fatigue. They believed that potassium loss was accomplished by a lowered tissue alkaline reserve. They advanced the idea that potassium loss might not be the initial factor in failure, but was a link in the production of subsequent episodes. The relation of potassium to overwork has been shown by Calhoun, Cullen, and Harrison (11), who produced this state by stimulating one sciatic nerve of a dog. The other was kept at rest. A diminished potassium content was found in the muscle of the overworked side as compared with the normal side when fatigue set in. There was no significant difference in the water content of the muscles. Calhoun, Cullen, Clark, and Harrison (10) and Sampson and Anderson (101) found that they were unable to raise the
potassium content of the failing ventricles by its administration.

Wilkins and Cullen (122) found sodium to be increased in failure. They found calcium to be somewhat decreased, but potassium, phosphorus, magnesium, and total solids were markedly lowered in the heart in failure. Scott (102), using a different method, found no consistent change in the mineral content of the heart. His method has been questioned by the previously mentioned workers.

Cruickshank has more or less verified the work of the others (22), and with McClure (23) did some work on the amino acid metabolism of the heart. They found that naturally occurring or other amino acids cannot be utilized in mammalian hearts in the absence of sugar in the circulating blood.

It can be seen that the chemistry of failure contains a great number of apparently disconnected links, but ultimately, they may all be united. Clark et al (14) state that the character of metabolism in contraction is similar in all forms of muscle. They believe that the recovery processes may vary slightly, but as yet have no proof of this. Only time will solve the significance of the various chemical changes tied up with failure.
Dynamics of Cardiac Failure

The production of cardiac fatigue brings about alterations in certain dynamic functions relative to the heart, and it is the change in these elements which determines what course failure ultimately follows.

The idea that a tiring heart is unable to propel sufficient blood to the various organs with a normal degree of promptness has fostered studies in cardiac output and circulatory rate. The well known factor of venous congestion associated with failure was instrumental in stimulating research on the venous pressure in this condition. Studies on the blood volume were induced by the fact that there was apparent at autopsy, congestion of so many organs.

Cardiac Output

The problem as to whether or not the heart maintained the normal amount of blood to the various portions of the body in any integral period through the greater and lesser circulations, and the dependence on this change as a constant finding in failure, make up controversial points in dynamics. Around the ability of the inefficient cardiac mechanism to maintain its output have arisen two theories of the mechanics concerned in decompensation.
Measurement of Cardiac Output

In the normal individual the basic regulator of the cardiac output is the oxidative metabolism (34). As the venous return to the heart is increased with an elevated metabolism, the rate is reflexly accelerated due to impulses arising in the right auricle and the great veins (2). In this way the output is maintained. Also, if the output is diminished, the lowered pressure in the carotid sinus, aorta, and heart, reflexly stimulate the rate. The output per beat may be lower, but that per minute is increased. The venous congestion is thereby reduced (34), (58).

In some forms of muscular exercise the venous return is greater than in others. Also, a further mechanism for increase in output has been presented by Patterson, Piper, and Starling (95). They found that as the venous pressure rose, the systolic discharge increased. This has been discussed in the section on dilatation and hypertrophy.

In order to determine the cardiac output direct measure not being feasible, a method of measuring this variable had to be devised. Physical methods have been advanced wherein x-rays of the heart are taken during systole and diastole, the volumes calculated, and the differences found. This method is highly inaccurate at best, as various factors such as position and phase of respiration are apt to vary it.
More accurate determinations are based upon the Fick principle (see definitions). Application of the Fick method to individuals with failure tended to show a diminution in output (76), (89a); although Eppinger, Von Papp, and Schwartz (quoted by Harrison (48)) found normal or elevated outputs. The method, though accurate is impractical for clinical work since it involves the risk of entering the right heart and the pulmonary vein.

With the inadvisability of using the above methods, a new procedure was devised using a foreign gas. The basic principle is that the amount of foreign gas in the inspired air which is absorbed by the blood is directly proportional to the volume of the blood flowing through the lung. Acetylene is the gas now most generally used and recommended by Grollman (43). The individual breathes into a bag containing an acetylene and air mixture. In health only two samples need be taken. The first sample is taken after the mixture in the bag is homogeneous and is in equilibrium with the blood in the pulmonary capillaries. The second sample must be taken before any appreciable amount of recirculation of the blood containing the gas occurs. If this is not done, there will be an appreciable alteration in the rate of gaseous absorption. In health the second sample is taken in twenty-two seconds. From the change in concentration of oxygen and the foreign gas
in the samples, and the knowledge of the solubility of the gas in the blood, one can calculate the volume of blood passing through the lungs and absorbing a liter of oxygen. If oxygen consumption of the subject at rest (found by the usual basal metabolism method) in liters per minute, be divided by the above figure; the result will be the liters of blood passing through the lungs of a resting individual. This will correct for the amount due to the exertion of attempting to get a homogeneous mixture in the bag (28), (34), (48), (49).

Grollman (43) proceeded to analyze the shortcomings of the various methods. He found that most of the foreign gas methods were subject to error in cardiac disease. He believed that the foreign gas most applicable to use was acetylene. In congestive failure, certain modifications must be made, however. Because of a diminished vital capacity and changed circulatory rate, there is often a delay in obtaining a homogeneous mixture until after recirculation has occurred. Therefore, the procedure is altered so that an accurate check can be made on whether or not recirculation has occurred. The first sample is taken twenty seconds after rebreathing has started, and this permits time for a homogeneous mixture to occur in the system. Subsequent samples are taken at twenty-five and thirty seconds. If the calculated value for the first
two samples correspond closely with those of the last two, the determination may be considered reliable. One can assume that a homogeneous mixture has been gotten by the time the first sample is taken, and recirculation has not occurred by the last (34), (43).

Recently Hamilton, Moore, Kinsman, and Spurling (46) have developed a method for calculating the output from the concentration of a dye in the blood. The method is quite accurate, apparently, but has as yet not come into general use.

With this as a basis let us consider the facts as they have been used in the establishment of the role of cardiac output in failure. In viewing this variable, there have arisen two schools of thought. We shall consider cardiac output from the point of view of each group.

Forward Failure Hypothesis

This theory which had found more favor in English speaking countries seemed doomed to discard by the work of Harrison and Grollman; but lately has been revived somewhat. It states in effect that the various manifestations which clinically constitute the condition of congestive heart failure are ascribable to a deficiency of blood supply to the tissues as a result of an inadequate cardiac output.
In support of a lowered output is the statement of that eminent clinician, Sir James Mackenzie (87), wherein he states that the signs of heart failure are shown by the organs whose blood supply is not sufficient. His belief was that heart failure sets in when the limitation of the reserve power of the heart is such that there is a lack of blood to body organs with exercise. A similar idea had been previously expressed by Jurgensen (15). Evans and Matsuoka (29) infer that heart failure starts by pulse retardation. This may be interpreted to mean that there is a lessened output. Smith agrees (104). Blumgart, Riseman, Davis, and Berlin (5) state that adequate flow of blood to tissues implies two things. They claim that there must be an adequate amount of blood expelled, and it must be transported to its site of utilization with a normal speed. They conclude that circulatory insufficiency consists of failure of the heart to maintain blood supply large enough for the ordinary needs of the tissues at a given metabolic level. This may imply that the cardiac output is reduced.

Experimental evidence has been brought forward in support of the above men. For example, Meakins and Long (90) claim that severe circulatory failure is accompanied by an increase in the level of the resting lactic acid in the blood, and that accumulation is in direct proportion to the clinical evidence of the severity of the
failure. Henderson, Haggard, and Dolley (59), claim that efficiency of the circulation is defined as the ratio of the circulation, its volume per minute, to the oxygen requirement of the body. If we accept the findings of Leakins and Long (90), it would not be too much to postulate that the oxygen supply to the tissues is inadequate to maintain metabolism and oxidize the lactic acid (74). However, Cullen, Calhoun, Harrison, Wilkins, and Tims (84) found that lactic acid in beginning or moderate failure was not increased.

More direct work has been done on this factor. Stewart et al (111) conclude from observations before, during, and following failure that with decompensation all the measurements of the circulation become subnormal and improve when failure is recovered from, but never to the pre-failure level. McGuire et al (84), (83), (85) found in nineteen of twenty patients tested, a subnormal cardiac output. They added that the volume of the circulation may not be diminished; but assign this fact to accessory factors, such as increased metabolism, increased venous pressure, long standing anoxemia, low grade fever, anxiety, or apprehension. They admit that this is as yet unproved, and it is not quite logical to assume that the above factors operate only in cases of failure. The workers believe that there is an association
between the degree of failure and lowered output. In three of four patients, there was an increased output with improvement. Stewart, Cohn, Steele, and others (19), (109), (110) find the digitalis raises the cardiac output. We will later give findings which contradict this.

The theory of forward failure has a great number of ardent advocates, and time alone will give the ultimate answer to this riddle. It is opposed by an alternate hypothesis which has a great deal of support, both in logic and in experiment.

Back Pressure Theory

Diametrically opposed and mechanically unrelated to the above recorded theory is one first advanced by James Hope (65), since then once discarded, and then again coming into ascendancy. As Hope first described it, "As an obstacle to the circulation operates on the heart in a retrograde direction, the cavity situated directly behind it is the first to suffer from its influence." This in effect is the gist of the back pressure theory. It postulates that the clinical syndrome designated as failure may be attributed to a rise in pressure back of the failing chamber. In its simplest form it may be summarized as follows: Overwork of the chamber of the heart leads to enlargement which usually is brought about by both hypertrophy and dilatation of that chamber subjected to the
greater work. As the dilatation becomes excessive, there results a rise in venous pressure in the veins entering the affected side of the heart. The increased venous pressure leads to congestion of the organs drained by these veins.

Harrison et al (52) have found by the acetylene method that the cardiac output in congestive failure may be ten to thirty per cent less, but it may also be normal. They performed the work on nineteen patients. Grollman, Friedman, Clark, and Harrison (44) had similar findings. Hamilton, Moore, Kinsman, and Spurling (46) using their dye injection method, from which they calculated cardiac output, found the patients in failure may have a greater output than normal. Harrison and Blalock (51) using the direct Fick method in dogs found that anoxemia caused a five to five-hundred per cent increase in cardiac output in dogs. This would seem to indicate that one of the very factors which is supposed to bring about heart failure, according to the forward failure theory, seems to be one element in elevating the cardiac output. This assumption, however, is not entirely justified since these dogs were not in failure. Harrison and Leonard (54) found that digitalis lowered the cardiac output. Friedman et al (37), (38) found the same thing in a number of patients. Harrison et al (52) believe also, following the same patient
through failure to be of more value than single observations. Accordingly, they found on fifteen patients no consistent change in output as failure improved. Harrison, Friedman, and Resnik (53) believe that the chief objection to the back pressure theory is that most of its opponents believe that it implies regurgitation through the a-v values. The authors do not believe this to be necessary, for auricular pressure may rise as a result of dilatation of the ventricle by residual blood; so a greater pressure gradient is required in diastole in order for the ventricle to receive a given amount of blood.

Before expounding further on the back pressure theory, let us consider two matters. One concerns the work of Starr (107). He recently presented evidence which seems to negate the back pressure theory. He has found that when an experimental animal is killed, the blood pressure does not fall to zero. This residual pressure is designated the non-cardiac blood pressure, since it is independent of the heart action. The author has found that part or all of the elevated venous pressure in congestive failure is not directly due to the heart. He has determined that in individuals dying with venous obstruction, the non-cardiac blood pressure was not elevated, although congestion was present. In twenty cases of congestive failure, the non-cardiac blood pressure was elevated. Twenty-two cases of
cardiac disease without decompensation showed a normal non-cardiac blood pressure. These findings have not been verified by any other worker. Furthermore perhaps the more generalized pooling of the blood due to congestion is more a factor here, than in the often less widespread pooling in venous obstruction. Finally a negation of backward failure does not substantiate forward failure, and retrograde failure may be the mode in which non-cardiac pressure acts. This has opened a field for further research.

The other consideration with which we deal now is ventricular imbalance. This has been used to explain all the dynamics of failure. According to this theory there is a difference in the amount of blood pumped by the two ventricles. This is in reality one of the mechanisms by which backward pressure may be effected in acute dilatation of one side of the heart. That it plays no large part in chronic congestive failure is demonstrated by clinical observations. The facts that patients develop symptoms of pulmonary or systemic congestion concurrently, and that these phenomena disappear together, as clinical improvement supervenes, are not compatible with the ventricular imbalance theory. If this were the essential factor, congestion of the lungs would become worse when systemic congestion improved and vice versa. Certain clinicians (45), (108), (117) call attention to the fact
that one chamber strain precedes general failure. This may be in harmony with either the ventricular imbalance or the backward failure theory. In considering these two theories further, the fact that the improvement of the phases of entire condition occur simultaneously, as previously stated, is only in harmony with the backward pressure theory.

It is not the purpose of this paper to consider the production of symptoms in heart failure. We must admit, however, that the dynamics should be able to explain the symptoms of failure. The three principal manifestations of failure are dyspnea, edema, and cardiac enlargement. If the mechanics are applicable to the situation, they must explain the first two symptoms. The adherents of the forward failure hypothesis explain dyspnea on a diminished cerebral blood flow with an increase of pH in the respiratory center. Their opponents answer by stating that neither arterial nor venous blood has a higher acidity in failure than normally (24), (48), (49). Disciples of the back pressure school hold that dyspnea is of reflex origin. They claim that several reflexes are concerned, but that the chief one is due to the effect of congestion on the efferent vagal endings. This is based on experiments (47), (48), (49) showing no increase in respiration on cutting nerves in animals in failure, with an intact
circulation. Edema is considered by some proponents of the forward failure theory (87) as essentially due to capillary injury by anoxemia, although other factors play a part. Harrison (47), (48), (49) negates capillary injury, since he says blood proteins are usually normal in failure, showing no leakage. The majority of authors, (33), (100) however, incline to the view that edema is due to congestion. Forward failure followers, favoring to this view, say that the congestion is secondary to diminished output. Their opponents counter by saying that congestion will cause the edema, even though there is a normal output.

Circulatory Rate

Although the output of the heart is normal, the blood may not be circulated with sufficient promptness to be of value in supplying the tissues with oxygen. Thereby methods were evolved to gauge the circulatory rate.

Methods

The modes of determining the rate of the circulation deal with the injection of some material whose time of arrival in another part of the body is manifest in some way. In determining the circulatory rate (see definitions), various materials have been tried (28), (34).

1. Radium emanation--A solution of radioactive sodium chloride is used, and its time of arrival at
another part of the body is noted by a special detector.

2. Histamine is used, and the time of its arrival in the face is noted by flushing of the superficial vessels.

3. Sodium taurocholate and sodium desoxycholate (Decholin) are used. The arrival of these substances in the mouth causes a bitter taste.

4. Sodium cyanide causes an increase in respiratory depth.

5. Ether is used by Hitzig and his co-workers (64). One can smell it on the patient's breath, and furthermore, it causes bitter taste on its arrival in the mouth.

6. Glucide, fluorescein, vital red, etc. have been used. The arrival of glucide is noted by a sweet taste. The dyes are recovered in the blood.

The substances are injected into the arm. The substances which go to the mouth determine the arm to tongue circulation time. Those substances which show themselves on reaching the lung, determine the arm to lung time. The difficulty with these methods is that they do not show the time it takes for the circulation to go through the pulmonary system only. This has been overcome to some extent by judging the arm to lung time, and then the arm
The difference between the latter and the former gives the "crude pulmonary circulation time". This forms an idea of the pulmonary time.

Determinations

The determination of this especial function entails more agreement than does the cardiac output. In one hundred patients with congestive failure, Tarr, Oppenheimer, and Sager (113) found an decrease in the circulatory rate of all. In ninety-six of these patients the rate was markedly lowered. Hitzig, King, and Fishberg (64), using the ether method, obtained results comparable to the above workers.

Attempts have been made to determine whereabouts in the vascular tree the slowing may be. Blumgart (4), in his extensive work on blood flow found that the arm to heart time was increased, by the radium emanation method, in patients with mitral disease; whether they were compensated or not. The pulmonary circulation time, as found by the same method was also increased. Hitzig et al (64) measured the arm to lung time by the ether method and the arm to tongue time by the glucide method. They found that in left heart failure the "crude pulmonary circulation time" was increased. In right heart failure the arm to lung time was elevated. Blumgart and Weiss (6), using the radium method, reached similar conclusions. Wood (126) has
advanced the idea that a prolonged circulation time with normal venous pressure is an indication of pulmonary congestion. In other words, he also found that in left sided failure the pulmonary circulation time is increased.

Blood Volume

The slowing of the circulatory rate does not necessarily mean a deficiency of oxygenation of the body tissues. The exchange of substances between the tissues and the blood is obviously dependent on the number of open capillaries also. The capillaries are the means by which the size of the stream bed varies. The best measure of the stream bed which we can muster is the blood volume. The distension of organs of patients with congestive failure, at autopsy, led many workers to surmise that the blood volume, and consequently the stream bed, was increased. Keith, Rowntree, and Geraghty (75) used a dye whose concentration could be determined, by a spectrophotometer, in serial samples of blood. They found the plasma volume. Then from hematocrit samples of venous blood and the plasma volume measurement, the total blood volume and red cell volume are calculated. Gibson and Evans (41) used the same method. All these investigators found an increased blood volume in decompensation. The latter workers found the increase to range anywhere from 5.7% to 85.7%. They found that the
average degree of increased blood volume paralleled the degree of failure clinically, in forty patients. None of eighteen normals had a lesser blood volume than any of the decompensated individuals, in relation to height and weight. Markson (88) found an increased viscosity of the blood in failure. The hyperviscosity was associated with an increased number and size of red cells. Their number varied from 5,612,000 to 7,000,000 cells per cu. mm. in six cases with failure. Hamilton, Moore, Kinsman, and Spurling (46) have found by a method of their own that the intra-thoracic blood volume may be doubled in patients dying with decompensation. In general, all findings seem to point to an increased volume circulating through the blood stream of an individual with an inefficient heart.

Venous Pressure

The congestion of the venous system is one of the most dramatic sequences of failure. The manner of measuring systemic venous pressure is not difficult, but the pulmonary pressure presents a different story. The establishment of the latter, directly, is obviously not a clinical feasibility or desirability (56).

In all cases of cardiac failure the systemic venous pressure has been found elevated (6), (9). This has been the result established in Eyster's comprehensive monograph (51). Dock and Tainter reiterate these same findings (27).
Griffith, Chamberlain, and Kitchell (42) used a simple method whereby a needle was inserted into a vein and connected through a side arm syringe to a manometer filled with saline. A pressure of over 140 mm. of saline was believed to be abnormal. Wood, Capaccio and Tainter (127), using the above method, found the pressure in twelve decompensated patients fluctuated between 145 mm. and 315 mm. In ten normal controls the pressure varied between sixty and 120 mm. Friedfield and Fishberg (36) found elevated cerebrospinal and venous pressure to parallel each other as far as intensity was concerned. Rytand (99) found that digitalis reduces the venous pressure as it changes a failing heart into a compensated one.

Although it seems logical that the pressure in the pulmonary circuit must ultimately rise in left heart failure with congestion, no direct data for this is available. The congestion of the lungs leads to a diminished vital capacity according to Drinker, Peabody, and Blumgart (quoted by Harrison (47), (48), (49)). Whether the diminished expansibility of the lung is associated with an increase in pulmonary pressure remains as yet unsolved.

Arterial Pressure

The arterial pressure surprisingly enough, is not one of the essential alterations in dynamics of failure. This
is often found to be maintained in the decompensated condition. If we accept that the cardiac output may be normal in failure, we would not expect a lowered blood pressure in those cases of cardiac failure. If this theme is not accepted, or in the cases wherein the output is not maintained, other mechanisms serve to maintain the pressure. According to Fishber, citing the law of Poiseuille, the pressure of fluid in narrow tubes varies directly with the first power of the viscosity and the minute volume and inversely with the fourth power of the radius of the tube. While this law does not hold exactly for a branching circulation, it forms a very close approximation. Therefore, it can be seen that halving the radius of the small arterioles increases the pressure sixteen times. By constriction of the arterioles the arterial pressure is maintained, if the minute output falls. Fishberg (34) believes this to be so in failure, and that a vasoconstriction in the muscles, skin, and splanchnic area leads to maintenance of cerebral blood flow and arterial pressure. He further states that it may be brought about as follows: A drop in arterial pressure due to diminished cardiac output reflexly stimulates the vaso-motor center through the carotid sinus and aortic nerves with resultant vaso-constriction and restoration of previous blood pressure.
Additional factors tending to affect the blood pressure in failure include abbreviation of diastole, changes in blood composition, slowing of blood flow, and increased venous pressure. Tachycardia, with an abbreviation of diastole may allow a smaller amount of blood to leave the arteries before the next systole, and this may be responsible for a raised diastolic pressure. Slowing of blood flow through the vasomotor centers are supposed to stimulate them. Increased venous pressure may cause a corresponding increment in peripheral resistance and arterial pressure. In severe failure, arterial anoxemia and carbon dioxide retention exert pressor effects.

There is a balance of a weakened heart and the mechanisms tending to elevate arterial pressure. The balance of all the influencing factors determines whether or not the pressure in failure is elevated, lowered, or remains the same.
SUMMARY

The individual afflicted with a chronic affection of one or more valves of the heart, in time develops a dilatation and hypertrophy of this organ. This individual will finally exit with congestive heart failure, if nothing else intervenes. At autopsy, pathological changes are usually insufficient to explain why the myocardium played out. Therefore, failure is probably best accounted for along lines of alteration in function.

As a valve is injured, it progresses to a stage where it becomes stenotic, insufficient, or both. The effect is such that the chamber behind the injured valve dilates and hypertrophies. This may continue on to involve all chambers back of the injured member. The point is still a matter of controversy, but it would appear that by undergoing hypertrophy, the heart may accomplish more work. Whether or not injury must be added to that heart for hypertrophy to take place, and whether that organ could have accomplished the same work more efficiently without this, are still moot questions. There does seem to be a true work hypertrophy of the myocardium. Hypertrophy is always preceded by dilatation, but what brings about the latter after the former has existed for some time is unknown.
As the heart hypertrophies, it still retains its original relationship of one capillary per fiber. The distance supplied by that terminal vessel is greater than normally. Evidence shows that the heart cannot operate in the face of an oxygen debt. The recovery period of the cardiac musculature is closely tied up with diastole and appears to be an oxidative process. This period prepares the myocardium for contraction. As long as the heart maintains a diastolic period sufficient for complete recovery, there will be no fatiguing. As diastole is decreased by the speeding up of the heart, or as the heart fibers become extremely thick, the time for diffusion becomes insufficient; there is an accumulation of metabolites; and the heart fails. A relatively lessened coronary flow appears to be present. Often factors initiating the insufficiency by calling for increased labor from the cardiac apparatus can be established. In arteriosclerotic and luetic valvular disease there is often the added factor of actual diminution of coronary flow. This seems to be an element of aortic insufficiency of any origin due to a lowered diastolic pressure.

The chemical changes in failure are as yet not definitely elaborated, but evidence shows that potassium and creatine phosphate play stellar roles, either in the causation or in the determination of fatigue.
As the heart fails, it produces an alteration in dynamics. There is some debate as to whether or not the output of the fatigued heart is diminished. It appears, at the present time, that although the output is often lessened, it may be normal, or even above this. The part which accessory factors play in the last two groups is unsettled. A lessened output does not seem to be an essential change produced by insufficiency. There is a definite slowing of the circulation, but an increased blood volume is constantly observed. The latter is evidently, according to many, a means of compensation for deficient oxygenation caused by the former. There is an increased venous pressure in the systemic circuit, and probably also in the pulmonic. Most authorities assign this to an insufficiency of the heart with congestion back of the failing chambers. Recently, the role of the non-cardiac blood pressure as an influence in the elevated venous pressure has been suggested, but this needs more work. The arterial pressure may rise, fall, or remain the same in failure.

Within the past five years many of the concepts referred to in this paper have been advanced. As more is understood about fatigue of the myocardium, more may be accomplished in the attempt to prevent this condition. With this note of hope for the future, we conclude this paper.
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