not to be used. We continue to encourage fluids.—I am, etc.,

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SIR,—I note with interest a recent letter referring to the use of stilboestrol in the suppression of lactation (7 December, p. 644). There seems little doubt that this is the commonest preparation used for this purpose in this country. Recently a senior consultant plastic surgeon commented to me that he noted that every parous woman referred to him for reconstruction and enlargement of the breast gave a history of having had lactation suppressed by stilboestrol. He found that no case ever came to him in which any other method had been used or when breast-feeding had been uninterrupted.

I contacted the midwives attached to our practice and asked their comments, and they also stated that the patients had complained to them of shrinkage of the breast tissues after suppression of lactation. Recently we have therefore changed our routine and eliminated stilboestrol, but it is of course too early to assess results.

I wonder if this is just a casual coincidence or whether anyone else has made a similar observation.—I am, etc.,

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SIR,—The paper by Professor T. N. A. Jeffcoate and others (5 October, p. 19) is interesting and thought-provoking. The increasing incidence of thromboembolic episodes before delivery poses a mystery. Were any of them on the "pill" prior to pregnancy, and, if so, could this be a factor? No information on this was given. Similarly, the group of patients given oestrogen empirically for recurrent abortion: did they have assays of circulating oestrogens prior to administration? If abortion was due to low hormone output, might not the oral stilboestrol still have left them below normal pregnancy levels and thus explain the absence of thromboembolism in this group?

Lastly, despite the conclusion that administration of oestrogen to suppress lactation does not increase the risk to "an unacceptable degree," might we not use the figures as an aid in promoting the course of breast-feeding? Most would agree it is in the best interest of the child; perhaps obstetricians could now try harder to convince the ladies they would also benefit.—I am, etc.,

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Polyglutamyl Forms of Folate Acid in Man

SIR,—Miss Janet Perry and Dr. I. Chanarin (30 November, p. 546) demonstrate that folate polyglutamate prepared from

brewer's yeast by adsorption on to charcoal and elution is about one-third as well absorbed in normal human subjects as folic acid.

As they point out, it has been known for some time that crude yeast folate polyglutamates are less well absorbed by normal subjects than pure folic acid. One possible explanation for this finding is the presence in yeast of a powerful folate-conjugase inhibitor.^{1,2} Folate conjugase is the enzyme present in human jejunal mucosa thought to be necessary for the splitting of folate polyglutamate to folate monoglutamate prior to its entry into the portal blood. Swendseid *et al.*² demonstrated that crude yeast inhibits the absorption of pure folate polyglutamates. They also reported that the conjugase inhibitor in yeast, like folates, could be adsorbed on to charcoal and eluted—thus the inhibitor is likely to be present in the impure folate polyglutamate preparation of Miss Perry and Dr. Chanarin.

This conjugase inhibitor has never been identified. However, while preparing folate polyglutamates from yeast by the use of D.E.A.E. cellulose chromatography,³ I performed the experiment detailed in the Figure, which suggests that, under the conditions of the experiment, the compound elutes from D.E.A.E. cellulose in company with "free" folate and can be separated from folate polyglutamates by this technique.

The lower graph shows the elution pattern of yeast folates from a D.E.A.E.-cellulose column using a gradient elution with phosphate buffer.³ The concentration of folate compounds with more than three glutamate radicals in the molecule (folate polyglutamates) is shown by the *Lactobacillus casei* activity after human small-intestinal folate-conjugase treatment, while the concentration of folate compounds with three or less glutamate radicals in the molecule ("free" folate) is shown by the *L. casei* activity without conjugase treatment. The upper graph shows the recovery of a constant known amount of folate polyglutamate added to a portion of each of the fractions before incubation with conjugase and *L. casei* assay. Recovery was less than 100% in tubes 12 to 22, with a minimum recovery of 28% at tube 17, suggesting that these fractions contain the folate-conjugase inhibitor.

Since the conjugase inhibitor content of individual foods may vary, the availability of folate polyglutamate may differ greatly from one food to the next. It may be therefore only justified to conclude from the results of Miss Perry and Dr. Chanarin on the avail-

ability to normal subjects of yeast folate polyglutamates prepared by their method, and not on the availability of pure folate polyglutamates, or of dietary folate polyglutamates eaten in other foods.—I am, etc.,

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Malignant Renal Lesions and Erythrocytosis

SIR,—The renal cell(s) which is responsible for the production or release of erythropoietin (or of an erythropoietin precursor) has not yet been characterized definitely. Osnes¹ was the first to implicate the juxtaglomerulus apparatus. Subsequent experimenters,²⁻⁶ however, have not conclusively demonstrated the relationship between the juxtaglomerular apparatus and erythropoietin production.

I have reviewed the pathological reports in the 83 cases of malignant renal lesions found in association with erythrocytosis. Eighty-two per cent. showed the clear-cell histology, 6% were tumours composed of cells with granular cytoplasm, and 6% had a mixed cytoplasmic appearance. There were also three sarcomas and four nephroblastomas.

According to Murphy and Mostofi⁷ the carcinoma with a preponderance of granular cells is the more frequently occurring renal tumour, accounting for 61% of all renal malignancies, with the clear-cell carcinoma found in 39% of cases. Comparing Murphy's data with those found when the paraneoplastic phenomenon occurs, one notes a reversal of the usual cytological frequency.

Erythrocytosis is also associated with the cerebellar haemangioblastoma in 9 to 20% of cases.⁸ This tumour is composed of cells which are very similar microscopically to the clear-cell renal carcinoma.⁹

There is evidence that the clear cell from the renal carcinoma has ultrastructural characteristics quite different from that of the cell with granular cytoplasm, such that one could more easily ascribe a secretory function to the clear cells.¹⁰

There thus seems to be an indication that the clear-cell renal carcinoma is involved to a greater extent than the cell with the granular cytoplasm in the production or release of erythropoietin.—I am, etc.,

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