CORRESPONDENCE

Correspondents are asked to be brief

Treatment of Malignant Melanoma A. W. Levene, F.R.C.S.	545	AHF-related Protein and Precipitation Reactions L. Holmberg, M.D., and Inga M. Nilsson, M.D.	549	Tubal Sterilization and its Reversal C. K. Vartan, F.R.C.O.G.; A. E. R. Buckle, F.R.C.O.G.	552
Central-Core Disease and Malignant Hyperpyrexia D. G. F. Harriman, F.R.C.P., and F. R. Ellis, PH.D., F.F.A. R.C.S.	545	Sympathomimetic Amines and Antidepressant Agents G. G. Wallis, M.D.	549	Afternoon Surgeries E. T. Griffiths, M.R.C.G.P.; R. N. Palmer, M.B.	552
Cost of Drugs J. D. P. Graham, F.R.C.P.ED.; D. K. Bose, M.R.C.G.P.	546	Classics and the Medical Student R. H. MacDougall, M.B., and D. W. Sinclair, M.B.	550	Vitamins in Illness Z. A. Leitner, F.R.C.P.GLASG.	552
Sarcoid Heart Disease L. Rossi, M.D.	546	Legalization of Cannabis C. E. Allen, M.D.	550	School Eye Clinics P. A. Gardiner, M.D.	552
Cutaneous Sarcoidosis in Venepuncture Sites A. Sakula, F.R.C.P.; R. F. Harvey, M.R.C.P., and others; I. A. Short, F.R.C.P.GLASG., and J. A. Milne, F.R.C.P.	547	Disseminated Intravascular Coagulation in Benign Tertian Malaria Barbara J. Bain, M.R.A.C.P.	550	Free Contraceptives R. D. Haigh, D.P.H.	553
Gastric Decompression after Abdominal Surgery D. M. Essenhigh, F.R.C.S.	547	Airgun Pellets and the Eye S. P. B. Percival, F.R.C.S.; B. R. Kesby, F.R.C.S.	550	Rigid Footwear A. W. Fowler, F.R.C.S.	553
Dangerous Patients A. I. Roith, M.R.C.PSYCH.	548	Radioimmunoassay Follow-up of Hydatidiform Mole Sir John Stallworthy, F.R.C.O.G.	550	Nitrazepam and the Elderly J. G. Evans, M.R.C.P., and E. H. Jarvis, M.R.C.P.	553
Working of the Mental Health Act S. J. G. Spencer, D.M., M.R.C.PSYCH.	548	Pathogenesis of Obesity B. N. Draznin, M.D., and Y. K. Marakhovskii, M.D.	550	Soaking Beds J. W. C. Leech, M.D.	553
Myocardial Infarction and Pulmonary Thromboembolism W. J. Windebank, M.R.C.P., and F. Moran, F.R.C.P.ED.	548	Cutaneous Polyarteritis T. Dyk, M.D.	551	Amoxycillin Rash in Infectious Mononucleosis R. Mulroy, M.R.C.G.P.	554
Fractured Lippen Loop and Pregnancy Z. Domány, M.D., and M. Hancsók, M.D.	549	Fluoride and Osteoporosis J. Dequeker, M.D., and A. Burssens, M.D.	551	Treatment of Dextropropoxyphene Poisoning Vanessa Hunt, D.A.	554
Childhood Leukaemia and Pregnancy Viraemia R. H. Lindenbaum, M.R.C.P.	549	Drugs in Infertility G. I. M. Swyer, F.R.C.P.	551	Chambers and the Periphery A. H. Holmes, F.R.C.S.ED.	554
		Potentialization of Neuroleptics by Catecholamine Inhibitors J. Walinder, M.D., and A. Carlsson, M.D.	551	Earnings of General Practitioners D. J. Anderson, M.B., and others.	554
				S.H.M.O.s and Medical Assistants I. M. Librach, M.B., D.P.H.	554

Treatment of Malignant Melanoma

SIR,—Your leading article (10 February, p. 306) presenting some aspects of contemporary thought on melanoma is, I believe, inadequate in certain respects.

It is misleading to state that cutaneous melanoma is unpredictable in its behaviour, the implication being that other malignant tumours are predictable in their behaviour or that it belongs to a group of tumours about which information is so scarce as to be inadequate for prognostic purposes. Neither is true. For example, there is a well-established relationship between prognosis and a large number of clinicopathological relationships—sex of the subject, anatomical location of the tumour, its size and histogenetic type, depth of invasion, clinical involvement of regional nodes, and radiosensitivity, to name the obvious ones.^{1,2} As in the case of the lymphomas there is an abundance of information of prognostic importance.

Again it is not "agreed that in the management of melanoma incisional biopsy must be avoided." On the contrary, I would suggest that it is a mandatory procedure to obtain a diagnosis on a large ulcerated cutaneous lesion of doubtful histogenesis before any treatment is given. Furthermore, informed opinion is that there are no known harmful effects from biopsy carried out on the ulcerated lesion.³ Where radiotherapy may claim to be the treatment of choice—that is, for the melanotic freckle and its conjunctival homologue—confirmatory biopsy should be an invariable preliminary. The final sentence

"External radiotherapy produces a poor response in most cases"—is misleading in its simplicity, which again has about it the suggestion that melanoma is one disease only, and an unpredictable one at that.

Finally, there is the statement that "the primary tumour must be excised with a very wide margin of skin at the earliest possible time and the defect covered with a skin graft." How wide? I have noticed that surgeons, the most frequent writers on the therapeutics of melanoma, either provide no guidance on dimensions, tailor it according to the anatomical site involved and the likely cosmetic problems presented, or resort to recommending one of the series of prime numbers 1, 2, 3, 5, 7, 11 cm as a suitable margin of clearance around the tumour, regardless of its size. So far as I am aware the choice of such numbers enjoys no pathological basis, nor sanction, but is an attempt to circumvent the subsequent appearance of satellite nodules. Since no method of surgical treatment guarantees freedom from this complication the recommended area of excision would still appear to be a debatable point, possibly to be determined by appropriate surgical research.—I am, etc.,

ARNOLD LEVENE

Royal Marsden Hospital, London S.W.3

- 1 Maillard, G. F., *Annales de Dermatologie et de Syphiligraphie*, 1971, 98, 5.
- 2 Clark, W. H., Jr., from, L., Bernardino, E., and Mihm, M., *Cancer Research*, 1969, 29, 705.
- 3 Epstein, E., Bragg, K., and Linden, G., *Journal of the American Medical Association*, 1969, 208, 1369.

Central-core Disease and Malignant Hyperpyrexia

SIR,—The report by Dr. M. A. Denborough and others (3 February, p. 272) of core-like areas in type 1 fibres in malignant hyperpyrexia myopathy is interesting, but they are not justified in referring to this myopathy as central-core disease as if it were a specific entity. Focal areas of absence of mitochondria in histochemically stained sections have already been reported by us in malignant hyperpyrexia myopathy,^{1,2} but we have preferred to use the term "moth-eaten fibres" to avoid any suggestion that the finding is specific. Our illustrations of the mitochondria-deficient areas, identical with those of Dr. Denborough and his colleagues, have been shown at international meetings and are shortly to be published.³ They are less numerous in our cases, possibly owing to a difference in the muscles examined.

Those with more than average experience of muscle biopsy realize that focal areas of mitochondrial absence, whether accompanied by preservation of myofibrils in electron micrographs (core-like fibres) or their disarray (target or targetoid fibres) are relatively common in neuromuscular disease in isolated fibres. To refer to all those with the former characteristics as central-core disease would clearly be ridiculous. Central-core disease is poorly defined, but the term should be reserved for cases which at least resemble the original descriptions.⁴ We believe that the patient described by Dr. Denborough and his colleagues suffered from malignant hyperpyrexia myopathy, and

we are pleased to note that in another report Moulds and Denborough,⁵ using the in-vitro method introduced by us,⁶ showed that the same patient's muscle exhibited one of the cardinal features of this myopathy—namely, contracture on exposure to halothane. Central-core disease, so far as is known, does not confer susceptibility to anaesthetic agents. Some years ago we examined a mother and a daughter by the lengthy procedure of motor-point muscle biopsy, and both were shown to have central-core disease. Halothane was used for general anaesthesia without incident.

In your leading article on the "Pathology of Malignant Hyperpyrexia" (3 February, p. 249) you showed that you were aware of the non-specificity of the structural changes that have been described so far, but we wish to draw attention to what appears to be a thoughtless remark, in which you say that "it would be interesting to see whether any further biopsy samples (obtained under local, not general, anaesthesia) . . . show similar histological changes." This could lead to susceptible patients or their relatives being subjected to muscle biopsy with little or no benefit. If investigation by biopsy is indicated, it should include examination at the motor-point (so that nerve terminals as well as muscle cells can be examined), a full histochemical and electron microscopical examination, and above all in-vitro examination of the susceptibility of muscle to anaesthetic agents. Patients are prepared to travel long distances for this examination, and we now have an experience of 20 cases in 10 families. We no longer use local anaesthesia, which is uncomfortable for the patient, impossible in children, and usually interferes with the identification of the motor-point. We employ general anaesthesia with nitrous oxide, oxygen, and minimal amounts of thiopentone, and the patients are carefully monitored, core and peripheral temperatures being continually measured. The in-vitro method for detecting susceptibility to anaesthetic agents, introduced by us, has proved consistently reliable in experienced hands.

Biopsy examination of patients for susceptibility to malignant hyperpyrexia should not be undertaken lightly, but if it is to be done at all it should be comprehensive.—We are, etc.,

D. G. F. HARRIMAN
F. RICHARD ELLIS

The General Infirmary,
Leeds

- 1 Ellis, F. R., *et al.*, *British Medical Journal*, 1972, 3, 559.
- 2 Ellis, F. R., Keane, N. P., and Harriman, D. G. F., *Proceedings of the Royal Society of Medicine*, 1973, 66, 66.
- 3 Harriman, D. G. F., Sumner, D. W., and Ellis, F. R., *Quarterly Journal of Medicine*, 1973, in press.
- 4 Bethlem, J., *Muscle Pathology, Introduction and Atlas*, p. 48. Amsterdam, North-Holland Publishing Co., 1970.
- 5 Moulds, R. F. W., and Denborough, M. A., *British Medical Journal*, 1972, 4, 526.
- 6 Ellis, F. R., Harriman, D. G. F., Keane, N. P., Kyte-Menasah, K., and Tyrrell, J. H., *British Journal of Anaesthesia*, 1971, 43, 721.

Cost of Drugs

SIR,—Those whose duty it is to teach medical students have been urged to include some account of the cost of the drugs in their courses of instruction. This is not so simple a matter as may at first appear when one remembers that the "cost" of an illness

includes the social benefits as well as the N.H.S. costs and that the "cheapest" drugs must therefore be the most effective one. The D.H.S.S. and its precursor the Ministry have for many years issued information sheets with tables or bar diagrams comparing brief lists of drugs of comparable therapeutic use by the cost to the N.H.S. of an average prescription or of an equal number of units, capsules, tablets, etc. This method of comparison ignores effectiveness and may therefore be misleading if one accepts the implication that the drug mentioned first in the list (the cheapest in terms of cost to the N.H.S.) is the drug of choice. There is a disclaimer (in small print) that it is not suggested that the drugs mentioned have the same actions or side effects. What then has been the purpose of this long-continued exercise?

A recent example, ECL 106/69 No. 14/72, which is devoted to the cost of antibacterial drugs, illustrates my point. The last page of the issue is devoted to drugs used in urinary tract infections. The cost of 25 tablets etc. of six frequently prescribed drugs is given—ampicillin cheapest at 91p, nalidixic acid (Negram) and co-trimoxazole (Bactrim or Septrin) roughly equal at £1 to £1.19p and nitrofurantoin (Furadantin) last at £1.38p. Now before I incorporated this information in my teaching I checked with my colleagues who are experienced in this field of therapy. They told me that this order would be reversed if the dosage schedules which they have found most effective or those recommended by the manufacturers were taken into account, that ampicillin should be omitted¹ on account of frequency of rashes (which need further treatment and delay the therapeutic attack on the primary condition), and that the choice of agent with which to begin is influenced above all by the sensitivity of the pathogen to the drug. Little bacterial resistance to the last three drugs has been encountered, and nitrofurantoin has the unique advantage of leaving the intestinal faecal flora unaltered so that any recurrence of urinary infection should be readily controlled by a repeat course of the same drug.

These sort of complexities make the information given in the D.H.S.S. pamphlets irrelevant. Only if and when they include a considered view on the whole matter—choice of drug, treatment schedules, and total "cost-effectiveness"—will they be useful teaching material. If this task is held to be fraught with too many difficulties the present series might well be abandoned and the practitioner left to work it out for himself.—I am, etc.,

J. D. P. GRAHAM

Welsh National School of Medicine,
Cardiff

- 1 McCallister, T. A., Alexander, J. G., Dulake, C., Percival, A., Boyce, J. M. H., and Wormald, P. J., *Postgraduate Medical Journal*, 1971, 47, Suppl. September, p. 7.

SIR,—I was shocked by the accusations of Dr. I. W. B. Grant (17 February, p. 416). He must be terribly misinformed about the facts of life in general practice. As a general practitioner, I am constantly aware of, and reminded time and again about, the cost of each brand of drugs we prescribe. Any conscientious general practitioner always takes into account the relative efficacy and cost

of any preparation. If any of us overprescribe, the Ministry of Health officers are always around to tell us to cut down the cost of our prescriptions.

Thinking back to when I was medical registrar for five years in the U.K., there was neither any check on the cost of drugs I prescribed nor any guidance on this point—these conditions still exist among hospital doctors. Hence, according to my personal experience of medicine in Britain during the past 15 years, it is the general practitioners who prescribe drugs more economically because they have to know what each particular brand costs and account for it if necessary.

Dr. Grant had better get his facts checked—there is official Government machinery to do this. He will then know who is spending N.H.S. money "carelessly."—I am, etc.,

D. K. BOSE

Wolverhampton

Sarcoid Heart Disease

SIR,—Your leading article (16 December, p. 627) and the work of Ghosh *et al.*¹ have rightly emphasized that sarcoid heart disease is a serious condition. As a cardiac pathologist I agree that in appearance the aggregates of sarcoid follicles may easily be confused with myocardial fibrosis secondary to ischaemic heart disease. I also agree that the presence of lesions in the right atrial wall, where ischaemic scarring rarely occurs, is of help in differentiating the two conditions at necropsy. However, in my opinion, certain histological features are also helpful in diagnosing sarcoid heart disease,² as in the following case.

A 67-year-old woman suffered for three years from complete heart block with recurrent Adams-Stokes seizures and episodes of cardiac arrest and ventricular fibrillation. She deteriorated progressively and died, notwithstanding endocardial pacemaking by catheter. At necropsy fairly large, whitish, hard areas were seen in the myocardium of the ventricular septum and left ventricular walls. There were similar nodules in the lungs, spleen, and some mediastinal lymph nodes, and altogether the microscopic picture was that of sarcoidosis. Involvement of the right atrium also became evident on

Fig. 1—Sarcoid granulomatous tissue in the right atrium (Tawara's node). (Haematoxylin-eosin ×90.)

histological examination of the conducting system. The node of Tawara, whose outline was still recognizable, had been almost completely destroyed by sarcoid granulomatous tissue (figs. 1, 2) and other parts of