Correspondence

Letters to the Editor should not exceed 500 words.

Keeping the Heart Going

SIR,—In your editorial entitled "Keeping the Heart Going" (19 June, p. 1566) we believe that incorrect emphasis has been placed upon the risks of the production of ventricular fibrillation by pacing on the T wave in patients who have returned to sinus rhythm.

All proved instances of ventricular fibrillation, in our experience, have occurred only with the epicardial system of pacing, and only in the immediate post-thoracotomy period.¹ It seems that the risk of ventricular fibrillation is highest when the threshold for the production of ventricular fibrillation is lowered from superficial myocardial damage caused by stitching the electrode on to the epicardium and from alterations in pulmonary ventilation due to the thoracotomy. Another factor was probably the unnecessarily high power of the earlier units.

Now that we use endocardial jugular systems for long-term pacing, thereby avoiding a thoracotomy, the risk of ventricular fibrillation must be greatly reduced, and we have never seen it in our experience of over 100 patients treated by endocardial pacing.—We are, etc.,

RODNEY H. BLUESTONE.
GEOFFREY M. DAVIES.
ALAN M. HARRIS.
AUBREY G. LEATHAM.
HAROLD M. SIDDONS.
EDGAR SOWTON.

St. George's Hospital,
London S.W.1.

REFERENCE

- 1 Sowton, E., *Brit. Heart J.*, 1965, 27, 311.

Thrombosis and Anticoagulants

SIR,—Drs. L. Poller and Jean M. Thomson (5 June, p. 1475) state, "There is a clinical impression that fresh thrombotic attacks are more likely to occur shortly after anticoagulant treatment is stopped." The evidence is stronger than a mere impression. During the three months following withdrawal of anticoagulant therapy from 61 patients with cerebrovascular disease I observed an incidence of 3.2 cerebrovascular accidents per 100 patient-months, as compared with 1 during the time on therapy and 2 during the fourth to twelfth month after stopping treatment.¹

The possibility of this difference occurring by chance was 1 in 50.—I am, etc.,

JOHN MARSHALL.

University Department of
Clinical Neurology,
The National Hospital,
London W.C.1.

REFERENCE

- 1 Marshall, J., *Circulation*, 1963, 28, 329.

Interstitial Pulmonary Fibrosis

SIR,—We were glad to see the article by Dr. Margaret E. A. Turner-Warwick and Dr. Deborah Doniach on auto-antibody studies in interstitial pulmonary fibrosis (3 April, p. 886). This appears to confirm our previously published findings,¹ details of which have now appeared in the May issue of the *Annals of the Rheumatic Diseases*.² In our series we excluded cases with clinical rheumatoid arthritis, but still found occasional unexpected radiological evidence of rheumatoid changes.

We were very interested in what Dr. Turner-Warwick and Dr. Doniach had to say about the correlation of the duration of lung symptoms with the presence of rheumatoid factor. We have been repeating the tests for rheumatoid factor on some patients now for over two years and have observed that where a change in the titre occurs it is usually to a less positive one; we have not yet come across a case which progressed to clinical rheumatoid arthritis as reported by Lee and Brain.³

We note that Drs. Turner-Warwick and Doniach found the antinuclear factor test positive in 28% of their cases. Only 12 of our 19 cases have been tested for A.N.F. These were done by Dr. Geoffrey Taylor, of the Manchester Royal Infirmary, and were all negative. This might perhaps be explained by a difference in sensitivity of the A.N.F. test as performed by different laboratories. The 4% of positive sera in the control group described suggests that the test as used by the authors is rather over-sensitive.

Fluorescent-antibody studies on post-mortem lung from one of our patients showed gamma-globulin lining the alveoli. The interpretation of this finding, which may merely represent terminal exudation of serum proteins, is, at the moment, impossible.—We are, etc.,

RICHARD WARD.
RANDAL STALKER.

Royal Infirmary,
Blackburn, Lancs.

REFERENCES

- 1 Ward, R., and Stalker, R., *Lancet*, 1964, 2, 477.
- 2 ———, *Ann. rheum. Dis.*, 1965, 24, 246.
- 3 Lee, F. I., and Brain, A. T., *Lancet*, 1962, 2, 693.

Screening Tests for Carcinoma of the Cervix

SIR,—I was very interested in Drs. C. B. Cameron and O. A. N. Husain's paper on 6-phosphogluconate dehydrogenase (12 June, p. 1529). In our own previous published series¹ we had three cases of carcinoma-in-situ, two of which were not associated with an elevated level of 6-phosphogluconate dehydrogenase, one of the cases not associated with an elevation of 6-phospho-

gluconate dehydrogenase showed micro-invasion, while the other did not. The one case associated with an elevated level showed micro-invasion. We have now collected nine cases of carcinoma-in-situ, of which five were not associated with an elevation of 6-phosphogluconate dehydrogenase. Of the five cases with no enzyme elevation, four of these showed micro-invasion.

It would seem that we are in disagreement as to how reliable a guide 6-phosphogluconate dehydrogenase is to the presence of invasive carcinoma. This may be due to a lack of a clear definition as to what groups of workers mean by invasive carcinoma. If the enzyme is to detect the "quiescent" from "incipient invasive," surely it must detect micro-invasion. It would be useful if one could clarify the meaning of the term "invasive" when used in reference to the use of 6-phosphogluconate dehydrogenase. If it can only reliably detect clinical invasive or stage I carcinoma, it has a very limited usefulness.

I feel that one must remember that the hexose monophosphate shunt may well be increased in malignant tissue, as has been shown,^{2,3} but where 6-phosphogluconate dehydrogenase is not rate limiting the enzyme will not necessarily be increased. This might certainly apply in the early stages of carcinoma-in-situ. Such a situation in which the enzyme became rate limiting would not necessarily develop at the same time as invasion of the stroma of the cervix.

An analogy can be drawn from McLean's⁴ work on the carbohydrate metabolism of the lactating mammary gland. During the early stages of lactation the yield of ¹⁴C-labelled carbon dioxide from glucose labelled in the carbon-one position with ¹⁴C is increased ninefold, while the increase in 6-phosphogluconate dehydrogenase activity is only two-fold. The proportionally greater increase in hexose-monophosphate-shunt activity compared with the increase in 6-phosphogluconate dehydrogenase is maintained throughout lactation. Surely a similar relationship may apply to carcinoma-in-situ and the early invasive stages of cervical carcinoma, and, though pathway activity is increased, the enzyme activity may not be.—I am, etc.,

GRAINGER MUIR.

Department of Clinical Biochemistry,
Luton and Dunstable Hospital,
Luton, Beds.

REFERENCES

- 1 Muir, G. G., Canti, G., and Williams, D., *Brit. med. J.*, 1964, 2, 1563.
- 2 Abraham, S., Hill, R., and Chaikoff, I. L., *Cancer Res.*, 1955, 15, 177.
- 3 Emmelot, P., Bosch, L., and Van Vals, G. H., *Biochim. Biophys. Acta (Amst.)*, 1955, 17, 451.
- 4 McLean, P., *ibid.*, 1958, 30, 303.

Deaths from Prolonged Ingestion of Phenacetin

SIR,—Although Spühler and Zollinger described "Primary Chronic Interstitial Nephritis" attributable to phenacetin in 1953,¹ it was not until January 1964 that Sanerkin and Weaver reported the first death