life Metchnikov strictly followed his own dietetic rules but nevertheless suffered from ischaemic heart disease and severe atherosclerosis.⁷ He died in Paris in 1916 at the age of 71.—I am, etc.,

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- 1 Burkitt, D. P., *Lancet*, 1970, 2, 1237.
- 2 Painter, N. S., and Burkitt, D. P., *British Medical Journal*, 1971, 2, 450.
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Predicting Survival in Terminal Cancer

SIR,—Dr. C. Murray Parkes (1 April, p. 29) reported on the inability to estimate survival of terminal cancer patients. Our experience with somewhat less ill patients has been that our colleagues are able to forecast survival with some accuracy.

In a controlled co-operative clinical trial designed to study the survival of lung cancer patients treated with methotrexate participating physicians were asked to predict survival prior to entering a patient onto study. Though protocol required that estimated survival be at least two months, seven patients with an estimated survival time of less than two months were admitted to the trial.

TABLE 1—Estimated and Median Actual Survival Times in 178 Patients with Lung Cancer

Estimated Survival (Months)	No. of Patients	Median Actual Survival (Weeks)
Two or less ..	33	6
Three or less ..	46	12
Four or less ..	44	19
Five or more ..	55	22

Table 1 shows the estimated and median actual survival times. The actual survival times are in good agreement with the estimated, and clearly our physicians can distinguish between a patient with a prognosis

TABLE II—Number of Underestimated and Overestimated Survivals in each Prediction Group

	Total	Prediction Group (Months)			
		Two	Three	Four	Five or More
Underestimated (Actual Survival greater than expected) ..	86	15	22	23	26
Overestimated (Actual Survival less than expected)	92	18	24	21	29
Percent underestimated	48	45	48	52	47

of two months or less and a prognosis of five or six months (only three patients had estimated survivals of more than six months). Survival curves in Fig. 1 (plotted on semi-log scale) also show that the physicians can separate the three-month group from both the two-month and the four month group. Differences in survival between the estimated four-month group and the five-month group are small but in the direction expected.

When one looks at data on the individual patient it can be seen that our physicians underestimated survival just about as often as they overestimated. Table II shows the number of underestimated and overestimated survivals for each prediction group. The proportion underestimated in the two-month prediction group was about the same as that for the five-month plus group (no trend in overestimating was seen with increased estimates of survival).

We believe that the ability of our colleagues to estimate survival may provide us with another parameter against which to measure the effectiveness of a treatment. A full report on the trial and on the effects of methotrexate is in preparation.—We are, etc.,

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Radioisotope Detection of Venous Thrombosis

SIR,—Dr. K. Jeyasingh and others (26 August, p. 500) make two assumptions for which they do not provide any evidence. The first is probably true except under particular conditions (for example, trauma) and is assumed by most investigators who use the ¹²⁵I-fibrinogen test. The second can rarely be made for two reasons.

Firstly, vasomotor and in particular venomotor tone is variable. Even if the limbs are elevated local changes of venous capacitance may produce pooling of radioopaque dye or radioisotope. Such changes may cause local alterations in radioactivity,¹ and though these often may not persist for 48 hours they must be taken into account. When comparison is made with the other limb over this period a diagnostic error is unlikely. However, comparison with the precordial count will permit bilateral changes of vascularity to appear as "thromboses." Secondly, the precordial count may be affected by myocardial infarction so that the reference point is not constant.²

It is necessary to establish a new test by some existing criteria—for example, pathological or venographic evidence. The latter may not show small thromboses which the established ¹²⁵I-fibrinogen technique demonstrates. If the latter is their criterion the new

test they are introducing has a high incidence of false-positive results. We still do not know the clinical importance of ¹²⁵I-fibrinogen-positive thromboses. Even the simplest test is time-consuming and must be proved before it should be generally applied.—I am, etc.,

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- 1 Griffiths, P. A., and Talbot, S., *British Medical Journal*, 1971, 4, 624.
- 2 Simmons, A. V., Sheppard, Margaret A., and Cox, A. F., *British Heart Journal*, 1972, 34, 711.

Guillain-Barré Syndrome after Measles

SIR,—One may question whether the two cases of Guillain-Barré syndrome after measles described by Drs. Gunilla Lidin-Janson and Ö. Strannegård (3 June, p. 572) had either disease. The morbilliform rash described may occur with a variety of viral and other diseases besides measles. Koplik's spots, a characteristic of measles,¹ apparently were not seen. The serologic data are not convincing either, indicating only that both patients had experienced measles at some time. The fall in complement fixation antibody suggests that infection was recent, without pinpointing the time, only if acute and convalescent sera were done in the same test.² Thus, neither the clinical nor laboratory data support the diagnosis of measles "beyond doubt."

Nor should one accept without question the diagnosis of Guillain-Barré syndrome in these patients—rather they would seem to have had primarily encephalomyelitis with a polyneuritis, which has been described previously following measles and other infectious diseases.^{1,3} To diagnose the Guillain-Barré syndrome one should find increased protein in the C.S.F. without an increase in cells.³ The latter data were not provided for either patient.—I am, etc.,

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- 1 Rake, G., in *Viral and Rickettsial Infections of Man*, eds., T. M. Rivers, and F. L. Horsfall, jr., 3rd edn., p. 741. Philadelphia, Lippincott, 1959.
- 2 Katz, S. L., and Enders, J. F., in *Diagnostic Procedures for Viral and Rickettsial Infections*, eds., E. H. Lennette, and N. J. Schmidt, p. 518. New York, American Public Health Association, 1969.
- 3 Brain, W. R., *Clinical Neurology*, p. 280, 306. London, Oxford University Press, 1960.

Levodopa and Arrhythmias

SIR,—I was interested to read the paper by Dr. R. B. Jenkins and others (26 August, p. 512) on levodopa therapy in 40 patients with Parkinsonism and heart disease. Since coronary heart disease and Parkinsonism often occur in the same age group it is reassuring to note that little increased hazard attended the administration of levodopa in their series of cases.

The unanswered question is whether levodopa may be dangerous immediately after a myocardial infarction. Levodopa sometimes produces ectopic rhythms in man and animals. Arrhythmias are common after a myocardial infarction, and it is logical to presume that a summation effect may well operate when levodopa continues to be given to a patient immediately after a myocardial infarction. A recent case treated at this hospital presented with this problem.

A man aged 61 had been taking 2.5 g of levodopa a day for Parkinson's disease since March 1971. Since 1969 he had suffered from occasional angina on exertion. In May 1972 he was admitted with a fairly extensive anterior myocardial infarction. Ventricular fibrillation occurred but sinus rhythm was restored, to be followed by multiple atrial ectopic beats. Six hours after these had subsided premature coupled ventricular beats began. The arrhythmias lasted for 36 hours altogether, and levodopa was continued throughout with constant monitoring of the rhythm. The levodopa would certainly have been stopped if the ectopic rhythms had persisted or if they had failed to respond to anti-arrhythmic therapy.

The patient's general condition remained satisfactory for about a week, when rapidly progressive heart failure developed. He died three weeks after admission. Levodopa was discontinued 48 hours before death when hypotension had developed.

Though it is obviously unwise to draw any definite conclusions from a single case, one wonders whether this patient's tendency to arrhythmias after myocardial infarction was increased by levodopa. The experiences of others are needed to substantiate a theoretical risk. Until more definite evidence is available careful monitoring of these patients is required after a myocardial infarction.—I am, etc.,

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Activated Charcoal Rediscovered

SIR,—Your excellent leading article (26 August, p. 487) on activated charcoal omitted to mention one of its modern therapeutic applications. Since 1960 we have used activated charcoal in uraemic patients. We had previously found that charcoal effectively adsorbed certain uraemic substances directly from plasma or gastrointestinal contents (creatinine, uric acid, urea, phenols, guanidines, organic acids). A dose of 20–50 g of activated charcoal daily often results in an impressive clinical improvement, mainly on the gastrointestinal disturbances of the patient (oral fetor, anorexia, nausea, vomiting). No side effects were noted during continuous treatment for 4–20 months.¹ More recently we have devised a simple apparatus for direct perfusion of blood through granular activated charcoal (charcoal artificial kidney), and we have reported the good results we have had with this method in cases of renal failure and severe barbiturate poisoning.^{2,5} Others have also published reports.^{6,7}—I am, etc.,

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¹ Yatzidis, H., *Nephron*, 1964, 1, 310.
² Yatzidis, H., *Proceedings of the European Dialysis Association*, 1964, 1, 83.
³ Yatzidis, H., et al., *Lancet*, 1965, 2, 216.

⁴ Yatzidis, H., *Proceedings of the 3rd International Congress of Nephrology*, p. 290. Basel, Karger, 1966.
⁵ Yatzidis H., in *Acute Barbiturate Poisoning*, ed. H. Matthew. Amsterdam, Excerpta Medica Foundation, 1971.
⁶ Dunce, G., and Kolff, W. J., *Transactions of the American Society for Artificial Internal Organs*, 1965, 11, 178.
⁷ Andrade, J. D., et al., *Transactions of the American Society for Artificial Internal Organs*, 1972, 18, 473.

Admitting the Mother

SIR,—Hospital planners should learn by heart Dr. Arnon Bentovim's superb article (2 September, p. 579) and the account in the epidemiology section of the same issue (p. 597) of the spread of *E. coli* enteritis. All district hospitals should have comprehensive facilities for patients of all ages with physical, intellectual, and emotional handicaps, and all such hospitals should have comprehensive facilities for the accommodation of patients of all ages with communicable disease.

The particular link between the minimization of cross-infection in small babies and the maintenance of the mother-baby relationship lies in the policy of regarding the admission of the mother with the baby as a vitally necessary step. If provision for "rooming in" is made and constantly encouraged it will usually come about; its value both to barrier nursing and to psychoprophylaxis is probably immeasurable but almost certainly immense. The shuffling of patients, either because of infection or of handicap, from one place to another is both dangerous and inhumane: we must "plan it" into the past.—I am, etc.,

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Serum Prolactin Periodicity

SIR,—In their paper describing a rise of human serum prolactin concentration during the night, Dr. J. Nokin and his colleagues (2 September, p. 561) refer to it as an example of "circadian periodicity." Had they described it as a diurnal variation I would have had no quarrel with them, but their term implies an autonomous rhythm that would persist in the face of widely differing circumstances.

There indeed seem to be circadian rhythms of blood constituents, plasma cortisol being an example. However, it is only a few years since human growth hormone secretion was so described because of graphs very much like the one shown by Dr. Nokin and his colleagues. Yet after pioneer work in Japan^{1,2} it was conclusively demonstrated that the rise at night was triggered by a certain phase of sleep and that it did not appear unless that phase of sleep occurred. I was among those present at the annual meeting of the Association for the Psychophysiological Study of Sleep in New York earlier this year and heard leading workers describing research which led to the conclusion that the rise in serum prolactin in men and women during the night was also associated with sleep, though we shall have to await their publications before coming to a firm judgement.

Dr. Nokin and his colleagues seem not to have used the technique that is now commonplace in many departments, including

the department in which I work, whereby blood is sampled frequently throughout the night by an indwelling catheter. They do not even tell us whether their subjects were asleep during the night prior to the four-hourly sampling, but one supposes that they were. In the circumstances the use of the term "circadian periodicity" is inappropriate, since the authors have not excluded the simple possibility that they were observing a sleep-provoked phenomenon.—I am, etc.,

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¹ Sassin, J. F., et al., *Science*, 1969, 165, 513.
² Sassin, J. F., et al., *Life Sciences*, 1969, 8, 1299.

Thymectomy for Myasthenia Gravis

SIR,—While the riddle of myasthenia gravis still remains to be solved I was glad to read in your leading article on thymectomy for myasthenia gravis (2 September, p. 543) that it is now agreed that good results are obtainable in both sexes after surgery.

I was, however, sorry not to read, as pointed out elsewhere,¹ that the sooner thymectomy is carried out in these unfortunate patients the better the prognosis. All too often patients are referred who have suffered from the disease for many years. In the early stages they had responded well to drugs but it was only with the passage of time, as the symptoms became intensified and larger doses of the cholinesterase inhibitors became necessary, that surgery was recommended.—I am, etc.,

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¹ Lange, M. J., *British Journal of Surgery*, 1960, 48, 285.

Handicapped Preschool Children

SIR,—Dr. Arnon Bentovim (2 September, p. 579) provides a useful guide to understanding parental attitudes to the young handicapped child. He rightly stresses the need for successful intervention at the beginning to enable parents to accept the child and work through their own emotional reactions. The value of a voluntary enterprise is worth recording in this respect.

Opportunity classes provide a nursery class for handicapped children from birth onwards, and important added features are the presence of normal children and a meeting for mothers. The most interesting point about the classes has been the response of attending mothers. Firstly, nearly all mothers choose to attend, and, secondly, the degree of acceptance of the child's handicap, reduction of their own anxiety, ability to verbalize their feelings about their child, and confidence in handling and responding to their child have increased remarkably, even in comparison with parents who have received traditional social-work support in a one-to-one situation. Professional social-work support to the classes rarely exceeds one session each month. Clearly the mothers are providing continuing support for each other by the mechanisms postulated by Bentovim.

It is not claimed that the classes provide