or had become depressed as a result of the demecolcine or the radiotherapy, or a combination of both. Further patients with this condition on treatment here by radiotherapy are having platelet counts undertaken, though formerly this was not routine practice during palliative radiotherapy at low daily doses.

We would be interested in any comments on these findings, but would suggest that if demecolcine plus radiotherapy is undertaken for superior mediastinal obstruction careful check should be kept on platelets as well as white blood count.

I am grateful to Dr. Wade for permission to publish this information about her patients.—I am, etc.,

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REFERENCE

- ¹ Sheehy, T. W., and Ransone, J. W., *Arch intern. Med.*, 1957, **100**, 85.

Treatment of the Climacteric Syndrome

SIR,—Your article in "To-day's Drugs" (10 April, p. 976) dealing with treatment of the climacteric syndrome led one to wonder whether the date was 10 April 1965 or 1945. We agree that the statement that "... the object of treatment is to convert an abrupt fall in oestrogen level into a more slowly declining one ..." but why should "... the dose used ... be insufficient to abolish all the symptoms ..." and why is "... the aim to stop treatment altogether as soon as possible"? One can only sense the suggestion that exogenous oestrogens are carcinogenic, although it is now well known there is no evidence to support this theory.¹⁻³

The degree of distress suffered by the menopausal patient is extremely variable, and this in itself appears to have led to the conclusion that the symptoms must, in the main, be psychological. No other endocrine function is based on such an assumption and we think it strange that no attempt is made to measure the oestrogenic activity. The most simple and accurate method of assessing this is by endocrine vaginal cytology, which also serves as a useful therapeutic guide. We have always found a good correlation between the severity of menopausal symptoms and the degree of oestrogen deficiency.

You state that chlorotrianisene (Tace) is not a very potent oestrogen but is of long duration, due to storage in the body fat. During our investigation of the original Tace capsules we found it to be both a rapid and potent oestrogen which gave excellent clinical results, including a marked sense of "well-being, which is rare following the majority of oral oestrogens. We did not, however, find any evidence of its prolonged action in the majority of patients.

In our experience the homoeopathic dose of oestrogen recommended is only suitable for a very small minority of the patients who seek medical help. Indeed, it is difficult to understand why the clinician's chief aim should be to withhold or curtail hormone substitution to the post-menopausal hypogonadal woman. Hormone therapy excites no comment in young hypogonadal women, nor is there any age barrier in thyroid, pancreatic, or adrenal deficiencies.

To-day, when the average woman can expect to reach her threescore years and ten,

it would seem unrealistic to deny hormone treatment, which not only alleviates all the troublesome and antisocial symptoms of the menopausal and post-menopausal phases but is also a prophylactic measure against osteoporosis, senile vaginitis, hypertension, and coronary heart disease, to mention but a few hazards of oestrogen depletion.^{4,5} Why, then, should this treatment be rather grudgingly limited to "months"?

It seems a little paradoxical that the same reasoning is not applied to the male patient following bilateral orchidectomy. Here the rationale is immediate and prolonged hormonal replacement, in spite of a possible deleterious effect on the cardiovascular system. Obviously what is sauce for the gander, is not sauce for the goose!—We are, etc.,

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REFERENCES

- ¹ Bishop, P. M. F., and Murray, M., *A.R. Brit. Emp. Cancer Campgn.*, 1957, **35**, 404.
² Larson, J. A., *Obstet. and Gynec.*, 1954, **3**, 551.
³ Wallach, S., and Henneman, P. H., *J. Amer. med. Ass.*, 1959, **171**, 1637.
⁴ Wilson, R. A., and Wilson, T. A., *J. Amer. Geriatr. Soc.*, 1963, **11**, 347.
⁵ Greenblatt, R. B., *New Engl. J. Med.*, 1965, **272**, 305.

Ischaemia and Anaesthesia

SIR,—We were interested in the work of Dr. Charles Sorbie and Dr. Pesi Chacha (10 April, p. 957). Their demonstration of slowing of conduction in the ulnar nerve after stimulation at the elbow by recording from the first dorsal interosseus agrees with our findings¹ after stimulating the ulnar nerve at wrist and elbow. We showed that the effect of lignocaine was on the peripheral part of the neurone and the neuromuscular junction and was probably partly preganglionic and partly post-ganglionic.

Studies of motor-nerve function, such as those of Sorbie and Chacha, do not demonstrate that ischaemia does not contribute to anaesthesia. This can be done only by studies of sensory nerve conduction. Our work showed that sensory conduction changed similarly under the influence of ischaemia alone and ischaemia plus lignocaine. Ring electrodes applied to the fingers seem, therefore, to stimulate sensory nerve trunks, and we draw the inference that lignocaine acts on sensory nerve endings. Experimental work by Diamond *et al.*² came to a similar conclusion.—We are, etc.,

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REFERENCES

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² Diamond, J., Gray, J. A. B., and Inman, D. R., *J. Physiol. (Lond.)*, 1958, **142**, 382.

Intravenous Regional Analgesia

SIR,—The high incidence of toxic phenomena associated with the technique of intravenous regional analgesia reported by Kennedy *et al.*¹ has not been observed in clinical practice with this method at the Westminster Hospital.

We are at present engaged in a study of the peak blood levels reached in volunteers after release of the cuff. Following the injection of a 0.5% solution of lignocaine hydrochloride (155–275 mg.) blood samples were analysed by a sensitive specific gas chromatographic technique. In order to simulate the worst conditions with regard to general blood levels likely to be met clinically, the cuff was deflated after only five minutes. Peak blood levels of 1 to 3.9 µg./ml. were reached within seven minutes of releasing the cuff and they fell in such a way that the half-life was approximately 20 minutes.

The 76.2-kg. patient of Kennedy *et al.*, who suffered cardiac arrest, is unlikely to have had a peak level as high as the above as he received only 190 mg. lignocaine hydrochloride and the cuff remained in place for 30 minutes. We found peak levels of 3.5 µg./ml. five minutes after direct intravenous injection of lignocaine (50 mg.) in two volunteers; no untoward reactions were observed.

Furthermore, blood levels of 1.1 to 3.6 µg./ml. were found after epidural injection of lignocaine (470 to 1,130 mg. during a period of up to five hours) to alleviate labour pains.

It is reported by Bromage and Robson,² using the methyl-orange method of determining lignocaine levels, that the minimum toxic concentration in the blood is about 10 µg./ml. Thus it seems improbable that the correct use of intravenous regional analgesia could lead, after the release of the cuff, to a sufficiently high blood concentration of lignocaine to cause untoward effects and certainly not to cause cardiac arrest. It would be unrealistic to abandon this excellent technique on the result of one report in which blood levels of the drug were not determined.—We are, etc.,

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REFERENCES

- ¹ Kennedy, B. R., Duthie, A. M., Parbrook, G. D., and Carr, T. L., *Brit. med. J.*, 1965, **1**, 954.
² Bromage, P. R., Robson, J. G., *Anaesthesia*, 1961, **16**, 461.

Darwin's Illness

SIR,—The diagnosis of Darwin's illness (20 March, p. 745) has been and apparently will remain a controversial subject. It is obviously now impossible to make a diagnosis with absolute certainty. All that one can do is to examine relevant facts, particularly events prior to his illness, and suggest a diagnosis based on a reasonable degree of probability.

The facts are as follows: (1) It is indisputable that during the voyage of *H.M.S. Beagle* Darwin displayed a degree of endurance well above the average. (2) It is indisputable that on 25 March 1835 he "experienced an attack (for it deserves no less a name) of the Benchuca, a species of *Reduvius* the great black bug of the Pampas." The known distribution and bionomics of triatomid bugs in South America leaves no