Some Sequels to Myocardial Infarction and their Treatment*

R. R. H. LOVELL,† M.D., F.R.C.P., F.R.A.C.P.

Brit. med. J., 1964, 2, 465-470

In no country with a National Heart Foundation are the citizens likely to be allowed to remain ignorant of the ravages of coronary artery disease. Doctors, of course, whatever branch of medicine they practise, are all too familiar with its problems. So, in Australia at any rate, are students, for sufferers from the disease provide a fair proportion of patients in teaching hospitals. In a recent survey in the Royal Melbourne Hospital we found that one-quarter of the occupants of general medical teaching beds had, as their main diagnosis, coronary disease, cerebral vascular disease, or peptic ulcer, and coronary disease was the commonest of these.

The clinical episode of myocardial infarction which leads to admission to hospital is, of course, just one incident in the long course of coronary disease, and it must be viewed in perspective. This is given by prospective studies such as those reported from Framingham (Kannel *et al.*, 1961) and Chicago (Paul *et al.*, 1963).

The Framingham study suggests that of 1,000 men aged 30-62 who at the beginning of a year have neither clinical nor electrocardiographic evidence of coronary disease nine will have developed evidence of the disease by the end of the year. Of these nine, three will manifest the disease as angina pectoris. One will die suddenly without pre-existing evidence of coronary disease and it will be assumed—and it will often only be an assumption—that his death was due to coronary disease. One will not know that he has had a myocardial infarction until, at the end of the year, the electrocardiograph reveals evidence of infarction not previously present. He will have had a "silent infarction." The other four will have presented with symptoms and electrocardiographic evidence of a heart attack. It is these four who provide the population we have to consider. They differ from the complete population of people suffering myocardial infarction because they have had symptoms which have led to their seeking medical help, and they have generally lived long enough to get at least through the doors of a hospital casualty department. The statistical approach becomes a little confusing at this stage if you have had an experience, such as I had a few years ago, of meeting in the lift a patient in transit from the casualty department to the ward. He was receiving *en route* both cardiac massage and artificial respiration because, while being lifted out of the ambulance, he had become statistically dead.

The outstanding sequel in this group of patients admitted to hospital with myocardial infarction is early death, and I shall consider this and its treatment first. I shall then discuss mortality after the acute phase of the illness is over, and I shall finally consider some features presenting long-term problems which have interested us.

Early Mortality

When, in 1960, we reviewed our experience we found that of 81 consecutive patients admitted to the University Department's ward with myocardial infarction from 1956 to 1959, 23 died in hospital. This mortality of about 30% is of the same order as that reported for patients admitted to hospital with myocardial infarction in many parts of the world.

Numbers of deaths related to days after admission with myocardial infarction. University of Melbourne Department of Medicine, 1956-9.

The accompanying Chart shows that when deaths were related to the time after admission it was evident that the peak mortality was in the first few days. Indeed, over half of this group of patients who died died in the first 24 hours after admission. Over these years we may possibly have been receiving a disproportionate number of rather ill patients, but this experience accords with other widely reported experience that upwards of two-thirds of patients who die die in the first few days after admission.

This early mortality presents an obvious challenge to therapeutic skills, because if patients could be saved at this stage a worth-while dividend in terms of reduced mortality from coronary disease might be attained.

In order to discover if patients who die early can be saved it is necessary to know why they die. Our own case notes over the period I have mentioned suggested that about half of our patients who died in the first few days died in so-called cardiogenic shock. Other patients died with acute pulmonary oedema, and others died suddenly and unpredictably. This again parallels general experience. However, it is hard to classify modes of dying precisely in retrospect, and it seemed clear that if there was to be any progress in treating these patients some fairly detailed studies would have to be made on them from the moment of their admission to hospital.

There has long been a mass of well-ordered information on the clinical features of the acute infarct state. Laboratory studies too, over the years, have established certain changes, such as leucocytosis, raised erythrocyte sedimentation rate, and raised serum enzyme levels, which are consequences of tissue injury. However, they bear no evident causal relation to early death.

* A London University Special Lecture delivered at St. Mary's Hospital, London, on 17 March 1964.

† Professor of Medicine, University of Melbourne; Honorary Physician to In-patients, Royal Melbourne Hospital, Victoria, Australia.

Other biochemical sequels to infarction have received less attention. Drs. M. L. Mashford, P. J. Nestel, A. E. Doyle, and I made some observations in 1957 in which we compared plasma concentrations and renal clearances of sodium, potassium, and creatinine in patients admitted with myocardial infarction. We tried to relate them to changes in arterial and venous pressure and to cardiac output. The technical difficulties in making observations in these ill people proved to be great and no very consistent pattern emerged. We sometimes found that creatinine clearances were low for several days after admission even though the patient's arterial pressure was not low, perhaps reflecting the consequence of transient impairment of renal blood flow at the time of infarction, or perhaps reflecting continuing low cardiac output. We also sometimes found relatively high potassium and low sodium clearances in the first 24 hours, a situation which commonly occurs as a non-specific response to injury. While pursuit of the mechanisms involved in these changes might have proved interesting, it seemed that, like the laboratory sequels mentioned earlier, these changes had little to do with the cause of early mortality. The heart itself held the key to this problem, and it was the heart and circulation which needed study.

Detailed knowledge of the pathological physiology and pharmacology of the acute infarction state has been meagre for two related reasons. The first has been an understandable reluctance to disturb, in the sense of setting up and using more or less elaborate equipment around, patients many of whom will die within hours whatever happens. The second reason has been, until lately, the feeling that there was little of therapeutic value to offer in these circumstances anyway. This whole situation has changed. Firstly, technological advances have made it possible to monitor circulatory changes with little disturbance to the patient. Secondly, there has been the development of methods of defibrillating the ventricles through the unopened chest. It has long been known that death after cardiac infarction usually reflects either ventricular fibrillation or standstill (Strand and Feil, 1948). A spur to therapeutic effort was initially provided by Beck's (Beck *et al.*, 1956) successful termination of ventricular fibrillation through the open chest after myocardial infarction, and later by the report of similar successful external defibrillation (Nast *et al.*, 1960).

Thirdly, there has been the demonstration of the efficacy of what might be called "holding operations," in the form of closed-chest cardiac compression for sustaining the human circulation together with simple direct methods of artificial respiration.

The stage has therefore been set for study, combined with therapeutic trial.

Observations on Early Death and its Treatment

My colleague Dr. Graeme Sloman of the Royal Melbourne Hospital Cardiac Department was well abreast of these developments when in 1962, with Drs. J. S. Robinson and Colin McRae, and with the support of the National Heart Foundation of Australia, a formal study of patients admitted to the hospital with myocardial infarction was started. The aim was to see exactly what happened to their hearts and circulations, and to attempt revival of those who died.

I would like at this stage to pay tribute to my colleagues on the staff of the Royal Melbourne Hospital. The study of Drs. Robinson, Sloman, and McRae, whose preliminary results I will summarize, as well as the study of more remote sequels to infarction with which I have personally been more directly concerned and which I shall describe later, have been made possible only by the collaboration and forbearance of all the physicians on the staff of the hospital. They have permitted

all patients admitted to the hospital who might benefit by being studied in these ways to come under the supervision of the various study groups. This is an example of co-operative effort which is essential for the advance of knowledge in many branches of medicine but which is nevertheless rather rare.

The preliminary report by Robinson, Sloman, and McRae, which they have kindly let me quote, concerns the first 36 patients with myocardial infarction admitted to the study (Robinson, Sloman, and McRae, 1964). All were males either in pain or within 72 hours of the last episode of pain. They were admitted to a special ward containing two beds, with boards under the mattresses and with bed-heads removed so as to permit easy access to the head. The ward contained equipment for artificial respiration and for external defibrillation, and pacemakers.

On admission the history was taken, physical examination made, and blood taken for various tests. Four electrodes were fixed on the chest wall, permitting free movement of the limbs. Continuous electrocardiographic monitoring was started, using oscilloscopes incorporating heart-rate meters and automatic recorders. Rate-activated alarms were triggered by eight seconds of asystole, or by rises or falls in rate to pre-determined levels. The object was to continue monitoring for 72 hours or until a significant arrhythmia was controlled or terminated.

Table I shows the results in the first 72 hours. On admission patients were grouped in accordance with a classification slightly modified from that proposed by Freis *et al.* (1952).

TABLE I.—*Circulatory Arrest in the First 36 Patients Admitted to the Study in the Royal Melbourne Hospital, and Monitored for 72 Hours (Robinson, Sloman, and McRae, 1964)*

Classification on Admission	No.	Circulatory Arrest with		Course in Subsequent 6 Weeks
		Failed Resuscitation	Successful Resuscitation	
Mild ..	15	0	1. Ventricular fibrillation (age 37) 1. Ventricular fibrillation (age 66)	Survived „
Severe ..	17	1. Asystole (age 71)	1. Asystole (age 55) 1. Asystole (age 76)	Died on 17th day Died on 11th day
Cardiogenic shock	4	1. Asystole (age 71) 1. Asystole (age 46) 1. Asystole (age 65) 1. Asystole (age 67)		
Total ..	36	5 deaths	4 resuscitations	

Of the 15 mild cases 2 had circulatory arrest due to ventricular fibrillation within 72 hours of admission. Both were successfully defibrillated and both survived to return to work. Of the 17 severe cases one had asystole following pulmonary oedema and hypotension, and resuscitation failed. Two had asystole, with successful resuscitation. The heart-beat was restored after external cardiac massage in one, and after external cardiac massage and then needle-prick of the heart in the other. However, both died within the next three weeks, one with sudden ventricular fibrillation and the other, aged 76, with renal failure which followed his asystole. All the four patients with cardiogenic shock died within 72 hours with asystole, and they could not be revived.

Thus, overall, among 36 patients admitted there were nine "deaths" in the first 72 hours, with "revival" in four. Two of the latter died 11 and 17 days later respectively, while two returned to work and are known to be alive many months later.¹

¹ By February 1964 the total number of circulatory arrests due to ventricular fibrillation in the first 12 hours after infarction, in which resuscitation was successful and the patient was discharged from hospital, was three out of a total of 59 patients admitted to the monitoring unit.

In searching for factors that may have precipitated sudden asystole or ventricular fibrillation in these patients, and in others followed, but not continuously monitored, for longer periods in hospital, Robinson, Sloman, and McRae thought that circumstances conducive to emotional stress were sometimes present. This is very hard to determine with certainty. The association of asystole or ventricular fibrillation with such events as visiting-hours or notification of impending discharge from hospital may be no more than a chance one. However, the suggestion that deaths after infarction may be associated with emotional factors is not new. It is interesting in this connexion that Dock in 1928 described a 36-year-old man who suffered recurrent syncope attacks in which, as he said, "the noise made by his children often was the precipitating factor." Dock reported that the electrocardiograph during an attack showed ventricular fibrillation. He proceeded to induce an attack with adrenaline given intravenously and to show that attacks could be prevented with quinidine.

Suggestions of this sort make it important to test the possibility of an association between circulatory arrest and emotion critically, and a prospective comparison is now being made of patients allotted randomly on admission to treatment with light or heavy sedation.

As has been found in other studies in which there has been continuous electrocardiographic monitoring after myocardial infarction (Brown *et al.*, 1963; Julian, 1963), the Royal Melbourne Hospital group have found that arrhythmias of all sorts occur frequently in the first 72 hours. They judge that 75% of their patients showed arrhythmias during this period. Observation of the effect of sedation on these in a controlled trial will be important. Obviously the possibility of recognizing arrhythmias which presage disaster is to be borne in mind.

In this connexion some observations recently made by Dr. Desmond Julian at Sydney Hospital, which he has kindly allowed me to quote, are interesting. He has monitored 100 unselected consecutive patients admitted with the confirmed diagnosis of myocardial infarction, of whom 31 died—the usual hospital mortality. He also found an incidence of arrhythmias of about 75%. Julian has been interested in frequent ventricular ectopic beats, defined as more than one ectopic beat in nine sinus beats. Of the 32 patients who developed those frequent ventricular ectopic beats 41% died, in contrast to 23% of those with less frequent ectopic beats.

I would make two comments on these studies. The first is that they prepare the ground for some clearly defined experiments in applied pharmacology in a situation in which treatment has hitherto been given rather blindly. The second is that at this stage it looks as if the routine monitoring, at any rate of the milder cases of myocardial infarction, and the attempted revival of those developing circulatory arrest, may prove rewarding in terms of lives saved. Many more observations are of course needed before the exact place of monitoring and resuscitation in this illness can be defined.

It also seems clear from these and other studies that cardiogenic shock is a separate problem from that of arrhythmias and cardiac arrest, and merits study in its own right. It seems to me to be a state whose mechanism we understand only dimly. Fejfar (1957) has observed that a low stroke-volume follows quickly on infarction, and Freis *et al.* (1952) have shown that it is this persisting low stroke-volume which chiefly distinguishes the patient in cardiogenic shock after infarction from other patients who have had an infarct. Why this gross impairment of cardiac output continues in some patients and not in others is not clear. So-called "shock" has traditionally been the perquisite of surgical teachers, yet one of the commonest causes of circulatory failure in civilian practice is cardiogenic shock following infarction. The study

of this disordered circulatory state and of its pharmacology presents a very real challenge.

Later Mortality

I am going to mis the sequels of infarction occurring between the first few days and the time of discharge from hospital. In my own wards, as in those of many others, practice during this period of the illness has changed greatly in the past decade. The completeness and duration of initial bed-rest are increasingly tailored to the individual patient, and we now start with the attitude: Is there any reason why the patient should not move about? As a result, most of our patients leave hospital much earlier than they did some years ago. Because of this change in practice I believe the whole story of the sequels occurring in the early weeks after recovery from the acute episode of myocardial infarction needs to be rewritten, and treatments need to be re-evaluated in the context of increased mobility.

With regard to the later sequels, sudden death, and re-infarction which may or may not be fatal, are outstanding. While one must rightly not bother one's patients' with this information, these sequels nevertheless present another challenge to therapeutics.

Ours has been one of a number of groups spread round the world which have been trying critically to evaluate long-term treatment with anticoagulants. Our trial was planned in 1958 and started in 1959.

A Trial with Heparin

Engelberg *et al.* had reported in 1956 that prolonged intermittent heparin treatment (250 mg. subcutaneously twice a week) reduced the mortality in patients who had previously had myocardial infarction. We set out to compare this regimen with a regimen of therapeutic doses of phenprocoumon and a regimen of phenprocoumon in doses insufficient to alter the prothrombin time. The trial was designed so that patients were allocated randomly to one of these three treatment groups.

We decided to limit the heparin regimen to twelve months because of its disturbance to the patient's daily routine, and we followed the results sequentially, using death within or survival for fixed periods as indices of success or failure. By March 1962, using death within or survival for six months as the yardstick, there was no positive indication that heparin treatment was likely to prove better than either phenprocoumon regimen (Denborough *et al.*, 1962). We therefore stopped entry of more patients into the heparin group, but continued treatment of patients already admitted into it so that they could all receive a 12-months course.

By March 1963 all 62 male patients admitted into the heparin group had had a chance to complete a year of treatment and we reviewed the results, comparing the 62 patients treated for a year with heparin with the first 62 patients who had been treated for one year in the other two groups (Lovell *et al.*, 1964). The results are summarized in Table II.

Among 62 patients in each group exposed to risk for twelve months there were nine deaths in the heparin group, eleven

TABLE II.—Results of First 12 Months' Treatment in First 62 Male Patients Entering Each Group

	Heparin Group	Low-dose Phenprocoumon Group	High-dose Phenprocoumon Group
Entered trial	62	62	62
Withdrawn or defaulted ..	5	3	10
Died	9	11	5

in the low-dose phenprocoumon group, and five in the high-dose phenprocoumon group. Patients who defaulted or withdrew were scattered through the groups. The average age of the high-dose phenprocoumon group was by chance, at this time, slightly lower than in the other groups.

Our heparin-treated patients were on average younger than those of Engelberg *et al.* and their myocardial infarctions were more recent. These factors may account for the apparent discrepancy between our findings and those of Engelberg *et al.* However, the highest mortality after discharge from hospital after infarction is in the first year, and we believe an effective treatment should show evidence of benefit in this period. Heparin given in this way showed no promise of doing so in this trial.

Our findings do not, of course, exclude the possibility that heparin in different dosage given with different frequency may modify the course of other clinical varieties of ischaemic heart disease. There are theoretical reasons for supposing that it may have a place, and there have been favourable reports from the U.S.A. on its use in angina which will need confirmation (Hughes *et al.*, 1963).

Our comparison of high- and low-dose phenprocoumon has continued; it has been extended, and now includes about 250 patients. The sequential analysis, in which death within and survival for one year are the indices of failure or success, permits no conclusion at present.

The Long-term Anticoagulant Problem

At this stage I should like to summarize a recent review (Lovell, 1963) of the evidence about long-term treatment with anticoagulants.

Seventeen years after the introduction of the regimen I can quote only six reports, published or summarized in English, of properly designed trials. Table III, which lists them, shows that the evidence we have to consider is derived from a total of about 1,300 patients, of whom about half have been in the "treated" groups. This total is made up by patients who have been studied for periods ranging from a few months to several years. The number studied for more than one year, for instance, is much smaller than these totals. The table

TABLE III.—Trials of Long-term Treatment with Anticoagulants

Authors	Place	No. of Patients
Bjerkelund (1957, 1961)	Oslo	251
M.R.C. (1959); Arnott (1961)	U.K.	383
McMillan <i>et al.</i> (1960); Brown <i>et al.</i> (1961)	Toronto	71
Clausen <i>et al.</i> (1961)	Odense	192
Harvald <i>et al.</i> (1962)	Copenhagen	315
Lovell <i>et al.</i> (1963)	Melbourne	124
Total		1,336

also shows that no single group of workers has studied as many as 200 pairs of patients. I shall give reasons later which suggest that even this number is insufficient to establish the reality of the sort of treatment effects with which we are likely to be dealing, if indeed there are any treatment effects at all.

In examining the results of these trials we are concerned not only with results within individual trials but also with comparing results between trials. The extent to which results of trials can be usefully compared depends on the extent to which the major features of their design and conduct are similar. In all the trials I have mentioned, patients were admitted to hospital initially and allotted to the treatment groups at random. Age ranges have varied from 30 to over 75 years in some trials, to 40 to 69 in others. Both sexes have been studied in some trials, males only in others. The use of anticoagulants in the acute phase has varied; so has the

interval between infarct and admission to the trial. Grounds for exclusion have varied, some medical conditions being excluded in some trials but not in others. The anticoagulants used and the methods for measuring their effects have varied. Evidence for changes in prothrombin time has not always been given. It has been possible to analyse results by age in most trials, but data are rarely sufficient to take sex fully into account. The presentation of a summary of results is made difficult by the mixing of sexes, the variable practice in statistical handling of patients withdrawing and defaulting, and the use of different indices of mortality by different groups. Because of these variations there is obviously no possibility of simply pooling results in the form in which they have so far been published.

Against the background of these limitations and difficulties, let us consider one question, and that is, whether there is a difference in mortality between people in treated and control groups in their first 12 months after entering a trial. Survival is used as a yardstick because it is what really matters, and there is no argument on how to recognize it. I have used a duration of treatment of 12 months because records beyond this are meagre, and peak mortality, which a treatment should influence, occurs within the first year.

Table IV summarizes the results of the first 12-months treatment in the six series. The results are expressed as survival rates. They are very crude, for reasons I have mentioned. For what it is worth Table IV shows, first, that the survival

TABLE IV.—Crude Survival Rates One Year After Entering Trials

Series	No.	Controls	No.	Treated
Bjerkelund (1957)	(118)	0.85	(119)	0.93
M.R.C. (1959)	(160)	0.86	(165)	0.92
Brown <i>et al.</i> (1961)	(22)	0.91	(22)	0.73
Clausen <i>et al.</i> (1961)	(93)	0.93	(99)	0.94
Harvald <i>et al.</i> (1962)	(170)	0.84	(145)	0.90
Lovell <i>et al.</i> (1963)	(62)	0.82	(62)	0.92

rate in control groups has varied from 82% to 93%, and in the treated groups from 73% to 94%. Secondly, it shows that Bjerkelund's and the Medical Research Council's treated groups did better than their controls, Brown and his colleagues' groups did worse, and the groups of Clausen *et al.* both fared practically the same. In Harvald and his colleagues' trial, and in our trial so far, the treated groups have done better than the control groups. In no trial have the differences between survival rates been greater than could have occurred by chance had the treatments been identical.

With regard to survival rates beyond one year, I would just observe that Bjerkelund's (1961) survival rates suggested that a possible initial favourable effect of anticoagulants was sustained over several years. The survival rates of Harvald *et al.* (1961) suggested the same thing when they published them; but by 1962 (Harvald *et al.*, 1962), when the same patients had been exposed to risk for a longer time, any possibly favourable sustained effect had disappeared.

These results favour the possibility that the survival rate in the first year after myocardial infarction may be improved with anticoagulant treatment. However, they certainly do not permit a firm conclusion. There is still a chance that anticoagulants do not modify survival at all. Why is the verdict "Not proven"? I think it is partly because we have only lately, and largely as a result of these studies, been in a position to specify one of the main questions which needs answering: what is the effect of 12 months' treatment on survival? Furthermore, what is involved in trying to answer this question? Consider again the crude overall survival rates at 12 months in Table IV. The survival rate of control patients at one year is somewhat over 80%. If treatment with anticoagulants modifies mortality, it appears possible that survival may be at most a little over 90%. Remembering

these survival rates, we can now state the question, using round figures, how many patients must we expect to study to ensure that an increase from 80% to 90% survival would demonstrate itself by giving a result of appropriate significance? Dr. G. H. Jowett, Reader in Statistics in the University of Melbourne, tells me that the answer depends on the design of the trial. In a trial of predetermined length we would need about 600 patients. In a sequential trial, such as we are using in Melbourne, with average luck we would expect to need about 450 patients, though there is a 1 in 40 chance that we might be unlucky enough to need 900. If the difference in survival were smaller, as it seems from Table IV that it may be, we would need more patients. The answer to "why is the verdict 'not proven'?" is simply that enough patients have not yet been studied in any of the trials. I have suggested elsewhere (Lovell, 1963) that this problem of numbers might be overcome at this stage by some international collaboration.

I want to make one final point about long-term treatment with anticoagulants. It seems possible that extension of studies such as these I have quoted could establish before long that survival rates, in the first 12 months of treatment, may be changed, on average, from between 80% and 85% to about 90%. All the work leading to this possible conclusion will have been done on patients admitted to hospital initially and supervised subsequently by small groups of physicians interested, experienced, and expert in coping with the problems and dangers of anticoagulants. It could not be assumed that similar results would necessarily be obtained in a population different from public-hospital patients and supervised by doctors with less opportunity to become interested and experienced. If a difference were proved in these hospital populations, and was considered worth attaining, I believe a compelling case would arise for examining this regimen in a broader field of practice before it could be regarded as standard therapeutics.

Re-employment

I have dealt so far only with the sequels to infarction, in terms of life and death. I should like now to consider briefly two sequels which, while less dramatic, nevertheless provide us with therapeutic challenges. One sequel involves financial disaster and the other is pain in the chest, and these are sometimes related.

A valuable dividend paid to the physician by a long-term trial of treatment is the insight it gives him into the problems which face many patients discharged from hospital after myocardial infarction. In this connexion we have been singularly fortunate in having Dr. Alan Goble, cardiologist at the Royal Melbourne Hospital, associated with our long-term trial at a time when he was also establishing a neighbouring work-assessment centre for cardiac patients. Goble has rightly emphasized that an outstanding problem which faces the average male patient after infarction is his fitness for re-employment. This is determined by many factors. A very small proportion of patients are left as cardiac cripples. A larger proportion come to believe for various reasons that they are cardiac cripples. This belief is induced in many ways. They know from press, radio, and television that the No. 1 killer has been at them. They anticipate sudden death. There arises a situation in which "patients dare not lift their hands above their heads, walk upstairs, lie on their left side, lift light objects, use their arms, or lose their tempers" (Goble *et al.*, 1963).

I doubt if, as doctors, we appreciate the size of this problem of unnecessary invalidism or near invalidism, nor do we realize our own contribution to it. Sometimes it is blatant. There is a story current in Australia of a patient who had a

myocardial infarction and returned from hospital to his home half-way up a gently sloping road. His doctor lived one block up. After a statutory period of continued but not clearly specified rest at home the patient one day set out to call on his doctor. Having feared to walk further than the lavatory for many weeks, he was not unnaturally a little breathless when he reached his doctor's consulting-room. "Doc," he said, "they've let me out of hospital, but I'm b—ed." "Jim," replied his doctor, "I knew you were b—ed the day you had your heart attack, but you're such a pigheaded old b—— that I thought I'd leave you to find it out for yourself."

I don't suggest that we often convey this idea to our patients in these terms, but I do think we convey it more subtly, albeit unwittingly, as Goble *et al.* suggest, by giving certificates for "fitness for light work" and by replying to the question "How am I getting on?" by saying "You'll be all right if you are careful," which to the patient may mean "If I'm not careful I'll drop dead or have another attack."

This is a complex problem with ramifications involving insurance and other benefits, policy in industry, public education, and so on. In Melbourne, at any rate, it appears to be quite a large one. Goble *et al.* assessed 42% of unemployed cardiac patients referred to the Work Assessment Centre as employable at initial assessment and only 21% as permanently unemployable. The rest were assessed as unemployable when interviewed, but as those who might become fit for work: they were predominantly disabled psychologically.

Chest Pains

Following up patients who have survived myocardial infarction, we have been impressed with the frequency with which pain or discomfort in the chest bothers both patients and their doctors and is a factor leading to anxiety and thence sometimes to the sort of unnecessary invalidism I have been discussing. While those of us working in the long-term treatment believed that most of the pains were angina, we realized that many were not, and in discussion it was evident that there was no unanimity on whether, after myocardial infarction, there was any other single common pattern of chest pain apart from angina. Dr. Aubrey Pitt and I, therefore, modifying a questionnaire designed by Dr. G. A. Rose of the London School of Hygiene (Rose, 1962), set out to examine this matter. We have questioned so far 118 unselected male patients attending our clinic who have all had myocardial infarction between six months and three years previously.

The first question was, "Since your last discharge from hospital have you had any pain or discomfort in the chest?" The second question was, "Can you recognize more than one type of pain or discomfort?" Forty-five per cent. replied "No" to the first question. The 55% who replied "Yes" were made up of 41.5% who recognized one type of pain and 13.5% who recognized more than one type. Thus the recognition by patients of more than one type of pain was not rare.

In order to classify pains we used Rose's (Rose, 1962) admittedly restrictive definition of effort angina. About two-thirds of the pains fulfilled his criteria and one-third did not.

Table V shows pains other than effort angina, classified by site. Some of these pains are certainly angina associated with circumstances other than effort. For instance, two of the ten sternal pains were evoked by emotion but not by effort. However, outstandingly the commonest pain other than effort angina is one confined to the left chest anteriorly. Unlike effort angina which may have preceded the myocardial infarct, this left chest pain always follows it. It differs from effort angina in other interesting ways, and while it may be likened to the pain of effort syndrome or cardiac neurosis, likening it does not explain it. It would be nice to know more about

TABLE V.—*Sites of Chest Pains Other than Effort Angina*

Site	No. of Pains
Over sternum	10
Left anterior chest only	24
Left anterior chest and left arm	1
Right chest	3
Total	38

it, but the point of immediate practical importance is not what we think it is but what patients think it is.

In reply to the question "Do you believe your pain is due to heart disease?" 73% of patients with effort angina and 71% of patients with left chest pain said "Yes." Thus patients generally believe left chest pain is due to heart disease, and, since it dates from an illness with severe chest pain, this is scarcely surprising.

The point I would stress is that these painful sequels of myocardial infarction are exceedingly common. Patients don't always volunteer them but they do often worry about them. Part of the treatment after myocardial infarction is to get the patient back to work physically fit and mentally unperturbed. This process of rehabilitation should include specific inquiry about chest pains, bearing in mind that these pains are often multiple and that the patient may find left chest pain and other non-anginal pains more frightening and disabling than effort angina, which he may come to tolerate as a predictable and familiar companion. Even though one may not be able to cure his pain, restoration of confidence to a patient with chest pain after myocardial infarction is a most rewarding therapeutic exercise.

Conclusion

These, then, are some of the sequels of myocardial infarction.

In the acute stage, monitoring of the circulation and resuscitation may prove useful though their place in routine practice is still uncertain.

Cardiogenic shock presents an outstanding challenge.

The long-term anticoagulant problem is falling into perspective. It seems clear that anticoagulants, if useful at all, will prove of pretty restricted value.

Imperfect rehabilitation after myocardial infarction produces a toll of misery, and this is often triggered by symptoms of chest pains whose mechanisms we have yet to discover.

Having sketched these headlines, I would end with the perhaps obvious comment that, though it is the sequels which engage us in day-to-day practice, in fact in treating them we are shutting the stable door after the horse has gone. Myocardial infarction, this epidemic disease of our time, presents above all else a problem in preventive medicine.

REFERENCES

- Arnott, W. M. (1961). In *Anticoagulants and Fibrinolysins*, edited by R. L. Macmillan and J. F. Mustard. Pitman, London.
- Beck, C. S., Weckesser, E. C., and Barry, F. M. (1956). *J. Amer. med. Ass.*, **161**, 434.
- Bjerkelund, C. J. (1957). *Acta med. scand.*, Suppl. 330.
- (1961). In *Anticoagulants and Fibrinolysins*, edited by R. L. Macmillan and J. F. Mustard. Pitman, London.
- Brown, K. W. G., Macmillan, R. L., Forbath, N., Meligrana, F., and Scott, J. W. (1963). *Lancet*, **2**, 349.
- and Noble, E. J. G. (1961). In *Anticoagulants and Fibrinolysins*, edited by R. L. Macmillan and J. F. Mustard. Pitman, London.
- Clausen, J., Andersen, P. E., Andersen, P., Gruelund, Sv., Harslof, E., Andersen, U. H., Jorgensen, J., and Mose, C. (1961). *Ugeskr. Læg.*, **123**, 987.
- Denborough, M. A., Goble, A. J., Lovell, R. R. H., and Nestel, P. J. (1962). *Med. J. Aust.*, **2**, 937.
- Dock, W. (1929). *Amer. Heart J.*, **4**, 709.
- Engelberg, H., Kuhn, R., and Steinman, M. (1956). *Circulation*, **13**, 489.
- Fejfar, Z. (1959). *Adv. Cardiol.*, **2**, 108. Karger, Basel, New York.
- Freis, E. D., Schnafer, H. W., Johnson, R. L., and Shreiner, G. E. (1952). *J. clin. Invest.*, **31**, 131.
- Goble, A. J., Adey, G. M., and Bullen, J. F. (1963). *Med. J. Aust.*, **11**, 975.
- Harvald, B., Hilden, T., Letman, H., Lund, E., Thaysen, E. H., and Worning, H. (1961). *Ugeskr. Læg.*, **123**, 983.
- and Lund, E. (1962). *Lancet*, **2**, 626.
- Julian, D. G., Valentine, P. A., and Miller, G. G. (1964). *Med. J. Aust.*, **1**, 433.
- Kannel, W. B., Dawber, T. R., Kagan, A., Revorskie, N., and Stokes, J. (1961). *Ann. intern. Med.*, **55**, 33.
- Lovell, R. R. H. (1963). *Med. J. Aust.*, **11**, 915.
- Denborough, M. A., Nestel, P. J., and Goble, A. J. (1964). *Arch. intern. Med.*, **113**, 267.
- Macmillan, R. L., Brown, K. W. G., and Watt, D. L. (1960). *Canad. med. Ass. J.*, **83**, 567.
- Medical Research Council (1959). *Brit. med. J.*, **1**, 803.
- Nast, P. R., Pennypacker, C. S., and Wagner, J. A. (1960). *Circulation*, **22**, 138.
- Paul, O., Lepper, M. H., Phelan, W. H., Dupertuis, G. W., Macmillan, A., McKean, H., and Park, H. (1963). *Circulation*, **28**, 20.
- Robinson, J. S., Sloman, G., and McRae, C. (1964). *Med. J. Aust.*, **1**, 427.
- Rose, G. A. (1962). *Bull. Wld Hlth Org.*, **27**, 645.
- Strand, M. W., and Feil, H. S. (1948). *Amer. Heart J.*, **35**, 910.

Nosematosis, a Microsporidial Infection of Rodents and Other Animals, Including Man

R. LAINSON,* PH.D.; P. C. C. GARNHAM,* C.M.G., M.D., F.R.S.

R. KILLICK-KENDRICK*; R. G. BIRD,* PH.D., M.B.

[WITH SPECIAL PLATE]

Brit. med. J., 1964, **2**, 470-472

The natural occurrence of aggregations of small organisms in the brain of mammals has been noted with increasing frequency over the past fifty years. Such parasites have variously been described as *Toxoplasma gondii*, *Trypanosoma cruzi*, "M" organism, or *Encephalitozoon*.

* From the London School of Hygiene and Tropical Medicine, London.

The identity of *Toxoplasma gondii* and *Trypanosoma cruzi* presents no serious problem in adequately prepared material, but the nature of *Encephalitozoon* has puzzled workers since the time it was first described and named by Levaditi *et al.* (1923) in the brain of rabbits suffering from encephalitis.

A connexion between *Encephalitozoon* and human disease was soon sought by these same authors (Levaditi *et al.*, 1924a);