Discussion

The six minute corridor walk[8] is an accurate, routine standard test of effort tolerance in patients with respiratory disease. Use of the test and the design of this study appeared to have been satisfactory in that variations in walking distances were not prejudiced by walking order, experience, or training effects. Patients were selected carefully so as to exclude only those who might be considered as suffering from chronic asthma. The population studied was therefore representative of patients whom we commonly encounter with chronic bronchitis due to cigarette smoking.

As with some single dose studies of theophylline in chronic bronchitis[2] the incremental dosages used here produced no useful improvement in spirometric values. Neither effort tolerance nor concomitant dyspnoea appeared to be influenced by the drug, even when unacceptably high dosages were used. The results were similar for those subjects who showed small improvements in PEFR and for those with or without accompanying emphysema.

Leitch *et al* reported a 6% improvement in 12 minute distances with oral slow aminophylline.[6] Their results, however, were not confirmed or reproduced by Eaton *et al* in patients with chronic airflow obstruction, who did show significant improvement in spirometric function with oral theophylline.[7] Interestingly, my results show that an improvement of 7% can be obtained with placebo alone.

Nineteen of the 20 subjects in this study with chronic bronchitis had previously been prescribed long term oral theophylline, and the use of the drug in this condition is common practice. The role of theophylline in chronic bronchitis appears to be less controversial than before, but the routine, indiscriminate use of the drug in these patients seems difficult to justify.

I thank Mr M S Pickering and Mr A Milbourn, East Anglian Regional Health Authority, for statistical advice and Miss J Ridout and Miss O F Jones for typing the manuscript.

References

1 Eaton ML, Green BA, Church TR, McGowan T, Niewoehner DE. Efficacy of theophylline in "irreversible" airflow obstruction. *Ann Intern Med* 1980;**92**: 758-61.
2 Jenkins PF, White JP, Jariwalla AJ, Anderson S, Campbell IA. A controlled study of slow release theophylline and aminophylline in patients with chronic bronchitis. *Br J Dis Chest* 1982;**76**:57-60.
3 Huidobro F. A comparative study of the effectiveness of 137 trimethylxanthine and certain dimethylxanthines (1, 3-dimethylxanthine and 3, 7-dimethylxanthine) against fatigue. *J Pharmacol Exp Ther* 1945;**84**:380-6.
4 Ritchie JM. Central nervous system stimulants: xanthines. In: Goodman LS, Gilman A, eds. *The pharmacological basis of therapeutics*. 5th ed. New York: Macmillan, 1975:367-78.
5 Aubier MA, De Troyer A, Sampson M, Macklem PT, Roussos L. Aminophylline improves diaphragmatic contractility. *N Engl J Med* 1981;**305**:249-52.
6 Leitch AG, Morgan A, Ellis DA, Bell G, Haslett C, McHardy GJR. Effect of oral salbutamol and slow release aminophylline on exercise tolerance in chronic bronchitis. *Thorax* 1981;**36**:787-9.
7 Eaton ML, Macdonald FM, Church TR, Niewoehner DE. Effects of theophylline on breathlessness and exercise tolerance in patients with chronic airflow obstruction. *Chest* 1982;**82**,5:538-42.
8 Butland RJA, Pang J, Gross ER, Woodcock AA, Geddes DM. Two-, six-, and 12-minute walking tests in respiratory disease. *Br Med J* 1982;**284**:1607-8.

(*Accepted 8 October 1984*)

How soon after myocardial infarction should plasma lipid values be assessed?

R E J RYDER, T M HAYES, I P MULLIGAN, J C KINGSWOOD, S WILLIAMS, D R OWENS

Abstract

Because acute myocardial infarction may affect plasma lipid concentrations it is commonly recommended that assessment of these concentrations should be delayed until about three months after the acute event. A study was therefore conducted of fasting plasma lipid concentrations in 58 patients with acute myocardial infarction. Measurements were made during their stay in hospital (days 1, 2, and 9) and three months later.

Triglyceride concentrations remained unchanged throughout. Values of total cholesterol, low density lipoprotein, and high density lipoprotein all fell significantly between the first two days and day 9. Total cholesterol and low density lipoprotein also showed significant falls between days 1 and 2. Nevertheless, fasting plasma lipid concentrations showed no significant difference at any time during the first 48 hours from values measured three months later. After the infarction 26 patients changed to eating less fat or less energy, or both. More patients had hypercholesterolaemia in the first 48 hours than at three months.

These results suggest that lipid state may be assessed as accurately, and possibly more accurately, during the first 48 hours after acute myocardial infarction than at three months.

Department of Medicine, University Hospital of Wales and Welsh National School of Medicine, Heath Park, Cardiff CF4 4XW
R E J RYDER, MB, MRCP, research fellow
T M HAYES, MB, FRCP, consultant physician
S WILLIAMS, AIMLT, research technician
D R OWENS, MB, BCH, lecturer

Department of Cardiology, University Hospital of Wales, Heath Park, Cardiff CF4 4XW
I P MULLIGAN, MB, MRCP, registrar

Llandough Hospital, Llandough, Penarth, South Glamorgan CF6 1XX
J C KINGSWOOD, MB, MRCP, registrar

Correspondence to: Dr R E J Ryder.

Introduction

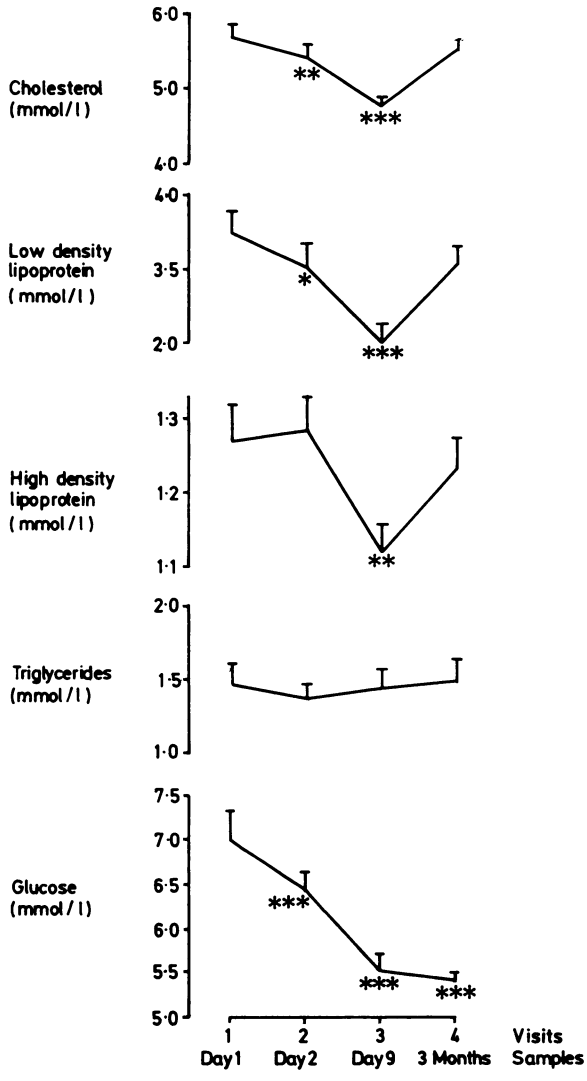
Current clinical convention dictates that because acute myocardial infarction may affect plasma lipid concentrations lipid measurement for the detection of hyperlipidaemia should be deferred until two to three months after the acute event.[1-4] We have re-examined the effect of acute myocardial infarction on plasma lipid values to see if these can be meaningfully assessed during the hospital admission.

Patients and methods

We studied 58 patients who survived for three months after myocardial infarction. All had been admitted to the coronary care

unit and were diagnosed as having had an acute myocardial infarction on the basis of history, unequivocal changes in the electrocardiogram, and a diagnostic rise in cardiac enzyme activities. Thirty eight of the patients were men and 20 women, and their mean age was 57 (range 26-73).

Fasting (overnight from 10 pm) blood samples were taken as soon as possible after admission (day 1; average 23 hours after estimated onset of infarction), 24 hours later (day 2), shortly before discharge (day 9), and, finally, about three months later (average 13½ weeks).



Mean fasting plasma lipid and glucose concentrations after myocardial infarction in 58 patients. Bars are SEM. Compared with day 1: *p < 0·05; **p < 0·01; ***p < 0·001.

Conversion: SI to traditional units—Glucose: 1 mmol/l ≈ 18 mg/100 ml. Triglyceride: 1 mmol/l ≈ 88·4 mg/100 ml. High density lipoprotein, low density lipoprotein, and cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml.

Concentrations of plasma total cholesterol and triglycerides (Boehringer enzymatic methods), low density lipoprotein and high density lipoprotein (heparin manganese chloride precipitation methods), and glucose (glucose oxidase) were measured in each sample. The results were not examined until after the end of the study, so that patient management—in particular, diet—was not influenced by them. Changes in dietary intake and smoking habits were noted at three months. Significance was assessed by the paired *t* test.

Results

The figure gives the results of analysis for the group as a whole. Triglyceride concentrations showed no significant change during the study. Total cholesterol ($p < 0·001$), low density lipoprotein ($p < 0·001$), high density lipoprotein ($p < 0·01$), and glucose ($p < 0·001$) all showed significant falls between days 1 and 9. Nevertheless, although there was a significant fall in total cholesterol by day 2, there was no significant difference in value of total cholesterol, low density lipoprotein, or high density lipoprotein between either day 1 or 2 and three months. Of the 19 patients who had raised total cholesterol concentrations (over 6·0 mmol/l (232 mg/100 ml)) three months after myocardial infarction, 13 (68%) had had raised values on day 1 or 2. Conversely, of the 27 patients whose total cholesterol concentration exceeded 6·0 mmol/l shortly after the infarct (day 1 or 2), only 13 (48%) had high total cholesterol values at three months. The only patient whose total cholesterol concentration was over 8·0 mmol/l (309 mg/100 ml) at three months also had similarly high values on days 1 and 2. Nevertheless, none of the other four patients (including the only patient in the study previously known to have type IIb hyperlipidaemia) with total cholesterol values over 8 mmol/l on day 1 or 2 had values this high at three months. During the three months these patients had lost weight and were eating less fat. Furthermore, 26 of all 58 patients studied (45%) admitted to eating less energy or less fat, or both, at three months.

The changes in glucose values were compatible with initial stress hyperglycaemia, which rapidly recovered. At the time of the infarct 27 (47%) of the patients were smokers; at three months 16 (60%) had stopped smoking and six (22%) were smoking less.

Discussion

Our study confirms reports that concentrations of plasma total cholesterol[5-13] and low density lipoprotein[12 13] fall significantly after acute myocardial infarction, whereas triglyceride values remain unchanged.[8 11] We also found a significant fall in high density lipoprotein. Other studies reporting that values of total cholesterol[14] and high density lipoprotein[12-14] do not change after acute myocardial infarction were carried out on smaller numbers of patients; they did, however, tend to show trends in keeping with our results. Those smaller studies also reported a significant rise in triglyceride values, which we were not able to confirm.

Lipid state is usually not assessed while the patient is in hospital immediately after myocardial infarction because of the effect of the infarction on plasma lipid concentrations, which we have confirmed. We, however, could find no significant difference between plasma lipid values measured during the first 48 hours after myocardial infarction and those measured three months later. This confirms the work of Fyfe *et al*, who concluded that hyperlipidaemic states could be identified during the 24 hours after myocardial infarction.[11] Twenty six of our patients (45%) changed to eating less fat or energy, or both, as a result of the heart attack, so it may be that the sample taken in the first 48 hours gave a more accurate reflection of previous lipid state than the one at three months. High total cholesterol values at three months were more likely to be detected during the first 48 hours than were high total cholesterol values in the first 48 hours to be followed by high values at three months. Thus underlying hypercholesterolaemia may be detected more easily in the first 48 hours than at three months.

The association between the incidence of coronary artery disease and total plasma cholesterol concentration is well established.[15 16] The low density lipoprotein subfraction is mainly responsible for this relation, while values of high density lipoprotein are inversely related.[17 18] In view of this close link between cholesterol concentrations and coronary artery disease and the accumulating evidence that treating hypercholesterolaemia in middle aged men may reduce mortality and morbidity from ischaemic heart disease,[19 20] plasma lipid assessment is very important in patients who have had a myocardial infarction.[21 22] It is frequently overlooked at the follow up attendances at busy hospital outpatient departments or general practitioners' surgeries in the months after discharge from hospital. In order to identify patients requiring follow up plasma lipid values may be routinely examined during the first two days after a myocardial infarction.

We thank Mr C J Davies and Mr S Luzio for technical help.

References

1 Buckley BM, Bold AM. Managing hyperlipidaemias. *Br Med J* 1982;**285**:1293-4.
2 Schlant RC, Digirolamo M. Modification of risk factor in the prevention and management of coronary atherosclerotic heart disease. In: Hurst JW, Logue RB, Schlant RC, Wenger NK, eds. *The heart*. 4th ed. New York: McGraw Hill Book Co, 1978:1311-44.
3 Levy RI, Manning F. Risk factors for coronary artery disease and their management. In: Braunwald E, ed. *Heart disease, a textbook of cardiovascular medicine*. Philadelphia: WB Saunders, 1980:1246-78.
4 Lewis B. Disorders of plasma lipid transport. In: Scott RB, ed. *Price's textbook of the practice of medicine*. 12th ed. Oxford: Oxford University Press, 1978:426-32.
5 Biorck G, Blomquist G, Sievers J. Cholesterol values in patients with myocardial infarction and in a normal control group. *Acta Med Scand* 1957;**156**:493-7.
6 Bjorntorp P, Malmcrona R. Serum cholesterol in patients with myocardial infarction in younger ages. *Acta Med Scand* 1960;**168**:151-5.
7 Dodds C, Mills GL. Influence of myocardial infarction on plasma-lipoprotein concentration. *Lancet* 1959;i:1160-3.
8 Kirkby K. Disturbances in serum lipids and in their fatty acid composition following acute myocardial infarction. *Acta Med Scand* 1972;**192**:523-8.
9 Tibblin G, Cramer K. Serum lipids during the course of acute myocardial infarction and one year afterwards. *Acta Med Scand* 1963;**174**:451-5.
10 Welin G. Serum cholesterol in myocardial infarction. *Nord Med* 1948;**37**:324-6.
11 Fyfe T, Baxter RH, Cochran KM, Booth EM. Plasma lipid changes after myocardial infarction. *Lancet* 1971;ii:997-1001.
12 Avogaro A, Bittilo Bon G, Cazzalato C, *et al*. Variations in apolipoproteins B and A during the course of myocardial infarction. *Eur J Clin Invest* 1978;**8**:121-9.
13 Ballantyne FC, Melville DA, McKenna JP, Morrison BA, Ballantyne D. Response of plasma lipoproteins and acute phase proteins to myocardial infarction. *Clin Chim Acta* 1979;**99**:85-92.
14 Heldenburg D, Rubenstein A, Levtov O, Berns L, Werbin B, Tamir L. Serum lipids and lipoprotein concentrations during the acute phase of myocardial infarction. *Atherosclerosis* 1980;**35**:433-7.
15 Keys A, Aravanis C, Blackburn H, *et al*. Probability of middle aged men developing coronary heart disease in five years. *Circulation* 1972;**45**:815-28.
16 Pooling Project Research Group. Relationship of blood pressure, serum cholesterol, smoking habit, relative weight, and ECG abnormalities to incidence of major coronary events. Final report of the pooling project. *J Chronic Dis* 1978;**131**:201-306.
17 Heiss G, Johnson NJ, Reiland S, Davis CE, Tyroler HA. The epidemiology of plasma high density lipoprotein cholesterol levels. The Lipid Research Clinics Program prevalence study: summary. *Circulation* 1980;**62**(suppl 4):116-36.
18 Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High density lipoprotein as a protective factor against coronary heart disease: the Framingham study. *Am J Med* 1977;**62**:707-14.
19 Lipid Research Clinics Program. The lipid research clinics coronary primary prevention trial results: 1. Reduction in incidence of coronary heart disease. *JAMA* 1984;**251**:351-64.
20 Lipid Research Clinics Program. The lipid research clinics coronary primary prevention trial results: 2. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. *JAMA* 1984;**251**:365-74.
21 Rosenhamer G, Carlson LA. Effect of combined clofibrate-nicotinic acid treatment in ischaemic heart disease. *Atherosclerosis* 1980;**37**:129-38.
22 International Society and Federation of Cardiology Scientific Councils on Arteriosclerosis, Epidemiology and Prevention, and Rehabilitation. Joint recommendations. Secondary prevention in survivors of myocardial infarction. *Br Med J* 1981;**282**:894-6.

(*Accepted 29 August 1984*)

Fast neutron treatment as an alternative to radical surgery for malignant tumours of the facial area

MARY CATTERALL, P R BLAKE, R P RAMPLING

Abstract

Thirty one patients with very advanced tumours of the maxillary sinus were treated with fast neutrons. Tumour regressed completely in 29 (94%) and subsequently recurred in four (14%). No surgical excision of bone, skin, or nerve was required, and an artificial eye was well tolerated in cases where the eye received the tumour dose and had to be removed. Complications occurred in 10 patients, two of whom had already received radical *x* ray treatment. The overall duration of neutron treatment was four weeks, and admission to hospital was usually unnecessary. These results compared well with those obtained with surgery. Surgery with curative intent for even moderately advanced tumours of the facial region, particularly the paranasal sinuses, results in deformity, which is often severe and always irreversible. Even so, the cure rate is only about 35%.

The high rates of tumour control and the avoidance of severe cosmetic and functional defects after fast neutron treatment make it an alternative to radical surgery in the management of malignant tumours of the facial area.

Fast Neutron Clinic, Medical Research Council Cyclotron Unit, Hammersmith Hospital, London W12 0HS

MARY CATTERALL, FRCR, DSC, consultant
P R BLAKE, FRCR, senior registrar
R P RAMPLING, MRCP, PHD, registrar

Correspondence to: Dr M Catterall.

Introduction

Coverage has recently been given in the national press and on television to a group of people whose aim is to give support to patients who have undergone radical surgery for the removal of tumours of the face. This has drawn attention to the plight of these patients, relatively few in number and rarely seen in public. Their disabilities result from removal of the entire bony orbit, maxilla, or facial nerve and from construction of forehead or chest skin flaps, leaving cosmetic results that often cause them severely to restrict their social lives.[1 2] Skilfully designed prostheses, understanding relatives, and support groups all help to lessen the effects of this morbidity. Morbidity is, however, unalterable for the rest of their lives unless the tumour recurs, when even further surgery, phototherapy, or laser beam surgery may be undertaken.

Tumours of the paranasal sinuses are often advanced when the patients are first seen and the bone is often affected. Some are "radioresistant" because of hypoxia or some other biological property and they also have a great propensity to spread along nerves or tissue planes.[3] These factors make their control by γ and *x* rays difficult because the high doses required to sterilise the tumour are beyond the tolerance of the adjacent normal tissues. Radiation damage to bone and nervous tissue often appears in addition to recurrence of tumour. Thus the management of these tumours usually consists of a combination of surgery and radiation.[2]

Fast neutrons have different biological effects from *x* rays, and these differences result in therapeutic advantages in treating locally advanced or radioresistant tumour in certain sites.[4] Neutrons are more effective against hypoxic malignant cells, and the damage they inflict is usually lethal rather than repairable as it often is after *x* rays. Furthermore, neutrons are absorbed by tissues in proportion to the concentration of hydrogen atoms. Consequently, soft tissues, which include tumours, absorb relatively more neutron energy and suffer greater damage than does bone. As bone is a dose limiting