from two patients with sarcoidosis was confirmed by sequencing of cloned polymerase chain reaction product and shown to be identical with the *M tuberculosis* sequence.

The importance of our findings should not be dismissed by ill considered interpretation of additional data.

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1 Eisenach KD, Cave MD, Bates JH, Crawford JT. Polymerase chain reaction amplification of a repetitive DNA sequence specific for Mycobacterium tuberculosis. *J Infect Dis* 1990; **161**:977-81.
2 Hermans PWM, Van Soolengen D, Dale JW. Insertion element IS986 from Mycobacterium tuberculosis: a useful tool for diagnosis and epidemiology of tuberculosis. *J Clin Microbiol* 1990;**28**:2051-8.
3 Bocart D, Lecossier D, De Lassence A, Valeyre D, Battesti J, Hance AJ. A search for mycobacterial DNA in granulomatous tissues from patients with sarcoidosis using the polymerase chain reaction. *Am Rev Respir Dis* 1992;**145**:1142-8.

Further clues from skin testing

EDITOR,—The polymerase chain reaction study of Helen M Fidler and colleagues showed that *Mycobacterium tuberculosis* DNA was present in the granulomatous tissues of seven of 16 patients with sarcoidosis.[1] Sarcoid granuloma can be reproduced in sensitised individuals by intradermal skin testing with the purified protein derivative of *M tuberculosis*.[2] We found that five of 50 black men developed histologically proved sarcoid granulomas at the sites of injection of 0·05 ml of first strength purified protein derivative (25 ng). Although these five men were healthy, without evidence of sarcoidosis, the findings showed that they had acquired a specific immune granuloma type sensitivity. Accordingly, they were at risk of developing sarcoidosis if exposed to sufficient numbers of *M tuberculosis* bacilli.

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1 Fidler HM, Rook GA, Johnson NM, McFadden J. *Mycobacterium tuberculosis* DNA in tissues affected by sarcoidosis. *BMJ* 1993;**306**:546-9. (27 February.)
2 Hurley HJ, Shelley WB. Sarcoid granulomas after intradermal tuberculin in normal human skin. *Arch Dermatol* 1960;**82**: 119-26.

Cardiac rehabilitation

EDITOR,—The recent article by T P Chua and David P Lipkin emphasises the importance of exercise in the role of cardiac rehabilitation.[1] Those of us who are exercise enthusiasts support such a notion and wonder why regular aerobic exercise is not prescribed more widely, as a prophylactic against the onset of coronary heart disease in the first instance, as well as for postinfarct rehabilitation. However, drug therapy also has an important role in reducing death from coronary heart disease. After an infarction, ß blockers are highly effective in reducing the risk of reinfarction and sudden death.[2] Patients might benefit from combined drug and exercise therapy during cardiac rehabilitation, providing of course that the two treatments are compatible. The choice of ß blocker is critical if the patient is to continue an exercise regimen. Some drugs may severely reduce a patient's motivation to exercise and also reduce the metabolic fuel available during exercise.

Percentage contribution of fat oxidation to total energy expenditure

	Mean	(SD)	Significance (compared to placebo)
Placebo	36·1	(10·3)	
Non-selective	25·5	(7·3)	p=0·0014
$ß_1$-selective	28·6	(10·6)	p=0·2494

Having observed that lipid lowering drugs differ in their impact upon exercise capacity,[3] we compared the effects of $ß_1$ selective and non-selective ß blockers on exercise metabolism, perceived exertion, and mood states of 20 healthy volunteers during one hour of treadmill walking at 50% of subjects' maximum oxygen consumption. At one hour, compared with placebo, fat oxidation was significantly reduced with non-selective ß blockade, whereas $ß_1$ selective blockade had no significant impact (table).

The advantages of selective ß blockers were also apparent from subjects' perceived exertion: a $ß_1$ selective drug did not significantly increase "leg effort" compared to placebo (p=0·1660), whereas a non-selective drug did (p=0·0099).

Non-selective ß blockers also altered mood (measured by the profile of mood states[4]), reducing "vigour" (p=0·0208), increasing "depression" (p=0·0428), increasing "fatigue" after exercise (p=0·0406), and increasing "confusion" (p=0·0483). A $ß_1$ selective drug had no adverse effects on mood states.

After a myocardial infarction, ß blockers and exercise should be compatible treatments, particularly with a $ß_1$ selective drug, since patients' motivation and capacity to exercise are not greatly altered. Our aim is to identify drugs which most suitably complement the valuable postinfarct exercise therapy, while simultaneously achieving the best possible cardioprotective effects.

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1 Chua TP, Lipkin DP. Cardiac rehabilitation. *BMJ* 1993;**306**: 731-2.
2 Olssen G, Wikstrand J, Warnold I, Manger Cats V, McBoyle D, Herlitz J, *et al*. Metoprolol-induced reduction in post-infarction mortality: pooled results from five double blind randomised trials. *Eur Heart J* 1992;**13**:28-32.
3 Head A, Jakeman PM, Kendall MJ, Cramb R, Maxwell S. The impact of a short course of three lipid lowering drugs on exercise metabolism. *Postgrad Med J* 1993;**69**:197-203.
4 McNair DM, Lorr M, Droppleman LF. *Profile of mood states*. San Diego, 1971.

Gangliosides in neurological diseases

EDITOR,—The evidence that the incidence of Guillain-Barré syndrome is increased after treatment with gangliosides has been robustly challenged,[1] but the possible role of immune responses to gangliosides should not be ignored. Although low titre antibodies to ganglioside GM1 are present in a wide range of neurological conditions and autoimmune diseases, high titre IgM antibodies, sometimes monoclonal, are associated with disorders affecting the lower motor neuron, and high titre IgG antibodies are associated with particularly severe Guillain-Barré syndrome.[2] Antibodies to ganglioside LM1, the most abundant ganglioside in peripheral nerve myelin, have been discovered more frequently in patients with Guillain-Barré syndrome and chronic idiopathic demyelinating polyradiculoneuropathy than in controls.[3] There is a strict association between antibodies to ganglioside GQ1b and the Miller Fisher variant of Guillain-Barré syndrome.[4]

Apart from a report that the serum from one patient with antibodies to ganglioside GM1 induced conduction block following intraneural injection,[5] we agree that there is little direct evidence that immune responses to gangliosides are harmful. However, immune responses to gangliosides are difficult to elicit in experimental animals. Strong immune responses to individual gangliosides occur in humans in clinically relevant settings and deserve further investigation as important components of the pathogenesis of some peripheral nervous system diseases. A possible increase in the incidence of a disease as rare as Guillain-Barré syndrome (incidence 1-2 per 100 000) after treatment with gangliosides is difficult to disprove, and continued vigilance would be appropriate as further trials are undertaken.

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1 Gibbs CJ, McKhann GM, Walsh FS, Yu RK. Gangliosides in neurological diseases. *BMJ* 1993;**306**:655-6. (6 March.)
2 Gregson NA, Koblar S, Hughes RAC. Antibodies to gangliosides in Guillain-Barré syndrome: antigen specificity and relationship to clinical features. *Quart J Med* 1993;**86**:111-7.
3 Fredman P, Vedeler CA, Nyland H, Aarli JA, Svennerholm L. Antibodies in sera from patients with inflammatory demyelinating polyradiculoneuropathy react with ganglioside LM1 and sulphatide of peripheral nerve myelin. *J Neurol* 1991;**238**: 75-9.
4 Willison HJ, Veitch J, Paterson G, Kennedy PGE. Miller Fisher syndrome is associated with serum antibodies to GQ1b ganglioside. *J Neurol Neurosurg Psychiatry* 1993;**56**:204-6.
5 Santoro M, Uncini A, Corbo M, Staugaitis SM, Thomas FP, Hayes AP, *et al*. Experimental conduction block induced by serum from a patient with anti-GM1 antibodies. *Ann Neurol* 1992;**31**:385-90.

Urinary albumin excretion

Timed urine collections advisable

EDITOR,—J Johnston and colleagues point out the great variability in the albumin concentration or albumin:creatinine ratio measured in first morning urine samples and suggest caution in their use in the diagnosis of microalbuminuria.[1] The correlation between albumin excretion rate and albumin concentration or albumin:creatinine ratio is, however, far from perfect. Thus most authorities recommend simple concentration or ratio measurements as an initial screening test only, emphasising the need for formal measurement of the albumin excretion rate in several timed urine collections before the patient is categorised[2-4] and for response to treatment to be monitored by albumin excretion rate. The purpose of measuring the albumin concentration or albumin:creatinine ratio in diabetic patients is not to obtain an absolute value but to identify those patients with a high chance of having microalbuminuria in a timed urine collection. Thus, it would be helpful to know from the data of Johnston and colleagues how many patients changed category on re-examination from normoalbuminuric to at risk, however defined, rather than the fluctuations in absolute levels.

It is well recognised that changes in blood glucose and blood pressure acutely alter albumin excretion, as will ingestion of drugs such as non-steroidal anti-inflammatory agents. Thus it is perhaps not surprising that, in a two year follow up that did not control for these variables, the coefficient of variation is so large. In addition, in a two year period an increase in the albumin excretion rate of 20% per year might reasonably be expected, at least in untreated microalbuminuric insulin dependent diabetic patients.[5] Thus some of the "variability" noted here might be due to natural progression of the disease. The authors