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## THE PRINCIPLES OF THERAPY IN PATIENTS WITH CONGESTIVE HEART FAILURE\*

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IN an address delivered before the Massachusetts Medical Society on May 30, 1860, Oliver Wendell Holmes made certain remarks which may be appropriately quoted in any discussion of the treatment of disease:

"A medical man, as he goes about his daily business after twenty years of practice, is apt to suppose that he treats his patients according to the teachings of his experience. . . . But it is easy to prove that the prescriptions of even wise physicians are very commonly founded on something quite different from experience. Experience must be based on the permanent facts of nature. But a glance at the prevalent modes of treatment of any two successive generations will show that there is a changeable as well as a permanent element in the art of healing; not merely changeable as diseases vary, or as new remedies are introduced, but changeable by the going out of fashion of special remedies, by the decadence of a popular theory from which their fitness was deduced, or other cause not more significant. There is no reason to suppose that the present time is essentially different in this respect from any other. Much, therefore, which is now very commonly considered to be the result of experience, will be recognized in the next, or in some succeeding generation, as no such result at all, but as a foregone conclusion, based on some prevalent belief or fashion of the time."

Parenthetically, we may note that we do not have to travel far in order to find an excellent illustration of the truth of Holmes' statement. Digitalis has been successfully used for many years in the treatment of congestive heart failure. Following the development of instrumental methods for the study of the heartbeat, it became apparent that the chief action of the drug, *when studied by these methods*, was in cases of auricular fibrillation. Accordingly, one school of clinicians taught that the drug's only value was in such cases, and this belief is still widely prevalent in Great Britain and to a lesser extent in the United States. The theory of that time, which further experimentation has

shown to have been incomplete, demanded that the drug *should* be useful in only such cases, and, accordingly, many physicians were willing to discount the results of daily experience, which pointed toward its value in many cases with regular rhythm as well and omitted to give digitalis to many persons who needed it. Fortunately—and for this Dr. Christian more than anyone else deserves the credit—we have learned what our grandfathers knew, that digitalis is useful in almost all cases of chronic congestive heart failure, regardless of the rhythm.

To return to Oliver Wendell Holmes, "There are, of course, in every calling, those who go about the work of the day before them, doing it according to the rules of their craft, and asking no questions of the past or of the future, or of the aim and end to which their special labor is contributing. These often consider and call themselves *practical men*. They pull the oars of society, and have no leisure to watch the currents running this or that way; let theorists and philosophers attend to them. In the meantime, however, these currents are carrying the practical men, too, and all their work may be thrown away, and worse than thrown away, if they do not take knowledge of them and get out of the wrong ones and into the right ones as soon as they may. Sir Edward Parry and his party were going straight towards the pole, in one of their arctic expeditions, travelling at the rate of ten miles a day. But the ice over which they travelled was drifting straight towards the equator, at the rate of *twelve* miles a day, and yet no man among them would have known that he was travelling two miles a day backward, unless he had lifted his eyes from the tract in which he was plodding. . . .

"Presumption is of vast importance in medicine, as in law. A man is presumed innocent until he is proved guilty. . . . The presumption always is that every noxious agent, including medicines proper which may hurt a well man may also hurt a sick one. . . . Throw out opium, which the Creator himself seems to prescribe, for we often see the scarlet poppy growing in the cornfields, as if it were foreseen that wherever there is hunger to be fed

\*The Henry Jackson Lecture delivered before the New England Heart Association, April 30, 1936.

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there must also be pain to be soothed; throw out a few specifics which our art did not discover, and is hardly needed to apply; throw out wine, which is a food, and the vapors which produce the miracle of anaesthesia, and I firmly believe that if the whole *materia medica, as now used*, could be sunk to the bottom of the sea, it would be all the better for mankind,—and all the worse for the fishes. . . . Suffer me now to lay down a few propositions, whether old or new it matters little, not for your immediate acceptance, nor yet for your hasty rejection, but for your calm consideration."

Those of us who are interested in the treatment of cardiac disease are unwilling to go so far as Oliver Wendell Holmes in the direction of therapeutic nihilism, for we believe that drugs, when properly used, are often of much value to our patients. How well grounded is this belief? Is it based upon wishful thinking, and if not to what extent is it supported by objective and quantitative measurements? Our discussion of today will be concerned with an attempt to answer these questions.

The first principle to be discussed is the following one: *Although we are, speaking broadly, unable to avoid or to remove the underlying causes of cardiac disease, we can, in large measure at least, successfully prevent and treat the precipitating causes of cardiac failure.* For the sake of convenience it is well to divide the underlying causes of heart disease into the more common factors and into the less common factors. The first group comprises vascular disorders, including both hypertension and arteriosclerosis, the rheumatic diseases (including rheumatic fever, chorea and allied disorders) and syphilis. Only in the last mentioned disease is the etiological agent definitely known and a specific therapeutic attack available. Even here, once cardiac complications have set in, the specific therapy has relatively little to offer. Among the more important of the less common underlying causes of heart disease are bacterial endocarditis, congenital lesions, and chronic fibrosing diseases of the lungs. Against none of these do we have satisfactory methods of therapeutic attack. Finally, as relatively uncommon underlying causes of cardiac disease we have thyrotoxicosis and pericardial infections, which are open to surgical attack; severe, long-standing anemia, which can often be treated successfully; and avitaminosis, which, when recognized, offers brilliant therapeutic possibilities. However, it is unfortunately true that until more is known about the nature of the common underlying disorders of cardiac disease, their prevention and treatment will remain in a most unsatisfactory state.

It is fortunate that, in the majority of patients, heart failure does not occur until some precipitating factor is added to the underlying

but relatively nonprogressive disease process. The transitions from the asymptomatic stage of the disease to that of diminished cardiac reserve, and from the stage of symptoms only on effort to that of frank congestion with manifestations at rest, are usually initiated by one of the following processes: infections (especially of the respiratory tract), changes in rhythm, cough, violent exertion, pregnancy, obesity, anemia, thrombosis, prolonged severe mental stress and tachycardia, however brought about. The important point is that these trigger factors are in large measure preventable and once having arisen can usually be successfully treated. The management of cardiac disease in its earliest stages therefore resolves itself largely into the question of the prevention and control of these complications.

Of these several trigger factors, infection is probably the most important. Persons with cardiac disease must be trained to avoid exposure to inclement weather, to keep away from individuals with colds, to shun public gathering places during the winter months, to change wet clothes immediately, and when possible to spend part of the winter in a warmer climate. When such individuals are especially subject to respiratory infections they sometimes seem to be benefited by the use of vaccines containing the organisms which are the common secondary invaders in colds.

Exertion is probably—except in manual laborers—less important as a precipitating cause of heart failure than is generally believed. However, one occasionally sees patients whose first manifestations of congestion can definitely be ascribed to some unusual violent effort, such as a dash for a taxicab or a trolley car on a rainy day. Proper education of the patient prevents such eventualities.

Cough is an important and common precipitating cause of heart failure. It can usually be readily controlled by cough syrups containing codein.

To discuss in detail the other trigger factors would lead us too far afield. Except for thrombosis, which usually arises in the later rather than in the early stage of cardiac disease, these precipitating causes of heart failure can usually be prevented or adequately treated, provided sufficient care is devoted to the education of the patient.

The second principle to be emphasized is as follows: *The several and—at first sight—dissimilar methods which are available in treating persons with congestive heart failure have one fundamental action in common: they all tend to rest the heart.* In order to avoid misinterpretation this statement needs to be clarified. Like any machine which performs mechanical work, the heart is subject to variations in efficiency. The heart may expend more energy because it

is doing more work (the term "work" as used here refers to accomplishment), its efficiency remaining constant, or because its efficiency has diminished, the work accomplished remaining constant. Conversely, the heart may expend less energy either as the result of a diminution in its work or an increase in its efficiency.

The work of the heart depends on three factors: the output of blood per unit of time, the average pressure against which this blood is expelled, and the velocity imparted to the blood. Under conditions of low output such as obtain at rest, the last-mentioned factor is sufficiently small to be neglected. Since none of the therapeutic measures which are ordinarily used produce constant changes in blood pressure, it is evident that their chief effect on the work of the heart must be reflected in changes in its output. Certain useful methods of treatment such as rest, sedatives, venesection, dietary restriction, and thyroidectomy have been shown to diminish the amount of blood pumped by the heart, and hence the work done. These therapeutic measures are therefore believed to diminish the energy expended by the heart and to rest this organ.

The mechanical efficiency of the human heart cannot be measured directly by any method which has yet been devised. However, it is known from experiments on animals that when other conditions remain the same the energy expended by the heart varies directly with its diastolic volume. It has also been shown that, when the work performed is kept constant, the energy expended per unit of time is greater at rapid than at slow heart rates. It is therefore evident that therapeutic procedures which either slow the heart or which diminish the size of the heart, tend to decrease the energy expended. Digitalis has both of these effects. The action of this drug on the work performed by the hearts of persons with heart failure is inconstant, the output being increased in some subjects, diminished in others and unchanged in a third group, but the size of the heart is almost always diminished and the pulse rate is usually slowed in significant degree by digitalis. The best available evidence indicates that the beneficial action obtained by this drug is to be ascribed to an increase in the efficiency of the heart which is enabled to carry on its work with a diminished expenditure of energy. The happy results of quinidine in conditions of regular and irregular tachycardia are likewise to be ascribed to increased mechanical efficiency of the heart as the result of slowing in rate. Whether diuretic drugs have any action on the heart directly is still an unsettled question. There is some evidence which indicates that in certain patients diminution in edema is accompanied by a lessening of the blood flow through edematous tissues, and secondarily by a de-

crease in the work of the heart. Edema of the myocardium also sometimes occurs in patients with congestive failure, and it is perhaps not too fanciful to believe that if diuretic drugs can lessen the accumulation of fluid between the cardiac fibers, they may increase the efficiency of this organ.

The available evidence therefore indicates that procedures which produce benefit in patients with congestive heart failure do so primarily by diminishing the energy expenditure of the heart, and that this is accomplished either by decreasing the work it has to do or by increasing the efficiency of its performance.

The third principle of therapy is this: *Congestive heart failure is a vicious cycle for some of the symptoms produced by it tend in themselves to exaggerate it, and therefore rigid treatment of some of the effects of heart failure tends to help the underlying functional disorder which produces heart failure.*

This conception may be well illustrated by a consideration of the effects of cough, which is a very common symptom of congestive heart failure. Coughing is a violent muscular effort and like other exertion causes an increased metabolism of the body. During coughing there is a marked rise in the intrathoracic pressure. It is important to remember that the right ventricle is normally only about one third as thick as the left, and that the pulmonary arterial pressure is a similar fraction of the systemic pressure; hence a rise of twenty or thirty millimeters pressure in intrathoracic pressure constitutes a serious strain for the right ventricle. Coughing also raises the venous pressure and it is known that a rise in venous pressure produces reflex stimulation of breathing and hence tends to cause dyspnea. One frequently sees patients who have attacks of cardiac asthma which are set off by cough and which can be prevented when this trigger mechanism is suppressed by proper sedation.

Dyspnea, which is usually the most prominent symptom in patients with congestive heart failure, may likewise exert harmful effects. The increased excursion of the diaphragm tends to favor the emptying of abdominal blood into the chest. Venous inflow is also favored by the lowering of the average intrathoracic pressure during the dyspneic state. In normal persons this increase in the blood expelled by the right ventricle is readily handled by the normal left ventricle, but in patients with congestive failure the left side of the heart is usually affected in greater degree than the right and the blood therefore tends to accumulate in the lungs. Hence, dyspnea, which is originally mainly due to congestion of the lungs, tends to cause more congestion and to aggravate itself. In patients who are subject to cardiac asthma, attacks can

sometimes be produced by voluntary increase in respiratory movements.

The labored breathing which accompanies cardiac dyspnea may cause a well-marked increase in metabolism. Dyspneic patients often have a basal metabolic rate as much as 40 per cent above normal, and occasionally as much as 80 per cent. This of course increases the load on the heart.

An important delayed effect of persistent dyspnea is morphine addiction which develops when the drug has to be given repeatedly over a long period, and induces a cachectic state of the body in general, in which the heart is probably not spared.

Edema, another result of heart failure, also tends to have harmful effects. Accumulations of fluid in the abdomen and in the pleural cavities interfere with expansion of the lungs and hence produce dyspnea. When hydropericardium occurs, a heart which already empties with difficulty, becomes impaired in its ability to fill. Subcutaneous edema renders the tissues liable to infection, and heart failure is occasionally terminated by a streptococcal septicemia originating in this manner. In certain patients the blood flow through the peripheral edematous tissues appears to be increased because of impairment to oxygen diffusion.

The evil effects of pulmonary edema are too well known to require comment. However, it should be pointed out that edema fluid is often an excellent culture medium and that patients with edema of the lungs are very subject to bronchopneumonia, which is one of the most frequent causes of death in persons with congestive heart failure. Even in the absence of subcutaneous edema the presence of numerous râles in the lungs of a patient with cardiac disease is usually an indication for the administration of a diuretic drug.

Myocardial edema is not rare in patients with congestive failure. It probably imposes a barrier to oxygen diffusion and interferes with the recovery process in muscle fibers which are in poor condition to tolerate such impairment.

These examples illustrate how certain symptoms, themselves the cause of heart failure, tend to aggravate heart failure. The treatment of these symptoms is therefore not simply a matter of making patients more comfortable but is a fundamental step in the breaking of a vicious cycle which when untreated leads to death. Such a conception explains the great benefit which can be obtained by codein when it abolishes cough, by morphine when it relieves dyspnea, and by diuretic drugs, even in patients with minimal edema. The last point needs to be especially emphasized because it is not generally appreciated. We are all cognizant of

the importance of maintenance doses of digitalis in persons who have recovered from outspoken congestive heart failure. Maintenance doses of diuretics are also very useful in such subjects. It is important that ambulatory patients, who have had edema recently, should weigh themselves daily and take theophyllin or some other diuretic drug whenever the scales, by showing sudden gain in weight, point toward the beginning of reaccumulation of fluid in the body. By this plan certain subjects who would otherwise remain practically bedridden can be kept in an ambulatory state and relatively free of symptoms for months and occasionally for years.

A final principle of therapy: *If the foregoing points are borne in mind and patients are treated accordingly, only a very small percentage of the patients who have congestive heart failure die of it, although a good many die with it as the result of various complications.*

During the past ten years the general plan which has been followed at the Vanderbilt University Hospital in the treatment of patients with congestive heart failure has remained relatively unchanged, except that the principles which have been discussed have been recognized as of great importance and have been applied with increasing enthusiasm. We have recently undertaken a survey of the fatal cases in an attempt to determine whether any real advances in therapy have been made in recent years. It was felt that a comparison of the patients dying in the last five years with those dying in the previous five years might be helpful in this regard. In order to eliminate errors in diagnosis, the studies have been limited to patients who have come to autopsy. The various types of heart disease were about equally common in the two five-year periods. The median duration of life after the onset of congestive failure was estimated as accurately as possible from the case histories. In the past five years the value has been eighteen months as compared with eleven months during the preceding five-year period. A study of the chief cause of death has been made in both groups of cases. Uncomplicated congestive failure has in the last five years accounted for 19 per cent of the deaths, while during the previous five years the figure was 32 per cent. Many of these patients died within the first two days in the hospital before therapy could be effective. When these are eliminated it appears that only 9 per cent of the deaths which occurred during the last five years in patients with congestive failure were attributable to uncomplicated congestive failure. The value for the preceding five-year period was 24 per cent. In the recent years uremia, pneumonia and massive pulmonary infarction have each accounted for more deaths than has uncomplicated conges-

tive heart failure. Since only about 20 per cent of the patients who entered the hospital with congestive heart failure died in the hospital, the remaining 80 per cent being discharged improved, and since only 10 per cent of the patients who have been treated for several days or longer and died were found at postmortem examination to have heart failure as the chief immediate cause of death, it is evident that our direct mortality at present from congestive heart failure is only about 2 per cent. The indirect mortality—for conditions like infarction and pneumonia are in such patients usually indirect effects of the heart failure—is of course very great. However, these figures seem to indicate that the application of the principles of therapy which have been discussed has led to prolongation of life and to relief of suffering.

To summarize: If the kindly, witty and skeptical Oliver Wendell Holmes were with us today asking his pertinent and disconcerting questions concerning the real value of the therapeutic measures employed in patients with congestive heart failure, we should have to admit that his statement that the general care of the patient is more important than drugs, is just as true in our day as it was in his. The most valuable thing we can do for persons with chronic disease of the heart is to prevent the progression of the disorder by avoiding those conditions which act as precipitating causes of heart failure. Restriction of physical effort to that which can be performed without symptoms, prevention of undue mental and emotional stress, immediate attention to arrhythmias

and other causes of tachycardia, abolition of cough, supervision of pregnancy, reduction of obesity, management of anemia, and above all, prevention of infections—these are our most important measures of treatment. When in spite of our care congestive failure supervenes, rest, a proper dietary régime, the restriction of fluids, withdrawal of blood, and the use of opium, which Holmes recommended, are of the greatest value. In addition to these things we would request that Dr. Holmes add digitalis, quinidine and the mercurial and xanthine diuretics to his small list of drugs which should not be cast into the sea. All of these measures appear to have one fundamental action in common, for either they diminish the work done by the heart without affecting its efficiency, or they increase its efficiency so that a given performance of work is performed with a smaller expenditure of energy. In the final analysis the one effect of all therapeutic measures which are useful in the treatment of congestive heart failure is that of resting the heart.

And now for a final quotation from the medical sage of New England, who closed his address as follows: "My friends and brothers in Art! There is nothing to be feared from the utterance of any seeming heresy to which you may have listened. I cannot compromise your collective wisdom. If I have strained the truth one hair's breadth for the sake of an epigram or an antithesis, you are accustomed to count the normal pulse-beats of sound judgment, and know full well how to recognize the fever-throbs of conceit and the nervous palpitation of rhetoric."

## CANCER OF THE BREAST

### End-Results, Massachusetts General Hospital, 1927, 1928 and 1929

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THE present communication is the sixth of a series of papers reporting the five year end-results of surgical treatment of cancer of the breast at the Massachusetts General Hospital. This report covers the three year period, 1927 to 1929, inclusive. The results of the surgical treatment of cancer of the breast have been studied and reported since 1894, a period of thirty-six years, with the exception of two periods totaling eleven years.

In 1907, the results of the cases observed at the hospital during the ten year period, 1894-1904, were reported on a three year basis.<sup>1</sup>

In 1921, a similar communication was made, reporting the cases seen in the three year period 1910-1913, on a five year basis.<sup>2</sup>

In 1926, a report was made on the cases admitted to the hospital during 1918-1921.<sup>3</sup>

In 1934, two reports were published one giving the results of treatment during the three year period, 1921-1923,<sup>4</sup> and another for the three year period, 1924-1926.<sup>5</sup>

In the last three reports the cases treated in the private ward were included with those seen in the General Hospital.

This communication is arranged, as far as possible, in a manner similar to that of the previous reports to allow comparison, but changing conditions have made certain alterations necessary. The study of groups of consecutive cases made in this manner, we believe, is the best method of ascertaining the results of a given method of treatment. On the other hand, many factors enter into the prognosis of the individual case, such as, the age of the patient, the extent and duration of the disease and the

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