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THE CHANGING AETIOLOGY OF HEART DISEASE*

BY

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Until very recently it was customary to classify heart disease under such structural headings as "aortic incompetence," "mitral stenosis," or "pericarditis." The last few decades have seen the development of knowledge of disordered function as well as of structure. The most satisfactory classifications of disease are those which are based on causes, for the good reason that effective prevention depends on knowledge of aetiology. At once, of course, one is up against the problem of multifactorial causation. There are few disease processes that can be assigned exclusively to a single cause. The *Treponema pallidum* is essential for the production of syphilitic aortitis, but it is only a small minority of those infected who develop aortitis. There must be other factors which determine localization of the organism in the aorta. The famous razor of the great Franciscan philosopher William of Occam, which runs somewhat as follows; "*Entia non multiplicanda praeter necessitatem*," is a useful intellectual tool to use initially but little more, as to reach anything approaching a satisfactory solution it is usually necessary to invoke many causes.

Turning now to heart disease as it presents to-day, it is obvious that three types predominate; these are rheumatic heart disease, ischaemic heart disease, and hypertension, the latter two frequently combining to cause disability and death, and possibly sharing some causal factors. This is true at any rate up to the age of 70, but at greater ages the Registrar-General reports that a high proportion of deaths are certified as due to myocarditis and myocardial degeneration. Not enough is known to say whether these are due to cardiac ischaemia or are the result of some much more subtle disorganization of biochemical function concerned with senescence. Before considering the rheumatic and ischaemic groups in more detail let us briefly look at some less prominent forms of heart disease.

Pulmonary heart disease is a more important cause of disability and death than is generally realized. It does not receive adequate recognition in the Registrar-General's returns, as the cause of death is usually, and quite reasonably, ascribed to bronchitis, emphysema, pneumonia, or status asthmaticus. The mechanism in these conditions is pulmonary hypertension caused by rigidity and obliteration of the pulmonary vascular tree, which robs it of its capacity to dilate sufficiently to allow the passage of a large volume of blood without elevation of pressure. This rigidity is

due partly to structural change in the vessel walls and partly to low alveolar oxygen content. Fundamentally, the prevention of this form of cardiac disability must await better knowledge of the causation and prevention of bronchitis, bronchiectasis, emphysema, etc. Thyrotoxicosis presents no great cardiac problem, as there are several ways of correcting hyperthyroidism. Syphilitic heart disease is now rare in this country, and theoretically there is no reason why it should not become extinct. There are signs that congenital heart disease, inaccessible as the problem seems, may prove susceptible to preventive measures—such as the avoidance of maternal virus infections in the early stages of pregnancy and of foetal anoxia at delivery (Record and McKeown, 1953).

Rheumatic Heart Disease

Numerically, the only important cause of heart disease below the age of 40 is rheumatism. A remarkable change has taken place in the incidence of rheumatic fever (using the term to include acute rheumatism) during the course of this century. There has been a steady decline in the incidence of the acute rheumatic manifestations—so much so that as long ago as 1930 Glover stated that rheumatic fever was an obsolete disease. Its mortality in 1940 was, at all ages, of the order of 25% of the rate at the beginning of the century, while in 1950 the rate was only half that in 1940. There has been an equally dramatic fall in deaths from rheumatic heart disease in people below the age of 20. This is not surprising, as it is only the most severe forms of rheumatic heart disease, usually associated with florid acute rheumatism, that kill so soon.

It is not easy to assess the relevant mortality from rheumatic heart disease in older individuals, as several changes in methods of classification have made it difficult to get comparative figures from the Registrar-General's returns. However, there is probably a moderate decrease, so that the rate for 1936–8 is approximately 75% of that for 1921–3 (Knowlton, 1949). A curious feature, however, is that most of this decline is in males, the rate for females having dropped comparatively slightly. It has to be remembered that rheumatic heart disease lasts on the average about twenty-five years, with extremes of from a few months to many decades. This means that, supposing a method were discovered now absolutely preventing acute rheumatism, the full effect on the death rate from chronic rheumatic heart disease would not occur until about 1980. In this respect it is not inappropriate to recall

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the belief current twenty-five years ago concerning the effect of arsenical therapy in syphilis. It was taught then that, whereas arsenic was effective in primary, secondary, and tertiary syphilis, it was comparatively ineffectual in preventing the late neurological complications, dementia paralytica, and tabes dorsalis. The fallacy in this belief was that these late forms occur some twenty to thirty years after the primary infection, and as arsenical therapy was not widely practised until after about 1915 its full effect could not be assessed until about a quarter of a century later. As a matter of fact, from the mid-thirties onwards there has been a striking decline in their incidence fully comparable with that in tertiary forms of syphilis.

Aetiology of Acute Rheumatism

Let us now consider what is known of the aetiology of acute rheumatism and its attendant heart disease, with the particular object of recognizing factors which may account for this decline in incidence and of deducing what should be done to minimize or entirely prevent its recurrence. In this I am greatly indebted to D. A. Long, whose Milroy Lectures on the pathogenesis of rheumatic fever have just been published (1954). It has long been recognized that acute streptococcal infection of the tonsils and upper respiratory tract plays a very important if not an essential part in originating rheumatic fever. Some have believed that such infections act as non-specific provocatives which incite the rheumatic reactions in susceptible subjects. This conception allows rheumatism to develop in other forms of injury in the absence of streptococcal infection. Workers such as Coburn (1931), Swift (1949), and others regard rheumatic fever as a specific reaction to infection with the group A haemolytic streptococcus. The weight of evidence supports this latter contention. Long considers that the bacteriological and immunological evidence that haemolytic streptococci cause rheumatic fever is at least as good as that suggesting that haemolytic streptococci cause scarlet fever.

Scarlet fever has declined both in incidence and in severity during the past fifty years, particularly so during the last fifteen. The reasons for this reduction in streptococcal infection are complex, but they probably include many aspects of the steady improvement of living conditions during this period. So far, no clear case has been made that any particular aspect of environment plays a dominant part in this change. Respiratory tract infections are contact infections, and one would expect them to be closely dependent upon crowding. The evidence, however, for this is conflicting, as the decline continued throughout the period of unparalleled overcrowding during and after the war. This does not invalidate that hypothesis, as other factors, such as antibiotic therapy, may have cancelled it out. Virtually all antibiotics are very effective against the haemolytic streptococcus, and the development of antibiotic resistance by this organism is uncommon. There is much evidence to support the belief that such prompt treatment of streptococcal infections minimizes the risk of acute rheumatism and that the prophylactic use of either sulphonamide or penicillin in those who have had rheumatism significantly diminishes the rate of relapse.

Recent studies (with adequate controls) by Wannamaker *et al.* (1951) on large numbers of sufferers from streptococcal tonsillitis in an American Army camp demonstrated conclusively that rheumatism was almost entirely prevented by prompt treatment with penicillin. In fact, at the present time, the most useful procedure aimed at preventing rheumatism and rheumatic heart disease is the treatment of tonsillitis by sulphonamide or penicillin. There is no need to await bacteriological proof that the tonsillitis is streptococcal in origin, as, apart from diphtheria, the other causes of exudative tonsillitis are unimportant, consisting in the main of the occasional case of glandular fever or Vincent's angina. The development of oral preparations of penicillin

of a potency sufficient to achieve in most people blood concentrations that will deal with all but the most severe streptococcal infections are a great help in this respect. It must also be remembered that the sulphonamides are highly effective against the streptococcus. I believe that if such prompt treatment of tonsillitis were extensively practised there is a reasonable prospect that rheumatic heart disease would in a quarter of a century be as rare as syphilitic aortitis at the present day. Sulphonamide and penicillin occasionally cause sensitivity reactions, but these seem to me trivial risks compared with the benefit that may well be achieved.

What a transformation would be effected if rheumatic heart disease, with its toll of life and liberty during the first half of life, could be banished for ever. I sometimes think that cardiologists, as individuals and collectively in their societies, have not devoted as much interest and enthusiasm to this object as it deserves. The explanation may well be that exploration in this field demands the outlook and techniques of a bacteriologist, immunologist, and social scientist. These are all fields which those of us brought up as conventional cardiologists are ill equipped to explore.

Group A Streptococcal Infection

Turning now from the seed to the soil, what determines the rheumatic reaction in sufferers from group A streptococcal infection? I suppose at one time or other almost everybody is infected with this organism. There is no good evidence that any particular member of group A produces a specific substance causing rheumatism. All the evidence points to some general property of the group which initiates the disease in a susceptible person. The infection must persist for some little time, perhaps as long as two to three weeks. There is much evidence that the cellular injury which determines the rheumatic reaction is the result of a reaction between the circulatory antigen derived from the streptococcus and a fixed antibody. D. A. Long marshalled evidence strongly in favour of regarding this reaction as similar to the bacterial allergy seen in tuberculosis. For instance, the response is delayed and can be passively transferred with cells; histamine plays only a minor part (hence the inefficacy of antihistaminics) and the reaction can be suppressed by cortisone. The factors which determine the sensitivity are not understood, although clues are by no means lacking. There is much to support the belief that interference with the chemical structure of collagen is important.

The relationship to ascorbic acid metabolism is not fully explored. For instance, there is no satisfactory explanation why sufferers from rheumatism, rheumatic fever, rheumatoid arthritis, and active tuberculosis can absorb large quantities of ascorbic acid without reaching saturation point. It is known that certain amino-acids are essential to normal antibody production; rheumatic fever is seldom associated with diabetes mellitus; there is some obscure association between thyroid dysfunction and rheumatic fever. These and many other clues point to disorders of tissue metabolism, perhaps inborn, as being at the basis of rheumatism. Such a conclusion does not mean very much, as similar general phrases might be used to cover many pathological reactions.

Coronary Heart Disease

This disease is not unknown in the third decade, occurs occasionally in the fourth, is quite common in the fifth, and exerts a heavy toll in the sixth and seventh decades. There is abundant evidence that in the last 30 to 40 years it has increased to an extent much greater than can be attributed to such factors as the changing age structure of the community and the increased awareness of the clinical and pathological features of coronary occlusion.

The evidence which supports this absolute increase comes from many sources. The standardized mortality from "diseases of the coronary arteries and angina pectoris" has almost doubled (Morris, 1951). Morris also analysed the incidence of spontaneous rupture of the heart in the records

of coroners' necropsies and found an increase of more than twofold from 1932 to 1949. This is a particularly impressive item of evidence, as this gross pathological lesion allows of no error in reporting and coronary infarction is virtually its only cause.

There is the evidence of the clinician. Ryle and Russell (1949) record that Osler was admitted to the Fellowship of the Royal College of Physicians before he had seen a case of angina pectoris in hospital or private practice, while Sir James Mackenzie, in 1923, two years before he himself died of a coronary occlusion, stated that only 380 patients had consulted him for angina pectoris. The first clear account of the clinical picture of coronary thrombosis in England was by Sir John McNee (1925). Nowadays the life of a cardiologist is literally dominated by ischaemic heart disease.

The present high morbidity and mortality of this disease is unusually striking, because it has a much greater incidence in the professional classes, in particular the medical profession, although this high incidence is in varying degree general throughout the occupations of the Registrar-General's Class I. For instance, the standardized mortality ratio of deaths from coronary disease among physicians and surgeons is 368, as compared with less than 40 among coalminers, quarrymen, and agricultural labourers.

The magnitude of the menace was emphasized by the study Morris *et al.* (1952) made of coronary heart disease in general practitioners. They made use of the records of the Medical Sickness, Annuity and Life Assurance Society, which covered clinical coronary heart disease diagnosed among 6,000 medical men aged 35–64 holding "immediate benefit" non-cancellable sickness insurance policies. The data indicate that a medical man under 45 years of age who has not yet had any coronary disease has a one in five chance of developing it before the age of 65, and a one in fourteen chance of dying of it before that age.

Another factor which must be considered is that the disease is occurring in younger people, although it remains very uncommon in women before the menopause and is at all ages less common in that sex.

The problem, then, is to isolate the important factors which lead to ischaemia of the heart muscle; ischaemia which frequently results in necrosis of the myocardium with fatal shock, arrhythmia, or ventricular rupture—an event which is commoner as age advances and in males in the "upper," especially professional, classes, and which has increased several-fold in the last generation.

Approach Through Morbid Anatomy

Let us first of all approach the problem along the road of morbid anatomy. The crucial event here seems to be the occlusion of a coronary vessel of such size as to cause muscle ischaemia that is beyond the aid of collateral circulation. I am aware that it is not established that structural vascular occlusion always occurs—in fact, it is quite possible, even likely, that an identical lesion of the muscle occurs without demonstrable occlusion, but this is uncommon. This critical blockage is usually due to a clot; and here at once we confront a complicated situation. The mechanisms whereby blood clots—or avoids clotting—are imperfectly understood. Much emphasis has been placed on coronary atheroma as the determining factor, but too much weight must not be attached to this alone. Duguid (1954) advances impressive evidence in support of the hypothesis that atheroma is the result of a thrombus having formed on the vessel wall. Morris (1951) has considered the place of atheroma in some detail, starting from the very reasonable assumption that if it is the principal cause then its severity in the coronary vessels should have increased proportionately to that of coronary occlusion. He has made use of the admirable records of the London Hospital Institute of Pathology, which extend back far enough to make it possible to compare the first decade of this century with the fifth. Calcification, about the presence of which there can be little dispute, was taken as the "touchstone" of atheroma.

Some 6,000 reports from 1907 to 1949 were studied, relating to both sexes and to ages 30–69 inclusive. While the number of cases of coronary heart disease showed a sevenfold increase over this period, advanced coronary atheroma showed a substantial decrease; this was seen in all the sex, age, and pathological categories (including hypertensive) studied. Although this inverse correlation between the frequency trend of ischaemic heart disease and that of coronary atheroma makes it unlikely that the latter is the principal factor in causing coronary occlusion, it may yet be a common denominator in the process. Perhaps calcification does not reflect adequately the incidence of atheroma in that it may be a less common feature of that condition, which itself is increasing. Much remains to be done in this field, in particular the development of some satisfactory quantitative method of measuring the extent of atheroma, ideally during life but at least at necropsy.

The Problem of Atherosclerosis

The last few years have seen a revival of interest in the problem of atherosclerosis, particularly in connexion with the level and control of the cholesterol content of blood. The precise significance of the cholesterol that is found in atheromatous lesions is unknown. Opinion ranges from regarding it as the cause of atheroma to relegating it to the role of an incidental deposit in tissues already injured. It can safely be said, however, that there is an important relationship between the concentration of cholesterol in the serum and the development of atherosclerosis (Keys, 1952).

Great play is made of the fact that if rabbits or chickens are given a diet containing an enormous amount of cholesterol extensive aortic atheroma follows within a few months. This observation may not have a very wide significance, as neither of these species normally eat much cholesterol, its only dietetic source being dairy produce and animal fat. In the dog, feeding a large amount of cholesterol produces atheroma only if combined with induced hypothyroidism; while in man it has been found impossible to influence the level of blood cholesterol merely by changing its dietetic level. This is hardly surprising in view of the fact that cholesterol is so easily broken down and synthesized in the body. The one point that is clear is that the level of blood cholesterol in man is not influenced by the cholesterol content of diet. Yet dietetic factors other than cholesterol play a very important part in determining its level. This can be raised by a diet which contains a high proportion of fat, or which, while not containing so much fat, has a calorie content considerably above energy requirements.

This susceptibility of the serum cholesterol to these nutritional factors becomes apparent only after the age of 30: it seems as if prior to that age there is some homeostatic mechanism which holds cholesterol content within narrow limits. Keys *et al.* (1952) have demonstrated these relationships very beautifully in their surveys of serum cholesterol levels in comparable groups in Minneapolis, London, Naples, and Madrid. They have also emphasized the important regression of serum cholesterol content on age. A figure that would be normal at the age of 60 would be abnormally high at 20; in fact the essential basis of clinical deduction from blood cholesterol estimations is a knowledge of the normal of the particular community concerned and its variability in relation to age and sex.

It appears, then, that after the age of 30 the "better" the diet the higher the blood cholesterol.

The word "better" in this context has, of course, a meaning based on the popular belief that the more dairy produce and animal food one eats the greater the benefit. In fact, dairy produce is sometimes classed as "protective" food in the sense that its vitamin content is supposed to raise resistance to pathogenic micro-organisms. While deficiency of these foods undoubtedly means serious malnutrition, excess may spell dangers of a quite different sort. Popular belief is very understandably biased by the sensuous pleasure derived from eating dairy and animal food.

Blood Cholesterol and Ischaemic Heart Disease

Now what is the relationship of blood cholesterol level and ischaemic heart disease? However one views the problem there seems to be a close positive correlation between these two variables. Whether one compares nations or groups within nations, the statement, "The 'better' the diet the higher the serum cholesterol of middle-aged males and the more coronary disease," seems to hold good. Coronary heart disease is one of the main causes of disability and death in the United States, Canada, Britain, Northern Europe, Australia, and New Zealand, and these are all countries which, nationally speaking, derive more than 30% of the food calories from fat. On the other hand, areas like Southern Europe, Africa, India, and the Orient in general have diets the fat of which contributes less, usually much less, than 20% of the calories. It is difficult to be certain that atheroma and coronary heart disease are much less in these countries. The extent and standards of medical, biochemical, and pathological work are, generally speaking, much inferior, while the vital statistics of the populations at risk are less clearly defined. Nevertheless, while the evidence is not of the same quality as in the materially more favoured countries, it is uniformly consistent with the conclusion that the diseases are comparatively very uncommon.

In man, certain disorders such as diabetes mellitus, myxoedema, and obesity are often associated with prolonged elevation of blood cholesterol and also with a high incidence of atherosclerosis and associated arterial occlusion and ischaemic heart disease. The rare disorder of "familial idiopathic hypercholesterolaemia" shows a high rate of ischaemic heart disease. Lastly, persons who have ischaemic heart disease as shown by definite angina pectoris or infarction tend to have higher serum cholesterol values than otherwise comparable people (Geier, 1949).

On the other side of the picture there is a general impression that sufferers from chronic intestinal disease of the malabsorptive type—for example, steatorrhoea—have low levels of blood cholesterol, scanty atherosclerosis, and little liability to ischaemic heart disease.

Circulatory Disease in the War Years

Another curious piece in this mosaic of causality is provided by the changes that occurred in the death rate from circulatory disease in Norway during the period from 1940 to 1945, when the country was occupied by the Germans (Strøm and Jensen, 1951). Within a few weeks of occupation there was a substantial decline in all forms of circulatory disease presumed to originate in arteriosclerosis; conversely, the upward trend of incidence of these diseases was resumed within a similar period after the termination of enemy occupation. Now, the period in question was naturally associated with many important changes in the environment of the population, among them being a reduction of the average daily food intake per head from 3,470 calories to 2,850, with a reduction in fat from 159 g. (37% calories from fat) to 71 g. (20% calories from fat). It was also noted that there was a concurrent reduction in the thrombo-embolic complications of major surgical operations in the large hospitals (Dedichen *et al.*, 1951). These changes are compatible with the hypothesis that abundant fat intake favours vascular occlusion, but it is difficult to understand how the effect of the changes could be so soon apparent unless one supposed that they alter the coagulability of the blood. This latter possibility is intriguing, and stimulates speculation.

It is more than likely that alteration in blood coagulability plays just as important a part as atheroma of the vessel wall in promoting coronary thrombosis. Liability to post-operative thrombophlebitis shares with coronary heart disease a background of later life, obesity, and a chronic low level of physical activity. If this be proved to be a substantial factor there is a prospect of favourably altering the course of established ischaemic heart disease by appro-

priate measures. In brief, repentance even late in the day may be rewarded by some remission of sentence.

The increase in incidence of ischaemic heart disease might be attributed to the improving nutritional status of the community, as it is beyond dispute that malnutrition in North America, Northern Europe, etc., has steadily decreased until it is now of negligible proportions. Yet one would expect that it would be accompanied by an approximation of incidence in the various classes. Of that there is as yet no sign, and there has been no increase in the nutritional status of the professional classes themselves, rather the reverse. One will watch with interest the mortality experience of coal-miners in this respect, as the last ten years has seen an outstanding improvement in their economic position and there is now no financial reason whatsoever why they should eat less of the relatively expensive "fat foods" than the professional classes.

Influence of Physical Activity

Reverting to the occupational incidence of ischaemic heart disease, it was pointed out by Stocks (1951) that a sedentary mode of life might be a predisposing factor. It is obvious that among the many differences that distinguish the professional and labouring classes is that the latter often earn their living by the sweat of their brow, while the former are in the main "chairborne." This factor has been the subject of an outstandingly able investigation by Morris *et al.* (1953). They studied the morbidity and mortality due to ischaemic heart disease in drivers and conductors employed in the London buses and underground railway, the postmen, telegraph operators, telephonists, etc., in the London postal area, and most of the established men in the executive and clerical grades of the Ministries served by the Treasury Medical Service (Registrar-General's Occupational Grades II and III).

The essence of the results was that there was a significantly higher incidence of fatal coronary disease in the "inactive" occupation groups—that is, drivers as compared with conductors, telephonists with postmen on the delivery round, etc. It seemed, however, that the incidence of angina pectoris was rather higher in the active group; this, taken in conjunction with the better mortality experience of that group, meant that heavy workers tended to have coronary disease in a more benign and chronic form than light workers, and to die more commonly in second or later episodes of the disease. Although the two groups seemed, apart from the amount of exertion in their work, to be in all respects comparable as regards social class, implying similar dietetic, recreational, and other habits, the additional precaution was taken of analysing the 67 deaths of married women from coronary disease obtained from the same source. These when grouped according to the husband's occupation showed no group difference, thus emphasizing that the cause of the difference in mortality experience of the husbands lay in their occupational environment rather than in their home life.

Psychological Factors

Psychological "stress and strain" has for long been popularly believed to play an important part in a wide variety of diseases, including ischaemic heart disease and essential hypertension. So far as I can see, this hypothesis has no scientifically credible basis whatsoever—in fact, most of the evidence adduced in its support is dubious and much of it absurd. The argument runs somewhat as follows. Ischaemic heart disease is steadily increasing in frequency in the technically more highly developed and therefore wealthier countries, and in these countries it affects principally the professional, executive, and managerial classes; therefore there is some factor inherent in such people, or in their environment, which favours this disorder. So far the argument is irrefutable, but it then proceeds to select as important in this respect the concept that this lethal influence consists of (a) the exacting character of sustained

mental work accompanying intellectual occupations and posts involving heavy responsibility; (b) the emotional tensions that frequently accompany business, professional, and intellectual life; and (c) the inheritance of an ambitious or conscientious personality pattern. To sustain this argument it is necessary to show that these factors are much more potent in the affected classes. This has never been done; indeed, I believe (without scientific proof) that a dispassionate consideration of the matter exposes the concept as a fantasy of wishful thinking.

The reverse of the argument implies that the labouring classes in the wealthy countries and the great majority of the agrarian inhabitants of the Orient live some sort of idyllic existence, close to the soil, securely insulated from the fierce competitive, intellectual, and emotional burdens which grind the life out of those unfortunates whose lot it is to think, direct, and govern. It seems to me more likely that the stress factor operates in the reverse direction. The life of a physician in Birmingham is surely much less stressful than that of a peasant in the Yangtse Valley, with the ever-present menace of flood, famine, pestilence, and war; or of the tribesman in Equatorial Africa tortured by the taboo and sanction of primitive belief, to which are now added the tensions of organized political agitation. To subscribe at all to this factor one has to believe that the capacity to "feel" emotionally, to think deeply, to love, to hate, to fear, to hope, to aspire, and to despair are all much more highly developed in these materially favoured classes who get ischaemic heart disease. Basically, the intensity of all these intellectual and emotional activities, however much custom and education may alter their outward manifestations, is probably fairly uniform throughout the human family. Surely if these were fatal influences war, with such catastrophes as befell Norway, would greatly aggravate ischaemic heart disease. All available evidence is to the contrary.

The ready acceptance of this "stress-and-strain" concept is very understandable. It nourishes the *amour propre* of the believer and it is readily acceptable to the unfortunate victim and his relatives. It places ischaemic heart disease in the position of being the unjust reward of virtue. How much nicer it is when stricken with a coronary thrombosis to be told that it is all due to hard work, laudable ambition, and selfless devotion to duty than to be told it is due to gluttony and physical indolence. I know of nothing that conclusively disproves this psychological stress-and-strain concept; my contention is that so far there is little to support it, and much that makes it unlikely.

Conclusion

In conclusion I must emphasize that I have only briefly considered three of the many possible factors underlying ischaemic heart disease. There are many others, such as heredity and the important part played by essential hypertension with all its complex environmental background. It is important to recognize that such studies as I have considered merely indicate significant (in the statistical sense) correlations, which must not be taken as proving a causal connexion. They merely show how measurable environmental factors vary in relation to the incidence of ischaemic heart disease. It is easy to establish similar significant correlations with innumerable other factors whose causal relation is in the highest degree improbable. For instance, the progressive increase in ischaemic heart disease probably correlates closely with the rise in income tax, with the number of telephones in the community, or (inversely) with the decline in knowledge of the classics.

No other field of medical science illustrates so well the fundamental contribution of that academic discipline known as "social medicine," with its technique of the group inquiry, its searching examination of the validity of evidence, and its secure foundation on the mathematically disciplined philosophy of probability. It is right that the clinician should always keep before him the supreme importance of the individual patient, but he must never lose sight of

the importance of the patient as a unit in a complex pattern of biological adaptation. The application to diseases in general of the epidemiological techniques which have yielded such a rich harvest in the infectious diseases is the most exciting feature of current medical science.

The implications as regards prevention of such diseases as those we have considered, or of carcinoma of the lung, point to control lying in the hands of the individual rather than in those of the State. The complete control of water-borne infections has been achieved virtually without the knowledge and co-operation of the individual citizen, but anybody who has had experience of training soldiers to practise effective individual antimalarial measures will readily realize how hard it is to secure sustained effective co-operation. When such prophylaxis means avoiding attractive things and practising austere measures the propaganda problems become really formidable. However, the science of propaganda—as we know to our cost—also develops.

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COEXISTENT MYXOEDEMA HEART DISEASE AND PSYCHOSIS

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The reports of the Committee of the Clinical Society of London (1888) and of Brun and Mott (1913) indicate clearly that an acute psychosis may arise spontaneously in myxoedema. More recent accounts (Stoll, 1932; Zondek and Wolfsohn, 1944; Asher, 1949; Miller, 1952) have focused attention on this fact. Indeed, Asher wrote, "Myxoedema is one of the most important, one of the least known, and one of the most frequently missed causes of organic psychoses." His report evoked editorial comment (*British Medical Journal*, 1949; *J. Amer. med. Ass.*, 1949; *Year Book of Endocrinology*, 1952) and has prompted us to describe two illustrative cases which we have treated in the past six months.

Our patients merited additional clinical and therapeutic interest, as one had associated "myxoedema heart" (Zondek, 1918), while the other had congestive cardiac failure with little cardiac enlargement. The combination of myxoedema heart disease and psychosis has not previously received special attention.