Early Diagnosis Paper 5

The Early Diagnosis of Ischaemic Heart Disease

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In July, 1965, the Office of Health Economics held a colloquium on Surveillance and Early Diagnosis in General Practice at Magdalen College, Oxford. It was apparent from the discussion at this meeting that General Practitioners believed that if they were to act effectively in this field, they had to have clear cut information on current screening methods and the impact of early diagnosis of disease on the long term health of the patient. As a result of this view the Advisory Committee set up by the Office of Health Economics came to the conclusion that the best method of furthering this issue was to ask experts in a number of relevant clinical fields to write short papers specifically for General Practitioners.
The Early Diagnosis of Ischaemic Heart Disease is the fifth of these papers in the ensuing series. Other papers in the series are:

1. *The Early Diagnosis of Raised Arterial Blood Pressure*
2. *The Early Diagnosis of Visual Defects*
3. *The Early Diagnosis of Cancer of the Cervix*
4. *The Early Diagnosis of Depression*
6. *The Early Diagnosis of Some Diseases of the Lung*

Two Shillings and Sixpence

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DEATHS from ischaemic heart disease are increasing amongst the early middle-aged in many countries. Over one quarter of all deaths amongst British males under the age of 45 are caused by arteriosclerotic heart disease and there is ample social and economic justification for attempting to detect asymptomatic and early disease—but only if effective preventive treatment is available.

While epidemiological studies have shown that it is possible to predict with certainty those groups in the apparently healthy population with an increased risk of developing ischaemic heart disease, in an individual prediction is not synonymous with presymptomatic diagnosis.

Screening tests and more complex investigations for the early diagnosis of ischaemic heart disease are outlined; they can be relied upon to identify less than half of those who will develop the disease in the foreseeable future.

These limitations, and the fact that it has not yet been shown that myocardial infarction can be prevented from developing in healthy people or from recurring in patients with pre-existing heart disease, indicate that surveys to uncover occult ischaemic heart disease should be deferred.

Advice should be given, however, to healthy individuals who are anxious about themselves—particularly to siblings of young patients with ischaemic heart disease—and an effort should be made to correct any identified risk factor. The general practitioner is particularly well placed to do this.

INTRODUCTION

SURVEYS to establish a presymptomatic diagnosis of a chronic disease are only justified if the chronic disease in question is a common cause of morbidity or mortality in youth and early middle age, if it harms the social and economic structure of the community and if an active programme of prevention is possible. Atherosclerotic vascular disease and particularly ischaemic heart disease (IHD) fulfils the first two of these conditions and more so than any other disease. But the whole question of whether the time has yet come for implementing IHD detection surveys hinges on whether an active programme of prevention is possible.

The arguments that the current prevalence of IHD is an inevitable consequence of an ageing population, that death from a myocardial infarct is often quick and by implication pleasant, and that successful prevention of IHD merely preserves people to become senile are heard with increasing frequency. The first contention is incorrect, as I shall endeavour to show. The second is misleading since it does not take into account the invalidism, loss of working power and distress to the family and the individual himself which can ensue from chronic IHD. The argument that we all have to die from something and so why try to defeat fate is the negation of the practice of medicine and is particularly inapplicable to IHD since this is a disease of great importance to the young and middle-aged.

A recent World Health Organisation report[1] indicates that there has been a greater percentage increase in male deaths from arteriosclerotic and degenerative heart disease (ICD 420–422) in the 35–44 age group than in any of the subsequent three decades (Fig. 1). Of the ten countries with the highest mortality, the only one that is out of line is the United States where there was a very slight percentage increase during the ten years in question and no predominance in the youngest age groups. The explanation is not clear. Even in Canada, where the percentage increase in the disease during these ten years was less striking than in the others, the rise in the 35–54 age group was double that of the 55–74 age group. The actual death rates and their increases are greater, as would be expected, in the older age groups.

In addition to this strong suggestion that IHD is causing an increasing number of deaths in the young and middle-aged, arteriosclerotic and degenerative heart disease is responsible for approximately one quarter of all deaths between the ages of 35 and 44 years in the six countries with the highest death rates and for more than one-third of the deaths in these countries between the ages of 45-54 (Table A).

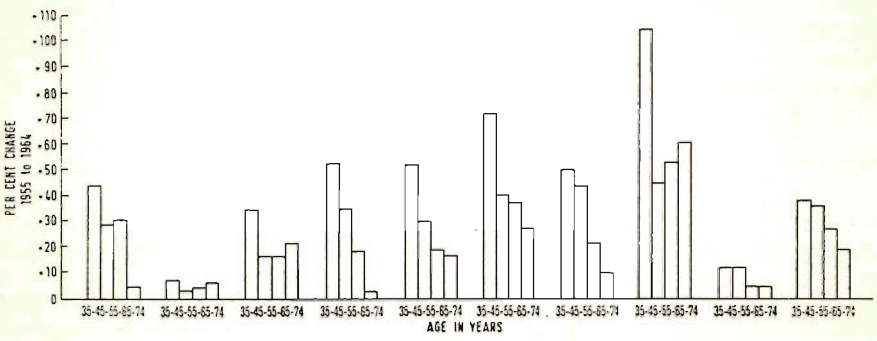
There can be no doubt, then, that atherosclerotic heart disease is a common cause of mortality in youth and early middle-age and that it is a source of major loss to the social and economic structure of these communities. On these scores, the arguments for presymptomatic diagnosis are commanding.

*This text is in part based on a paper 'Problems in the presymptomatic diagnosis of ischaemic heart disease', to be published in 1969 in *Modern Trends in Cardiology* (edited by A. Morgan Jones) by Butterworth & Co.

Figure 1

The percentage increase in male death rates per 100,000 population from arteriosclerotic and degenerative heart disease (ICD 420–422) from 1955 to 1964. Ten countries with the highest overall male mortality rates from arteriosclerotic and degenerative heart disease are shown and all have more than 5000 male deaths from these diseases annually (World Health Organisation, 1967).

	SCOTLAND	U.S.A.	SWEDEN	ENGLAND & WALES	AUSTRALIA	DENMARK	FINLAND	NORWAY	CANADA	W. GERMANY
DEATH RATES PER 100,000 MALES AT ALL AGES FOR 1964	406	382	353	346	342	329	321	304	303	243



EXPECTED YIELD

The expected yield from presymptomatic diagnosis of IHD depends on the prevalence in the normal population of 'risk factors' known to be associated with the disease. This depends on the relative weighting given to each risk factor and on the decision of when a biological index should be regarded as having departed from normal. Let us consider blood cholesterol levels as an example.

Assessment of the prevalence of a risk factor such as hypercholesterolaemia is seriously complicated by the difficulty in deciding when serum cholesterol levels should be regarded as elevated. These are influenced by race, age, sex, season, nutrition and genetic factors and it is misleading to define hypercholesterolaemia by stating a figure. There are striking differences in the cholesterol distribution in normal men between different populations and these are illustrated for the three countries with the greatest mortality from IHD in Table B. Even within a homogenous population such as that which exists in the Edinburgh area there can be

Table A

Death rates due to arteriosclerotic and degenerative heart disease (420–422) and per cent of deaths from all causes in men aged 35–54 years in 1964. (World Health Organisation 1967.)

	Death rates per 100,000 males		*Per cent of deaths from all causes*	
	35-44 yrs.	*45-54 yrs.*	*35-44 yrs.*	*45-54 yrs.*
Finland	118	442	26·4	39·4
Scotland	92	358	28·4	38·4
USA	94	354	24·6	36·7
Australia	74	324	23·6	39·5
Canada	73	311	25·2	41·3
England & Wales	63	245	23·6	33·3
West Germany	47	182	16·0	23·6
Denmark	37	181	17·2	29·5
Norway	38	164	16·5	29·0
Sweden	26	124	11·7	23·9

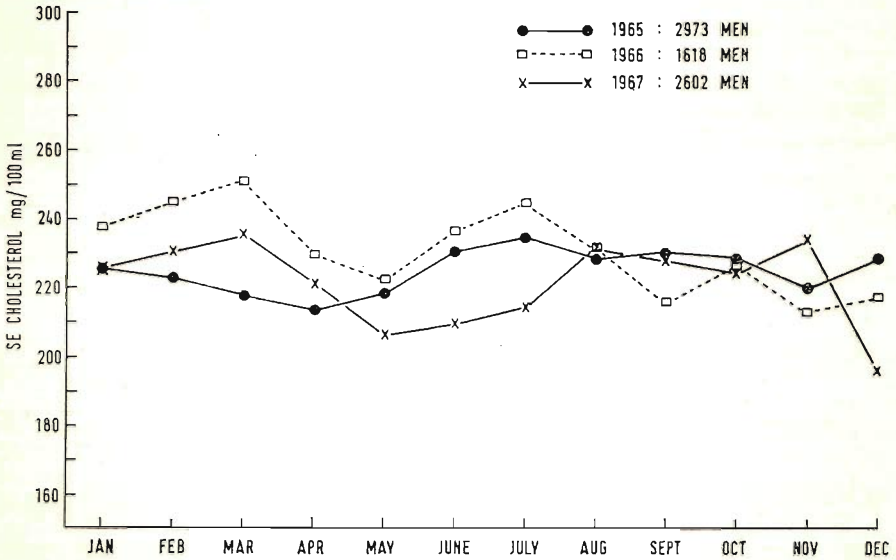
considerable variation and it is obvious from Figure 2 that it would be meaningless to fix any arbitrary level to indicate the presence of hypercholesterolaemia. These figures amplify those of Doyle et al[2] who studied seasonal variations in the same 69 men over a year. He showed that almost 50 per cent had a maximum difference of at least 50 mg./100 mls; no person had a difference of less than 20 mg./100 mls. and two had differences in excess of 100 mg./100 mls. Thus it is difficult to estimate the prevalence of this abnormality. It is necessary, therefore, for surveys to be conducted in each population as a preliminary to presymptomatic diagnosis in order to establish the range of normality and from these surveys the top percentiles of the population under study can be defined and used thereafter as an indication of increased risk. Similar surveys are necessary for other risk factors, such as physical inactivity and excess weight, since risk increases steadily with increasing severity of all factors.

Considerable reliance can be placed upon certain indices, such as elevated serum cholesterol levels, elevated blood pressure and excessive cigarette smoking as a means of predicting this disease. The relationship of these to coronary atherosclerosis has been fully reviewed by Moses[3] and the main epidemiological sources of this information are outlined below.

The twelve year follow-up figures of the Framingham prospective study[4] have

Figure 2

Spontaneous variations in the monthly assessment of the top tertile cut in the distribution of serum cholesterol obtained from healthy males, aged 30–59, in South-East Scotland for the years 1965, 1966 and 1967 (each point has been derived from more than 150 males).



recently been analysed by decile of risk[5]. In 789 men aged 30–39 years, 38 out of the 40 new cases of ischaemic heart disease occurred in those classified as being in the top half (five highest deciles) of risk, and in 742 men aged 40–49 years, the equivalent figures were 67 out of the 88 new cases observed. In this study it was shown that hypercholesterolaemia, excessive cigarette smoking, electrocardiographic abnormalities and hypertension were the most important risk factors; a multivariate analysis using discriminant functions showed that the combined effect of all these factors is greater than any singly. Relative differences between the highest and lowest deciles of risk were most marked at the younger age groups both in men and in women.

Morris et al[6] have made a comparable appraisal of prediction using London busmen, postulating stages of development of IHD. These stages of development were designated 'causes' (age, parental history, stature, skinfold thickness, occupation, cigarette smoking), 'precursors' (casual systolic blood pressure and plasma cholesterol)

Table B

Percentage of healthy population with 'high' serum cholesterol levels in the three countries with the highest mortality rate from IHD.

Country and Group	*Numbers*	*Per cent with se.cholest. more than 270 mg/100 mls.*	*References*
East Finland—men 40–59	834	46	Keys et al
West Finland—men 40–59	853	26	1967
Los Angeles civil servants, men			
21–39	540	49	Chapman and
40–49	334	63	Massey, 1964
50–59	356	70	
US railroad men 40–59			
Switchmen	835	24	Keys et al
Clerks	859	24	1967
Executives	251	22	
Scotland—Edinburgh men 30–59	2602	5	Personal observations
Country and Group	*Numbers*	*Per cent with se.cholest. more than 260 mg/100 mls.*	*References*
US PHS Framingham Study			
men 30–49	1535	18	Kagan et al
50–59	592	23	1962
women 40–49	904	23	
50–59	758	43	
Scotland—Edinburgh men 30–59	2602	8	Personal observations

and 'early disease' (ST-T wave abnormalities in the ECG). Examining the relationship of these to the subsequent development of IHD, the causes appeared to operate largely through the two precursors and the predictive power of these predominated over all others. Three-quarters of the new cases of IHD occurred in men who were in the top quarter of the distribution of either systolic blood pressure or plasma cholesterol. In Morris' population, 40 per cent of the men had either or both indices 'high' and they postulate that these are responsible for the epidemic disease.

There are comparable studies. For example, simultaneous consideration of four risk factors—high serum cholesterol levels, elevated blood pressure, heavy cigarette smoking and excess weight—indicates that 44 per cent of men with these features will develop clinical evidence of IHD within a projected ten year period[7]. Additional information should soon be available to allow accurate assessment of the predictive value of other factors such as personality type[8], abnormal glucose tolerance[9], hyperglyceridaemia[10] and physical inactivity[11,12].

The same association is true for fatal strokes. The risk of developing a fatal stroke in later years has been calculated to increase progressively according to the number of risk factors detected in youth[13].

However, predictability is not synonymous with presymptomatic diagnosis. The confidence with which we can conclude that certain groups of men—for example, those with hypercholesterolaemia—have an increased risk of IHD cannot be projected into the field of presymptomatic diagnosis. Here one is endeavouring to identify *individuals* in order to offer them advice to enable them to prevent the development of the predicted disease. The majority of these men, even although at preferential risk, will not get IHD in the foreseeable future. Taking elevated serum cholesterol and hypertension alone, Epstein[14] has estimated that for the ages 30–39 years between one-third and one-fourth of men with these risk factors will develop IHD over a ten year period and for the age group 40-59 years, the figure would be one in five. For a five-year period, Morris et al[6] estimate that the individual risk of developing IHD when these risk factors are present is only one in seven.

This should put into sharp relief the limited yield which can be expected from attempting the presymptomatic diagnosis of IHD in the community at large.

AVAILABLE METHODS FOR A PRESYMPTOMATIC DIAGNOSIS:

There is no single investigation or test which can be employed in order to reach a diagnosis of incipient IHD. The prevalence and relative importance of the various risk factors known to be associated with this disease determine the methods of approach to presymptomatic diagnosis. These can be considered at two levels. Methods which are readily available for initial screening of the population (first-stage screening) and those which are more complex and are usually only available in major centres (second-stage screening).

FIRST-STAGE SCREENING:
There are certain characteristics which can be elicited easily during the course of a simple screening examination.

1. Clinical examination:
It has been accepted for too long that clinical examination is unrewarding in patients suspected of having IHD and in those at risk and it is still not sufficiently appreciated that hyperlipidaemia may be associated with specific clinical signs. A positive effort should be made to search for these stigmata. The presence of a complete or partial arcus senilis is a significant finding in the young and early middle-aged and usually indicates raised serum lipids[15]: it is of no significance over the age of fifty. An arcus in the upper quadrants is often missed unless the upper eyelid is retracted when the patient looks down. The examination should be made with the subject facing a good source of light. Xanthelasma are usually fairly obvious but it should be a routine to examine the upper eyelid with the eyes gently closed. Xanthelasma occur most commonly just above the inner canthus but also on the lower eyelid. Their presence in young patients usually indicates hypercholesterolaemia[16] but is of less significance as age advances[17]. The prevalence of IHD in young patients with xanthomatosis is increased. Often the elbows and knees are not examined during clinical examination. With tuberous lesions, it is common to find an increase in serum cholesterol and triglyceride levels, and in both the low density and very low density lipoprotein fractions. It should be a routine for the examining doctor to run his fingers along the dorsal tendons of the hand and fingers, of the feet and toes and of the tendon achilles. Tendon xanthomata are more commonly associated with isolated elevation of serum cholesterol and low density lipoproteins. The palm of the hand should also be examined since occasionally small cholesterol deposits can be detected in the flexural folds.

2. Hyperlipidaemia:
Some of the evidence incriminating hypercholesterolaemia as a presymptomatic sign of IHD has already been described. (With advancing age, it is less common and becomes a less important risk factor.) All that is required at first-stage screening is measurement of serum cholesterol. This might well be amplified by standing a specimen of blood at room temperature for two or three hours in order to allow for clot retraction and for plasma or serum to separate; in the event that the plasma or serum is lactescent, arrangement should be made for serum triglycerides to be estimated. It must be remembered, however, that it is usual for there to be a certain amount of turbidity following a meal.

Estimation of serum cholesterol alone can be relied upon to detect the large majority of individuals with hyperlipidaemia. In young patients with IHD the usual

findings in order of frequency are (1) elevation of serum cholesterol, (2) normal levels of serum cholesterol and triglycerides and (3) elevation of both serum cholesterol and triglycerides and (4) elevation of serum triglycerides alone[18].

The value of estimating serum triglycerides and of more detailed methods, such as typing of lipoproteins, will be mentioned briefly in the section on second-stage screening.

3. Hypertension:

Several studies, notably the Framingham Study[19], have indicated that the presence of systolic as well as diastolic hypertension increases considerably the risk of developing IHD. The importance of this risk factor, unlike serum cholesterol, continues to operate during the sixth decade. Therefore, recording of the blood pressure should be a standard procedure in all screening examinations. It is usually not practicable to obtain a basal blood pressure reading during the course of screening programmes and it is probably adequate to record the blood pressure twice within a ten minute period when the individual is in the sitting position. The measurement of blood pressure has been considered in the first of the O.H.E. Early Diagnosis papers[20].

4. Cigarette smoking:

The risk of heavy cigarette smokers developing IHD is well documented[21,22,23], particularly in younger males. Under the age of 44 years, those who smoke more than twenty-five cigarettes daily are nearly fifteen times more likely to die from IHD than non-smokers[24]; for those who smoke between fifteen and twenty-four cigarettes daily, the death rate from coronary thrombosis is increased between four and five times. In heavy cigarette smokers the risk of dying from IHD is five to ten times greater in men under 45 than in those over 55. This correlation between heavy cigarette smoking relates particularly to myocardial infarction but less to the development of angina. Information concerning this habit should be recorded with care. Once again, the difference between prediction and presymptomatic diagnosis is brought out when it is realised that a relationship with cigarette smoking is characteristic of only a little more than half of the total deaths attributed to coronary thrombosis[25].

5. Obesity:

In practically all the prospective studies, excessive weight does not appear by itself to be a characteristic associated with an increased risk of IHD. Many individuals who are overweight also have hyperlipidaemia or hypertension, and their risk of developing IHD appears to be related more to these risk factors than to the presence of obesity itself. In the absence of these features therefore, it need not be regarded as an adverse sign. However, a rapid gain in weight is associated with an increase in

serum triglyceride levels and this may be a more important pointer to IHD than the presence of long continued excessive weight[26].

6. Family history:
Familial aggregation of deaths occurs in the relatives of young, but not in old, patients with IHD[27]. It has been assumed that this family clustering is related to the higher frequency of certain risk factors in these younger patients but Epstein[28] has postulated from a theoretical mathematical model that the known degree of familial resemblance of the two principal risk factors—hypercholesterolaemia and hypertension—fails to account for all IHD in families. Whatever the cause, a family history of IHD or other vascular disease is important information to be recorded in the young.

7. The Menopause:
In women, it is important to document the age of the menopause. Premature cessation of ovarian activity, either spontaneously or as a result of operation or irradiation, is often associated with the premature development of IHD[29].

8. Electrocardiographic abnormalities:
In the Framingham Study, the presence of an ECG abnormality at rest proved to be one of the most important predictive factors. Most disease detection surveys and health centres will have an electrocardiograph available and the recording of a resting record should be used as part of the screening procedure. Particular care must be taken, however, not to read too much into minor abnormalities. Several systems of classification and coding of electrocardiograms have been worked out in recent years. The Minnesota Code is one which is widely used[30]. This code grades the importance of electrocardiographic abnormalities. Certain categories indicate the presence of myocardial infarction and others code myocardial ischaemia. An effort tolerance test is unnecessary at the stage of initial screening.

SECOND-STAGE SCREENING:
The following investigations are not suitable for application during the initial screening procedure, since they will not generally be available outside a major hospital or special detection centre.

1. Hyperlipidaemia:
When the serum cholesterol is within the range of the top quarter for the population under study, then a fasting specimen should be obtained for estimation of serum triglycerides and for typing of serum lipoproteins. The most quantitative technique for estimation of serum triglyceride depends upon the direct determination of glyceride glycerol. Electrophoretic separation of serum lipoproteins[31], the use of a scatterlight nephelometer[33] or ultracentrifugation will allow classification of serum lipoproteins.

No prospective study has yet been reported on the significance of hyperglyceridaemia in healthy communities. Brown et al[33] believe that hyperglyceridaemia is related to the prevalence of IHD but do not regard it as a separate risk factor. Hyperglyceridaemia is often induced by a high carbohydrate intake[34], and in patients with IHD hyperglyceridaemia is sometimes associated with hyperglycaemia and both may be sometimes carboyhydrate-induced[35].

2. Glucose tolerance:
An abnormal blood sugar level one or two hours after ingesting 50–100 gm. of glucose should lead one to suspect that an individual may be at risk not only in terms of developing diabetes mellitus but also of IHD, although there are no precise figures to allow calculation of the degree of increased risk. The Bedford[36] and Tecumseh[37] studies have shown that IHD is significantly more prevalent in individuals with a hyperglycaemic response to a standard glucose load compared with those having a normal response.

3. Effort Electrocardiogram:
When one of the minor electrocardiographic abnormalities, such as flat or diphasic T waves, has been detected in the resting record, an ECG during or after effort can be informative. It is the most certain method of disclosing the presence of occult myocardial ischaemia which is, after all, the essence of attempting a presymptomatic diagnosis of IHD and is best done under standardised conditions. A maximum or near maximum effort tolerance test, followed immediately by sequential electrocardiograms during the period of recovery, increases the yield of pathological changes considerably[38]. The occurrence of myocardial ischaemia under these conditions correlates well with the presence of other risk factors, such as hypertension and hypercholesterolaemia. It is a late finding and it has been shown that one in four with post-effort ischaemia will develop overt symptoms of IHD within five years[39].

4. Hyperuricaemia:
Serum uric acid should be measured since Gertler and White[40] have shown that hyperuricaemia may precede the development of IHD in some young patients.

5. Radiological investigations:
The use of an image intensifier to disclose the presence of calcification in the coronary arteries has proved a reliable, safe and rapid method of detecting the presence of advanced coronary atherosclerosis[41]. It is a technique to demonstrate coronary atheroma and should not be regarded as a measure of an ischaemic myocardium. Its usefulness is that the demonstration of coronary calcification obviates the need for coronary angiography since it can already be deduced that there is extensive coronary atheroma present.

If the evidence from the screening stage and from the more complex investigations indicates that an individual may have incipient IHD but without symptoms, the question may arise as to whether a coronary angiogram should be undertaken. The contribution of this technique lies in the negative finding of healthy coronary arteries; under these circumstances, a presymptomatic diagnosis of IHD is less likely. The majority of adults have atheromatous involvement of the coronary arteries to a greater or lesser extent and the demonstration of this does not indicate IHD. Coronary angiography is not without hazard and complications in one form or another arise in approximately 8 per cent. It is not advocated as a second-stage screening test and is only indicated exceptionally in order to help to resolve a difficult diagnostic problem or a coronary neurosis.

LIMITATIONS OF PRESYMPTOMATIC SCREENING

The main limitations to attempts to implement widespread screening of the population for the detection of occult IHD are that the methods available cannot be relied upon to disclose more than half of those who will ultimately develop the disease, that cardiac neurosis may ensue, that the cost of such programmes could be prohibitive and, most important and perhaps completely limiting at present, that effective intervention is not yet possible.

These are formidable problems. The first has already been considered. The second, cardiac neurosis, requires comment. Whether we like it or not, the public knows a certain amount about IHD and anxious individuals may want to know how they stand. Provided IHD detection surveys are accompanied by sound advice, they need not cause alarm. In my experience, two distinct reactions have been apparent—relief that there is no evidence of developing heart disease or, if an abnormality has been detected, relief and gratitude that it has been found at an early stage. Attendance at IHD detection centres should remain entirely voluntary and there should be no persuasion or advertising until we are able to offer advice which will reduce the chances of developing the disease.

The cost of screening the population for occult IHD cannot be calculated. Screening programmes represent only a fraction of the total cost since individuals who are found to have a high risk of developing IHD and are offered treatment must adhere to it indefinitely and this will require surveillance from doctors, dieticians and nurses. The general practitioner can be involved in a very valuable way in helping vulnerable individuals and families to alter their ways of living. This may entail additional training although the interest is already growing. Backett[38] has made a plea for a detailed study of the economics of this kind of medical care and points out that it is assumed too readily that a cost-benefit analysis would show a deficit. We need to know how many man- or woman-years are saved by screening the population before the economics of detecting IHD can be appraised.

Of all these limitations, the most restrictive is our ignorance about preventing IHD.

THE PRESENT POSITION OF PREVENTION

It is economically and morally indefensible to promote on a national basis surveys for the presymptomatic diagnosis of IHD until it can be shown that this disease can be controlled. This has not yet been accomplished.

The current position can be summarised succinctly by stating that there is no conclusive evidence yet available that control of any of the risk factors has been followed by reduction in the incidence of IHD whether on a secondary or primary preventive basis. The position so far as control of hyperlipidaemia is concerned has recently been reviewed[43]. The conclusion reached was that the results of secondary prevention trials employing a diet rich in polyunsaturated fats are contradictory and equivocal, and that there is no case yet for departing from the recommendation of the World Health Organisation (1966) that 'no definite advice can be given with regard to specific change in the dietary habits of a nation'. More trials of dietary and drug control of hyperlipidaemia are necessary. Trials of the treatment of severe hypertension are notable for the absence of any striking reduction of mortality from IHD and formal large-scale trials of the control of moderate hypertension have yet to be conducted. It is only in ex-smokers that any difference has been observed[24].

The effect of controlling any or all of the risk factors can only be tested by establishing well designed prevention trials, and there are two complementary approaches. One is to show that a particular regime will reduce morbidity and prolong life in patients who have already developed IHD—secondary prevention. The other is to prove that it is possible to prevent at least a proportion of high risk individuals from developing IHD—primary prevention.

It is sometimes argued that if the control of a risk factor by secondary prevention improves the prognosis of patients who have developed IHD, then it would not be necessary to embark on primary prevention trials. There are obvious attractions in this, since all primary prevention trials must be very large, vast in cost and complex to organise. But the influences which cause a recurrence in survivors of myocardial infraction may be appreciably different from those which determine the initial onset of IHD. For example, successful reduction of hyperlipidaemia after infarction may be effective by altering mechanisms, such as thrombogenesis and myocardial function, which are more important in determining the outcome at this stage than before the infarct occurred. Therefore it should not be assumed that control of hyperlipidaemia after infarction will reduce the subsequent development of atheromatous lesions in the coronary arteries—the main aim in primary prevention—or that such an effect on atheroma is beneficial at this stage. A further and perhaps more potent argument against application of the results from secondary prevention trials to primary preven-

tion is that only approximately half of all patients survive their first myocardial infarction and are therefore able to participate in any secondary prevention study; and it is by no means clear that the same risk factors operate to an equal degree in those who die suddenly during the first infarct and in those who survive. At present, there are insufficient data to allow us to decide whether the pathogenesis of the second attack differs from the first and whether those who survive the first attack have a different pathogenesis from those who do not. Thus, there is no short-cut; long-term and large-scale primary prevention trials should be implemented in parallel with secondary prevention trials.

The views expressed here may need to be altered within the next few years and we should study carefully the results of all secondary and primary prevention trials. If it is shown that the primary prevention of IHD is possible, then large scale surveys to detect occult disease should receive the backing and close attention of national and international authorities. Meanwhile, one is bound to conclude that surveys to establish a presymptomatic diagnosis of IHD are not yet justified.

Advice should be given, however, to healthy individuals who are anxious about themselves—particularly siblings of young patients with IHD. If any of the major risk factors are found to be present, then it is justifiable to try to correct them. At the same time, it should be explained that in the present state of our knowledge the treatment is logical but unproven. The general practitioner is particularly well placed to handle this situation. His knowledge of the man—his smoking and eating habits, his occupation and hobbies—should enable the doctor to give tactful advice to each individual on occasions when he is consulted for other reasons. The general practitioner is also the ideal person to graduate advice according to the emotional make-up of the individual and an opportunity exists here for the personal implementation of preventive medicine.

1 WHO. *Epidemiological and Vital Statistics Report* (1967). *Epidem. Vital Statist Rep.* **20.** Cardiovasc. Dis. Suppl.

2 DOYLE, J. T., KINCH, S. H. and BROWN, D. F. (1965). *J. Chron. Dis.*, **18,** 657.

3 MOSES, C. (1963). *Atherosclerosis, H.Kimpton*, London.

4 KAGAN, A., DAWBER, T. R., KANNEL, W. B. and REVOTSKIE, N. (1962). *Fed. Proc. Suppl.* 11, 52.

5 TRUETT, J., CORNFIELD, J. and KANNEL, W. (1967). *J. Chron. Dis.*, **20,** 511.

6 MORRIS, J. N. KAGAN, A., PATTISON, D. C., GARDNER, M. J. and RAFFLE, P. A. B. (1960), *Lancet*, **2,** 553.

7 STAMLER, J. (1964). *Conn. Med.*, **28,** 675.

8 ROSENMAN, R. H., FRIEDMAN, M., STRAUS, R., WARREN, M., JENKINS, D., MESSINGER, M. B., KOSITCHECK, R., HAHN, W., and WERTHESEN, N. T. (1966). *J. Amer. Med. Ass.*, **195,** 86.

9 OSTRANDER, L. D., FRANCIS, T., HAYNER, N. S., KJELSBERG, M. O., and EPSTEIN, F. H., (1965). *Ann. Intern. Med.* **62,** 1188.

10 ALBRINK, M. J., and MAN, E. B. (1959). *Arch. Intern. Med.* **103,** 4.

11 MORRIS, J. N., HEADY, J. A., RAFFLE, P. A. B., ROBERTS, C. G. and PARKS, J. W. (1953). *Lancet*, **2,** 1053, 1111.

12 MORRIS, J. N. and CRAWFORD, M. D. (1958). *Brit. Med. J.*, **2,** 1485.

13 PAFFENBERGER, R. S. and WING, A. L. (1967). *Lancet* **1,** 753.

14 EPSTEIN, F. H. (1967). *Israel J. Med. Sci.* **3,** 594.

15 SHANOFF, H. M., and LITTLE, J. A. (1961). *Canad. Med. Ass. J.*, **91,** 835.

16 PIPER, J., and ORRILD, L. (1965). *Amer. J. Med.* **21,** 34.

17 VACCA, J. B., KNIGHT, W. A., and BROWN, G. O. (1959). *Ann. Intern. Med.* **51,** 1019.

18 OLIVER, M. F. (1966). *Proc. Roy. Soc. Med.* **59,** 1180.

19 KANNEL, W. B., DAWBER, T. R., FRIEDMAN, G. D., GLENNON, W. E., and MCNAMARA, P. M., (1964). *Ann. Intern. Med.* **61,** 888.

20 HOLLAND, W. W. (1967). *Office of Health Economics.*

21 HAMMOND, E. C., and HORN, D. (1958). *J. Amer. Med. Ass.*, **166,** 1159, 1294.

22 DOYLE, J. T., DAWBER, T. R., KANNEL, W. B., HESLIN, A. S., and KAHN, H. A., (1962). *New Engl. J. Med.* **206,** 796.

23 Report of the Advisory Committee to the Surgeon General of the U.S. Public Health Service (1964). *Smoking and Health. Pub. Health Ser. Publ. No.* 1103, U.S. Govt. Print Office, Washington, D.C.

24 DOLL, R. and HILL, A. B., (1964). *Brit. med. J.* **1,** 1939, 1460.

25 DOLL, R., and HILL, A. B., (1966). *National Cancer Institute, Monograph* **19,** *p.* 205.

26 ALBRINK, N. J., MEIGS, J. W., and GRANOFF, M. A., (1962). *New Engl. J. Med.* **266,** 484.

27 SLACK, J., and EVANS, K. A. (1966). *J. Med. Genet.* **3,** 239.

28 EPSTEIN, F. H. (1967). *J. Amer. Med. Ass.*, **301,** 795.

29 SZNAJDERMAN, M., and OLIVER, M. F., (1963). *Lancet*, **1,** 962.

30 ROSE, G. A., and BLACKBURN, H., (1966). *Wld. Hlth. Org. Rep. Appendix* 10—*Revised Minnesota Code.*

31 FREDRICKSON, D. S., LEVY, R. I., and LEES, R. S., (1967). *New Engl. J. Med.* **276,** 34, 94, 148, 215, 273.

32 STONE, M. C., and THORP, J. M. (1966). *Clin. Chim. Acta*, **14,** 812.

33 BROWN, D. F., KINCH, S. H., and DOYLE, J. T., (1965). *New Engl. J. Med.* **273,** 947.

34 AHRENS, E. H., HIRSCH, J., OETTE, K., FARQUHAR, J. W. and STEIN, Y. (1961). *Trans. Ass. Amer. Phys.* **74,** 134.

35 OSTRANDER, L. D., NEFF, B. J., BLOCK, W. D., FRANCIS, T. and EPSTEIN, F. H., (1967). *Ann. Intern. Med.* **67,** 34.

36 KEEN, H., ROSE, G., PYKE, D. A., BOYNS, D., CHLOUVERAKIS, C. and MISTRY, S. (1965). *Lancet*, **2,** 505.

37 EPSTEIN, F. H., OSTRANDER, L. D., JOHNSON, B. C., PAYNE, M. W., HAIJNER, N. S., KELLER, J. B., and FRANCIS, T. (1965). *Ann. Intern. Med.* **62,** 1170.

38 DOAN, A. E., PETERSON, D. R., BLACKMAN, J. R. and BRUCE, R. A. (1965). *Amer. Heart J.* **69,** 11.

39 RUMBALL, A. and ACHESON, E. D. (1963). *Brit. med. J.* **1,** 423.

40 GERTLER, M. M. and WHITE, P. D. (1954). *Coronary heart disease in young adults.* Harvard Univ. Press, Cambridge, Mass.

41 OLIVER, M. F., SAMUEL, E., MORLEY, P., YOUNG, G. B., and KAPUR, P. L., (1964). *Lancet*, **1,** 891.

42 BACKETT, E. M. (1966). *In 'Surveillance and Early Diagnosis in General Practice'. Office of Health Economics*, p. 38.

43 OLIVER, M. F., (1967). *Control of hyperlipidaemia. Modern Trends in Pharmacology and Therapeutics, ed.* W. F. M. Fulton, Butterworths, London, p. 221.

44 WHO (1966). Euro. **179,** 4.

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