therefore be estimated to be well in excess of 400. This compares with the present number of 349 consultants in England and Wales, and indicates the probability of expansion rather than contraction in the specialty.

Of the 349 consultants in diseases of the chest, 242 (nearly 70%) are stated to be over the age of 50, and only two below the age of 40. This peculiar age-distribution is consequent upon the contraction in the specialty which followed the decline of tuberculosis. But other respiratory diseases continue unabated, or even increasing in relative importance; and, unless recruitment to training in the specialty is expanded, within 15 years there will be a grave deficiency of consultant physicians trained in chest diseases. It is therefore to be hoped that the Ministry's gloomy assessment of prospects will not discourage recruitment to training in what appears likely to be an expanding specialty.—We are, etc.,

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J. G. SCADDING. E. E. KEAL.
N. C. OSWALD. P. A. ZORAB.
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Radiation Hazards of High Altitude Flight

SIR,—Few of your many medical readers will be called upon to advise on "longer space voyages" and so to recall your very topical leading article (21 December, p. 719). The omission of mention of the high concentration of electrons in the Van Allen¹ belts is therefore of little consequence. Your readers may, however, soon be asked about radiation in high altitude flight in Concorde, etc. Other experts are not nearly so sanguine as yours on the practicability of prediction of solar flares. The Space Radiation Study Panel² and a Task Group of Committee I of the International Commission on Radiological Protection³ suggested that the vast majority of visible solar disturbances do not result in significant radiation near the earth; those that do, and notably those that result in potentially dangerous giant flares, are not distinguishable from the others. The likely warning period is not always the 24 hours you give but may be as little as 10 minutes.—I am, etc.,

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Factors in Host-Virus Relationship

SIR,—The interesting paper "For Debate," by Dr. H. E. Webb (14 December, p. 684) raises many controversial points. In relation to his suggestion that dual virus infections may produce unusual clinical manifestations, I wish to continue the debate by pointing to

some evidence which might incriminate the following dual virus infections in certain diseases.

Measles and herpes simplex are both common infections of early childhood. Both viruses produce stomatitis, and both are potentially neurotropic. If herpes stomatitis were superimposed on a measles stomatitis it would probably not be detected clinically, and a dual infection would not be suspected. It seems possible that primary infection with herpes simplex (a D.N.A.-virus) occurring during the acute stage of a primary infection with measles (an R.N.A. virus) might so modify the measles infection, perhaps by production of interferon, that in some cells production of infective measles virus might be defective or incomplete. These cells might survive and replicate with accompanying replication of incomplete virus. If such were the case infective virus would not be found, but antibody might be produced as has been shown in incomplete infections of certain mammalian cell lines by influenza virus.¹ That such a dual infection with measles and herpes simplex might result in subacute sclerosing panencephalitis (S.S.P.E.) finds some support from the serological findings reported by Legg² in 22 patients and 23 controls; not only were there high antibody levels for measles in the S.S.P.E. patients, but also complement-fixing antibody for herpes simplex (but not for mumps, lymphocytic choriomeningitis, influenza A, influenza B, influenza C, and adenovirus) was found in a significantly greater number of the patients than the controls.

Recent reports suggest that herpes simplex and varicella-zoster viruses are antigenically related.^{3,4} These are well-recognized potentially latent viruses, and their cell membranes contain host material.⁵ Although the majority of the adult population have been infected with both of these viruses only a small proportion of such individuals have recurrent herpes simplex or develop zoster. It seems possible that subsequent attacks of recurrent herpes simplex or of zoster may be determined by which of these two viruses causes the first infection, and also perhaps by the interval between the two primary infections. If this interval is at least several weeks, and if the first infection in an individual is herpes simplex, that virus will become latent after the acute infection has subsided; it seems possible that latency of subsequent infection with varicella-zoster might be prevented by the boosting of the antigenically related herpes simplex antibody. Thus such an individual may be liable to attacks of recurrent herpes simplex but not to zoster. Similarly, if varicella is the first infection followed thereafter by herpes simplex, the varicella-zoster virus may become latent and thereafter cause zoster, but that individual might be free from recurrent herpes simplex infections. This possible relationship could, of course, be substantiated by showing that attacks of recurrent herpes simplex and zoster generally affect different individuals—an ideal investigation for general practice. If by coincidence there is combined active infection—that is, a dual infection—with two antigenically related viruses such as herpes simplex and varicella-zoster, or measles and an as-yet-unknown related human pathogen, it seems possible that there might be interference with the normal development of specific IgM and IgG antibodies. Such a

dysfunction might explain the pathogenesis of conditions such as S.S.P.E., or multiple sclerosis, where there are high antibody levels to various viral agents accompanied by abnormalities in immune globulins.—I am, etc.,

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Inhibition of Lactation with Oestrogens

SIR,—With respect I must disagree with Professor D. Llewellyn-Jones (9 November, p. 387) when he states that "inhibition of lactation using oestrogens is still the treatment of choice."

Three years ago I reported¹ that we were using no oestrogens and were getting perfectly satisfactory results by encouraging an extra fluid intake during the first three days. The rationale of this treatment is that engorgement is detrimental to breast feeding.² Waller used small doses of oestrogens to damp down engorgement, and this increased the mother's milk yield. Giving extra fluids may increase engorgement and thus be harmful to lactation.

During the last three years we have kept records and have learned that in 217 patients whose lactation was suppressed with water 55 had no discomfort, 50 slight, and 53 fair to moderate discomfort. Twenty-one had quite severe discomfort. This severe discomfort is adequately treated with analgesic drugs. Aspirin, Panadol (paracetamol), D.F. 118 (dihydrocodeine bitartrate), codeine, and Zactirin (tablets containing ethohaptazine citrate) have all been used according to the whim of the residents. In 109 instances, however, no analgesic was required or given.

It has of course been suggested that the giving of extra fluids cannot influence the result. However, in a group given no extra fluids the results were not so good.

In 106 patients who had been given extra fluids lactation had ceased,

by the 3rd day in	94 patients
" " 4th " "	1 patient
" " 5th " "	2 patients
" " 6th " "	2 "
" " 7th " "	1 patient

In three instances lactation was not suppressed.

In a group of 42 patients who had been given no treatment at all,

31 ceased lactation in hospital	
2 " " "	at 12 days
1 " " "	" 2 weeks
1 " " "	" 4 "
5 " " "	" 5 "
2 " " "	" 6 "

It does seem that the promotion of engorgement is a help in suppressing lactation.

I agree with Mr. S. J. Steele (30 November, p. 578) that oestrogen need not be used, and, since there is the unpleasant suggestion that thrombosis may be promoted, then I would go further and say that they ought

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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