

Reference	No. of Patients	% with Positive Insulin Tests One Week After H.S.V.	% Developing Recurrent Ulcer	Comment
Kronborg and Madsen ¹	50	58	22	High incidence of incomplete vagotomy; high incidence of recurrent ulceration.
Wastell <i>et al.</i> ⁵	16	28	13	Intermediate incidences both of incomplete vagotomy and of recurrent ulceration.
Kennedy <i>et al.</i> ⁴	50	4	2	Low incidence of incomplete vagotomy, low incidence of recurrent ulceration.
Johnston and Goligher (unpublished)	100	3	1	Low incidence of incomplete vagotomy, low incidence of recurrent ulceration.

Belfast,⁴ at any rate, it has been found that very few of these patients develop recurrent ulceration.

What does matter, in our opinion, is the insulin test that is performed 5-10 days after H.S.V. (see table) because the results of this test seem to have a considerable bearing upon the subsequent incidence of recurrent ulceration. Drs. Madsen and Kronborg say that their acid secretion figures obtained from this test "revealed no relationship between the completeness of H.S.V. . . . and recurrent ulceration." They seem to deduce from this that no such relationship exists. An alternative explanation—and a much more likely one in our view—is that the method which they employed was not adequate to reveal the relationship. Specifically, we think that they need more data on larger numbers of patients. It is striking (even if not statistically significant) that no fewer than 10 of the 11 patients in Drs. Madsen and Kronborg's series who developed recurrent ulceration after H.S.V. showed some secretory response to insulin 10 days after operation and that their mean acid response to insulin (minus basal) was 4.9 mmol (mEq)/h, which is quite a big response. In contrast, the mean acid response to insulin (minus basal) after H.S.V. in our first 100 patients in Leeds was 0.1 mmol/h. If Drs. Madsen and Kronborg were to look at their own and others' results in a different way (table) we feel that they might reach a different conclusion about the prognostic value of the insulin test that is performed soon after operation. As shown in the table, Drs. Madsen and Kronborg's patients had a significantly higher incidence of positive insulin tests after H.S.V. and significantly more recurrent ulcers than our patients in Leeds or the patients of Kennedy *et al.* in Belfast. Post hoc ergo propter hoc? We certainly think the latter.—We are, etc.,

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- 1 Kronborg, O., and Madsen, P., *Gut*, 1975, 16, 268.
- 2 Johnston, D., *et al.*, *Gastroenterology*, 1973, 64, 12.
- 3 Amdrup, E., *et al.*, *Annals of Surgery*, 1974, 180, 279.
- 4 Kennedy, T., *et al.*, *British Medical Journal*, 1975, 2, 301.
- 5 Wastell, C., *et al.*, *British Medical Journal*, 1972, 1, 28.

Variations in Leucocyte Count during Menstrual Cycle

SIR,—The recent paper by Drs. Barbara J. Bain and J. M. England (31 May, p. 473) relating variations in leucocyte counts during

the menstrual cycle to cyclical changes in endogenous oestrogen levels prompts me to report some recent experimental observations.

Magarey and Baum¹ described an increase in the phagocytic activity of the reticulo-endothelial system in patients receiving oestrogen therapy. Expanding on this initial finding I have postulated that the benefit of endocrine manipulation for certain human cancers may in part be related to stimulation of host factors.² The macrophages that populate the sinusoidal system of the liver and spleen, and in addition take part in a wide variety of cellular immune mechanisms (including the host response to cancer), arise from rapidly dividing precursors in the bone marrow. The new formed cells discharged from the marrow appear as monocytes in the peripheral blood before taking on a variety of morphological characteristics depending on which site within the reticulo-endothelial system they are eventually found.³ It would seem reasonable to assume, therefore, that oestrogen would stimulate these precursor cells with the resulting monocytosis providing an enlarged peripheral pool of phagocytic cells capable of clearing injected particulate matter from the blood.

To test this hypothesis I have studied the proliferation of macrophage precursors in mice treated with oestrogen. Male Swiss T.O. mice were injected intraperitoneally with 10 µg of oestradiol benzoate in 0.1 ml of arachis oil. Twenty-four hours after the injection the mice were killed and bone marrow was harvested from the femurs under aseptic conditions. In each experiment the marrow from three animals was pooled and aliquots containing 10⁵ nucleated cells were added to each of a replicate series of 10 tissue culture plates containing a semisolid medium prepared according to the method of Bradley and Metcalf.⁴

After seven days' incubation under controlled conditions the numbers of macrophage colonies per plate were counted, giving an index of the number of monocyte/macrophage precursors proliferating at the time of sacrifice. Control animals injected with 0.1 ml of arachis oil were studied in the same way. The experiment was repeated four times, providing 40 observations. The results are summarized in the table:

	Mean Colonies per Plate (±S.D.)
Oestrogen group	127±63
Controls	191±86

t=3.68, P<0.01

The results suggest that oestrogen in the dose used, far from increasing the number of macrophage precursors dividing, may actually have the reverse effect. The only

explanation for this unexpected finding that occurs to me is that oestrogen promotes the release of mature monocytes from the marrow reserve (as suggested by Drs. Bain and England) and that the increased peripheral pool of monocyte/macrophage produces an inhibitory factor, as has already been postulated by Ishikawa *et al.*⁵

Whatever the complete explanation for the effect of oestrogen on the mononuclear phagocytic system, there is no doubt in my mind that the endocrine system plays an important role in regulating cellular immunity and that the inter-relationship of these systems remains to be unravelled. Such research would be of the utmost value to clinical oncologists and transplant surgeons, as well as to haematologists.

I wish to acknowledge the invaluable technical assistance of Mrs. Maree Breese and the generous financial support of Tenovus, Cardiff.

—I am, etc.,

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- 1 Magarey, C. J., and Baum, M., *British Medical Journal*, 1971, 2, 367.
- 2 Baum, M., in *Host Defence in Breast Cancer*, ed. B. A. Stoll, p. 130. London, Heinemann, 1975.
- 3 Leder, L. D., *Blut*, 1967, 16, 86.
- 4 Bradley, T. R., and Metcalf, D., *Australian Journal of Experimental Biological and Medical Science*, 1966, 44, 287.
- 5 Ishikawa, Y., Dluznick, D. H., and Sachs, L., *Proceedings of the National Academy of Sciences of the U.S.A.*, 1967, 58, 1480.

Rewards of the Academic Career

SIR,—Dr. R. A. North says (7 June, p. 555) that "academic professorships" are paid almost as well as "consultantships." They are not. In this university the differential is at least £3500 per annum in favour of the consultant.—I am, etc.,

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Dying for a Number

SIR,—“No man ever died for a number” (Dr. J. S. Bradshaw, *Personal View*, 14 June, p. 611). Oh didn't he?

Just read what Sir John Fortescue, not normally a writer much given to emotional writing, had to say about the Battle of Albuera (1811). This was a "soldiers' battle" if ever there was one. The Portuguese had made Beresford a marshal. God had not made him a great general. It was all up to the soldiers; "and hence it was that when one man in every two, or even two in every three, had fallen in Hoghton's Brigade, the survivors were still in line by their colours, closing in towards the tattered silk which represented the ark of their covenant—the one thing supremely important to them in the world." For me, these are among the most moving words ever written in the English language.

The King's or Queen's colour is important; but the ark of the covenant is the regimental colour. In those days of our small army's growing fame this, and many another scrap of tattered silk, bore a number.—I am, etc.,

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