THE MECHANISM AND MANAGEMENT OF CIRCULATORY FAILURE *

WILLIAM DOCK

Professor of Medicine, State University of New York, State University Medical Center at New York, College of Medicine, Brooklyn, New York

CIRCULATORY failure exists when any tissue, or the body as a whole, receives less than an optimal blood flow. Often the failure is local, as when the retina receives inadequate blood in a pilot pulling his airplane out of a dive, or when the myocardium is poorly perfused because of coronary sclerosis. General failure occurs when the minute volume flow of blood into the aorta fails to meet the needs of the whole body. This happens in all of us on exertion, and leads to oxygen debts of varying magnitude. Such deficits in flow are made up after exertion ceases. Acute failure also occurs after severe hemorrhage, or with venous pooling due to reclining at a $75°$ angle on a tilt table, or after taking nitrites while quiet and erect. In all these conditions the roentgen shadow of the heart decreases, the rate becomes rapid, and blood pressure is normal or low. As the systolic pressure falls toward or below 90 mm Hg., and the patient develops nausea and apathy, circulatory failure progresses into shock. This can occur from dehydration, adrenal insufficiency, or hepatic necrosis as well as from trauma and hemorrhage.

Peripheral circulatory failure may be due entirely to decrease in blood volume, or, as in spinal cord lesions, entirely to loss of vasomotor and venomotor tone. In many acute infections and intoxications, both factors are present. Restoration of blood volume by transfusion will not completely relieve the disorder if venomotor and vasomotor tone are lost, nor will restoration of vascular tone, by norepinephrine infusion, give complete relief if blood volume is greatly reduced. Combinations of both forms of therapy now permit far better control of peripheral circulatory failure than ever before. Shorr's investigations of the epinephrine antagonists have not yet led to specific therapy for the loss of tone in arterioles and precapillary sphincters due to high levels of vaso-

depressor material of hepatic origin, although this type of shock has been corrected by dialysis of the blood in the artificial kidney.

Circulatory failure of the acute peripheral type is compensated for by the body, as we may see after hemorrhage, by rise in venomotor and arteriolar tone, and by conservation of sodium chloride and water. The latter, effected by endocrine control of the kidney, permits restoration of blood volume and tissue turgor. Also there is a new formation of plasma protein and of red cells, so that the blood lost is soon fully replaced. Cardiac output falls when we are in the sitting or erect posture, and in studies of patients with postural hypotension, whose beds are tilted so the shoulders are well above the legs throughout both day and night, a rise of several hundred ccm. in blood volume occurs in a week or two.[1] The body brings into play all these restorative reflexes, whether circulatory failure is due to hemorrhage, posture, or to any other cause.

In peripheral failure cardiac output falls because venous return and ventricular filling are inadequate. When the pericardial sac is distended with fluid, or the pericardium scarred and drawn tight around the ventricles, heart failure is due largely to inadequate diastolic filling of the ventricles. These conditions usually develop slowly, and as the compensatory reflexes come into play, there is a rise in blood volume and in body water far above the normal level. Combined with the rise in tone of venules, this raises pressure in the auricles, but does little to improve ventricular filling when there is high resistance due to pericardial disease.

These forms of circulatory failure might be considered as preventricular, in analogy with prerenal uremia or edema, while the common form of circulatory failure, congestive heart failure, is in most instances ventricular or myocardial. The fundamental problem of myocardial failure is one with which only those who have Prof. Szent-Györgyi's experience and imagination can deal. It is the problem of muscular fatigue in the special biochemical setting of the heart muscle, fatigue in a muscle which must contract at least thirty times a minute to maintain our vital functions. Why do hearts carry their heavy burdens for decades, and fail even when less is demanded of them in senescence, and why is this sort of failure reversed, to some degree, by digitalis glucosides? These are the problems now being attacked by the biochemist. It is simple enough for the clinician to explain to himself the failure of

a muscle inflamed by myocarditis, or of myocardial cells filled with glycogen or buried in amyloid. Since none of these simple causes are present in most cases of heart failure at ages over 40, the clinician seeks an explanation from the biochemists, whose progress is most exciting, even though we catch only fleeting glimpses through our fog of ignorance.

In chronic cardiac failure—failure of the ventricles to expel in systole the blood which overfills them in diastole—all of the compensatory mechanisms seen after hemorrhage are at work, and the patient has a high blood volume, excessive extracellular fluid, and yet continues to retain sodium and water.[2] If depleted of sodium, his renal function may fail and his plasma sodium fall to critical levels, because he still retains water in excess of his osmotic needs. These results of the body's compensation for inadequate output of blood cause most of the symptoms of heart failure, and will be considered in detail by other speakers. But it must be emphasized that the rate at which symptoms increase, and the severity of the symptoms observed do not give a valid index of ventricular fatigue, but are usually functions of the excess of the patient's salt intake over the normal needs of the mammalian body. The latter, for sedentary people in temperate climates, does not exceed 200 mgm of sodium per day, while American diets provide three to eight thousand mgm a day. This excess makes rapid accumulation of edema easy, even with mild degrees of ventricular failure which would not be apparent with physiologic levels of sodium ingestion.

The physician is chiefly concerned with congestive failure occurring in middle age, in sedentary people, with the usual excessive salt intake. Symptoms develop rapidly in such patients whenever cardiac output falls a little below optimal needs of the body and when salt ingestion suddenly rises. The optimal needs for flow include not only the blood to keep oxygen tension at proper levels in all organs and replace oxygen debts due to exertion, but blood to maintain normal flow to the renal filter, to the dermal heat-radiating system, and to any leaks or shunts in the circulation. When thiamine deficit sets in, additional cardiac output is needed. Pyruvate seems to act as a vasodilator and keeps the vascular bed open even when all other needs have been met. In cirrhosis of the liver, open shunts in the skin and elsewhere may double blood flow in relation to normal basal needs. Failure to meet all such excessive demands may lead to severe symptoms of heart failure at

cardiac outputs far above normal. This is similar to uremia in a patient with two or three times the normal daily output of nitrogenous metabolites, due to high protein intake or rapid break-down of body protein.

It might be thought that such increases in demand for blood flow would be important direct causes of heart failure. Actually the cost to the heart muscle of increasing stroke volume when the peripheral resistance falls is remarkably small. During exercise in normal people stroke volume rises but heart volume falls. Since oxygen use by the heart varies with heart volume,[3] the fall in resistance must more than compensate for the rise in stroke volume, which can thus be maintained at reduced levels of oxygen use per beat. We may conclude that the burden on the heart, due to increased volume flow of blood, is usually less than one would think from the rise in pulse rate. Such acceleration regularly occurs with increase in venous return.

Arterial hypertension, whether systemic or pulmonic, also adds to the burden of the ventricle, but we have no way to measure how much. Systemic pressure may gradually double, and pulmonic pressure rise four or five-fold yet heart failure may not set in, and ventricular volume increases far less than one would calculate from Starling's curves relating cardiac work to cardiac volume.[4] The curves deal with acute situations, and with an acute rise of pressure, heart failure may occur as would be predicted. In chronic disease, the muscle cells become thick, not long, and the work is done very efficiently. In such patients, rise in rate, not the level of pressure, is the best clue to the cardiac burden per gram of muscle. Even in acute experiments, doubling the systemic pressure level increases work per gram of muscle only 25 to 30 per cent.

Doubling the rate imposes on the heart, beating at constant volume, an increase in oxygen need of only 50 per cent per minute, and reduces oxygen used per beat.[4] But rise in rate also shortens the time available for restoration of the molecular arrangements and high energy chemical bonds needed for contraction. The evidence from clinical experience points to slowing down of these chemical reactions in myocarditis and in the aging heart, thus making the ventricles especially prone to fatigue or partial exhaustion of contractile force if driven at rapid rates. While elderly patients with complete heart block may have low minute volume flow, and are unable to increase this much on exertion, they do maintain high stroke volumes against normal or high arterial resistance, and rarely show classical evidence of congestive failure. Even when they

have had previous myocardial infarction and have bundle branch block, they usually have large ballistocardiographic waves of normal contour. This indicates vigorous ejection of a large stroke volume by the slowly beating heart.

At the opposite extreme we see that when young people with normal hearts have an attack of paroxysmal tachycardia, heart failure develops in a day or two. In the first hours, the heart is small, as seen by x-ray, just as with the tachycardia of exercise, but it gradually dilates as it becomes fatigued by sustained rates over 180 per minute, and in one or two days, venous pressure rises, rales develop in the lungs and the liver becomes swollen and tender. With termination of the rapid rate, everything returns to normal in a few days. There can be no doubt in the minds of those who study cases of block on one hand and of tachycardia on the other that that acceleration of the heart is the most potent factor in causing heart failure. Because increase in minute volume flow is regularly associated with acceleration in rate, it too has a causative role far greater than would be the case if stroke volume alone were increased. Cardiac acceleration is a common sequel of anger, apprehension and related moods, so that heart failure may be precipitated by emotional storms, just as it is by fever and by other conditions, such as beriberi, hyperthyroidism or cirrhosis which accelerate the pulse. As the average age groups of patients increases, heart failure occurs more often as a result of a given degree of acceleration, or of change in stroke and resistance. Also, acceleration causes failure to develop more quickly in older people and the rise in rate required to cause failure becomes less marked. At age twenty-five, heart failure does not occur in normal hearts driven less than 150 per minute; at ages over fifty it often occurs at rates of only 100 to 120, and disappears when the rate falls below 80.

It was long taught that failure of the coronary bed to grow, and inability of oxygen to diffuse into thick fibers, could explain myocardial failure in hypertrophied but otherwise presumably normal ventricles. Bing and Goodale[5] have shown that flow is normal and oxygen uptake is high in hypertrophied hearts without coronary sclerosis, and it is now realized that oxidation can occur by electron transfer along long molecules so that the calculations on diffusion into fibers have become less significant.[6] Today we can assume that chronic heart failure due to anoxia occurs only with coronary occlusion or with anemia of extreme severity. Acute anoxia due to ischemia or anemia can develop

swiftly in shock and hemorrhage, and may precipitate failure of the myocardium and acute pulmonary edema. But, in striking contrast to these types of failure is the extreme infrequency of chronic myocardial failure with congestive phenomena in younger subjects with fatal coronary sclerosis. This was evident in the hundreds of soldiers under thirty-five years of age, whose deaths were studied at the Army Institute of Pathology[7] and also in young civilians.[8] Even with myocardial necrosis and ischemia, heart failure is most uncommon before the age of forty. In the light of our present knowledge, myocardial necrosis and scarring, and coronary insufficiency, contribute to the work of the ventricles, cause pain, cardiac irregularities and tachycardia due to apprehension, but coronary insufficiency or failure of the coronary bed to hypertrophy are not the direct causes of the fatigability of the ventricular muscle which underlies myocardial failure. Pain, not fatigue, is the result of ischemia in voluntary and in cardiac muscles.

The failure of a heart which has lost myocardial efficiency or the ability to restore its molecular machinery rapidly after each beat is therefore hastened more by acceleration than by other factors, while the rate of evolution of symptoms depends largely on the daily intake of sodium. Symptoms also are aggravated by other stimuli to salt retention, the most common being operative shock and premenstrual steroid stimulation of renal reabsorption of sodium. The most readily demonstrable and easily corrected cause of myocardial fatigability are abnormal levels of plasma potassium and a deficiency of water-soluble vitamins, specifically thiamine. All the other causes are vague and hypothetical, but some of them may be corrected, in part, by digitalis. The cardiac glucosides may also reverse the ill effects on the heart of high or low potassium levels, and of excessive dosage of desoxycorticosterone.

From this schematic description of heart failure, the general principles of therapy are obvious. Therapy is most successfully directed at the phenomena due to attempted restoration of optimal output—that is, the increase in blood volume and the retention of sodium. Bleeding, when hemoglobin levels are over 12 gm per cent, the liver large and the neck veins full, not only relieves the engorged venous system but may actually lead to a rise in cardiac output, by relieving over-dilation and tachycardia. Sodium depletion, by diet, mercury and cationic exchange resins, not only relieves pulmonary edema but by reducing myocardial edema may improve the function of the ventricles. Thus,

therapy directed at secondary phenomena which cause distress may actually improve cardiac function.

Slowing the heart is of utmost importance, and this may occur merely through relief of fright, when the patient has confidence that the doctor is competent and diligent. This deceleration is further helped by judicious use of a narcotic for a day or so, and sedation thereafter. It may be greatly assisted by a cool oxygen tent, if the patient is not alarmed or annoyed by this device. A decrease in symptoms is often effected by proper posture alone. Often in urgent dyspnea the most restful posture is sitting in the arm chair before a table piled with pillows on which the patient can lean forward. In some cases an ordinary bed, with the head end tilted up so the whole bed is at 30°, is more comfortable than the propped-up Gatch bed. On a tilted bed the patient can roll on his side, or lie prone.

Digitalis is of greatest value when it slows the ventricles in auricular fibrillation, but it may have striking effects on failure with regular rhythm. When given with mercury, diet, sedation, etc. its value can not be assayed; when given after some days on a constant regime it causes no striking benefit in more than half these cases, but in about one-third of the older patients, and occasionally even in children, it clearly is responsible for great improvement in myocardial vigor and relief of symptoms. It should always be given until it gives a good result, or causes coupled rhythm, nausea, or other toxic signs. These latter may be caused by half the average digitalizing dose (1.5 mgm digitoxin, 1.5 gm folia, 0.6 mgm ouabain), or may not occur until twice this dose has been given within 36 hours for digitalis or 6 hours for strophanthin. Perhaps the highest praise a doctor can hope to deserve is the remark my father made of a colleague he greatly admired: "He knows how to use digitalis."

Correction of anemia is an urgent matter in some patients with heart failure and can safely be done with packed red cells. Starvation, disguised as Karrell diet, is usually wrong, although weight reduction is frequently necessary as a long term project. The cardiac needs a simple solid diet, with small frequent feedings and minimal salt intake as long as blood urea is below 80 mgm per cent. Five mgm a day of thiamine is adequate for correction of beriberi heart disease, and is a simple supplement needed by many cardiacs, so that we use it routinely. If there is good reason to suspect Graves' disease, suitable tests and antithyroid

therapy should be undertaken at once. Creatinuria and basal metabolism do not fall in the first few days of therapy, but radioactive isotope studies and protein-bound iodine determination should not be deferred until after therapy is started. All tests are more satisfactory if completed before antithyroid drugs are given. It may, however, be unwise to defer therapy in some cases where the diagnosis is strongly suspected and heart failure is not easily brought under control.

The management of heart failure, which so often begins as an emergency, usually develops into a permanent way of life. In the future, surgery will be more often undertaken to lessen the load on the heart and hypothyroidism eventually induced in cases not otherwise held in check. The fundamental elements for effective control of heart failure are a hopeful, well-instructed patient and a physican who appreciates the hazards of over-cautious regimes, the value of maintaining good morale and bodily fitness, and the need for exhausting simple and reversible forms of therapy before considering those which are costly, hazardous, and irreversible.

REFERENCES

1. MacLean, A. R. and Allen, E. V. Orthostatic hypotension and orthostatic tachycardia, J. Amer. med. Assoc. 115: 2162-67, 1940.
2. Dock, W. Congestive heart failure, J. Amer. med. Assoc. 140:1135-42, 1949.
3. Evans, C. L. and Matsuoka, Y. The effect of various mechanical conditions on the gaseous metabolism and efficiency of the mammalian heart, J. Physiol. 49:378-405,1914-15.
4. Starling, E. H. and Visscher, M. B. The regulation of the energy output of the heart, J. Physiol. 62:243-261, 1926-27.
5. Bing, R. J., Hammond, M. M., Handelsman, J. C., Powers, S. R., Spencer, F. C., Eckenhoff, J. E., Goodale, W. T., Hafkenschiel, J. H. and Kety, S. S.,

The measurement of coronary blood flow, oxygen consumption and efficiency of the left ventricle in man, Amer. Heart J. 38:1-24, 1949.
6. Szent-Györgyi, A. Chemistry of muscular contraction. New York, Academic Press, 1947.
7. Yater, W. M., Traum, A. H., Brown, W. G., Fitzgerald, R. P., Geisler, M. A. and Wilcox, B. B. Coronary artery disease in men eighteen to thirty-nine years of age, Amer. Heart J. 36:334-72; 481-526; 683-722, 1948.
8. Gertler, M. M., Driskell, M. M., Bland, E. F., Garn, S. M., Lerman, J., Levine, S. A., Sprague, H. B. and White, P. D. Clinical aspects of coronary heart disease, J. Amer. med. Assoc. 146:1291-95, 1951.