with tritiated thymidine. Thrombosed vessels were occasionally seen in the bases of the oesophageal ulcers, with gross epithelial hyperplasia and numerous mitotic figures which were distinguishable from carcinomas only by the absence of muscular invasion of the disorganised epithelial overgrowth. Most of these lesions cleared with parenteral riboflavin.¹

Despite these widespread and severe changes in the squamous epithelium, ocular and respiratory abnormalities such as are found in vitamin A deficiency were not seen.

There were considerable resemblances between these lesions and those produced in the skin of mice by painting with carcinogens.³ Wynder⁴ and Warburg⁵ commented on the similarities between the oesophageal lesions in riboflavin-deficient mice and the precancerous oral and oesophageal changes in the Plummer-Vincent syndrome.

In all the B₂-deprived baboons there was intense adrenal cortical fibrosis and changes in 11- and 17-hydroxycorticosteroids and 17-oxosteroids before and after corticotrophin stimulation⁶ as well as changes in the serum protein pattern and tryptophan metabolism. There were no significant changes in liver histology such as occurs in pyridoxine-deprived baboons.² There is some evidence that analogues of vitamin B₂, like galactoflavine, produce side effects over and above those associated with deficiency of vitamin B₂ only, and these effects should be considered in any experiments involving the use of vitamin analogues.

We think then that riboflavin deficiency has an important place in the development of squamous epithelial derangements.

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¹ Foy, H., Gillman, T., and Kondi, A., *Medical Primatology*, Proceedings of the 3rd Conference on the Experimental Medicine and Surgery of Primates, part 2, pp 159-168. Basel, Karger, 1972.

² Foy, H., et al., *Journal of the National Cancer Institute*, 1974, 53, 1295.

³ Wynder, E. L., and Klein, U. E., *Cancer*, 1965, 18, 167.

⁴ Wynder, E. L., et al., *Cancer*, 1957, 10, 470.

⁵ Warburg, O., Nobel Laureate's Lecture, 1931.

⁶ Foy, H., Kondi, A., and Verjee, Z., *Journal of Nutrition*, 1972, 102, 571.

Skin testing in hospital

SIR,—Skin testing is a useful tool in incriminating a possible "allergic" cause for symptoms of hay fever and asthma. Prick tests using standard, commercially available allergens are now employed in a widespread way. The number of allergens tested varies considerably, however, and recent reports¹⁻³ have shown that testing with a limited number of allergens would identify over 98% of those asthmatic individuals who react to at least one allergen. We have been able to find only one report⁴ in which the limited form of skin testing has been assessed in "normal volunteers." We have therefore analysed the results of prick tests carried out in a general hospital over an 18-month period to see if a change in policy to include only a limited range of allergens would be equally effective.

A total of 582 patients with suspected nasal or pulmonary allergy were referred for skin testing from various departments in the hospital. Tests were carried out with a control and 12 common allergens (house dust mite, house dust, mixed grass pollens, mixed tree

pollens, mixed flower pollens, mixed shrubs, mixed feathers, mixed animal danders and feathers, mixed hair and furs, *Aspergillus fumigatus*, mixed moulds, and tobacco) provided by Bencard Ltd and Dome Laboratories.

Altogether 303 patients were positive to at least one allergen and 279 negative to all allergens. A result was regarded as positive if a weal greater than 1 mm in diameter was found in the presence of a normal control. The numbers of positive reactions are shown below; 247 subjects (82%) reacted to more than one allergen.

House dust mite	192	Mixed feathers	78
House dust	169	Mixed tree pollens	43
Mixed grass pollens	187	Mixed flower pollens	43
Mixed animal dander		Mixed moulds	14
and feathers	166	Tobacco	14
Mixed hair and furs	101	<i>Aspergillus fumigatus</i>	4
Mixed shrubs	81		

If only house dust mite, mixed grass pollens, and mixed animal danders and feathers had been used 97.4% of the individuals reacting to at least one of the 12 allergens would have been identified. Of the eight patients who would have been missed, six were positive to one allergen only. We suggest that, as a screening procedure, it is necessary to use only these three allergens plus a control. Further testing could be performed on the positive individuals at the physician's discretion and other allergens added to the screen should the patient's history indicate them.

Limited skin testing would not, of course, be appropriate to a specialist allergy unit but would provide a useful service in the general hospital, saving both time and expense.

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¹ Russell, G., and Jones, S. P., *British Journal of Diseases of the Chest*, 1976, 70, 104.

² McCarthy, O. R., *British Journal of Diseases of the Chest*, 1973, 67, 238.

³ Hendrick, D. J., et al., *Thorax*, 1975, 30, 2.

⁴ D'Souza, M. P., and Davies, R. J., *Lancet*, 1973, 2, 325.

Klinefelter's syndrome with hypogonadotrophic hypogonadism

SIR,—We were very interested in the short report by Dr J. N. Carter and others (22 January, p 212) of a patient with Klinefelter's syndrome and low serum gonadotrophin levels. In 1975 Rabinowitz *et al*¹ described a similar patient with undetectable serum follicle stimulating hormone (FSH) levels. We have had the opportunity to study a third patient with this unique combination of findings.

A 38-year-old man was referred to the endocrine clinic for evaluation of his defective sexual intercourse. On physical examination he was eunuchoid (height 177 cm, span 186 cm) with a high-pitched voice, scarce beard growth, gynecomastia, and a female escutcheon. The testes measured 1 × 1 cm and were of firm consistency. The phallus was small (3 cm). Radiographs of the sella turcica were normal. A clinical diagnosis of Klinefelter's syndrome was confirmed by a positive buccal smear and a karyotype of 47XXY from peripheral blood. The growth hormone response to insulin-induced hypoglycaemia and thyroid and adrenal gland function were normal. However, the thyroid stimulating hormone (TSH) response to thyrotrophin releasing hormone (TRH) (ΔTSH maximum 4.6 mU/l, normal range 7.5-18.5 mU/l) was diminished. The serum testosterone

level was 2.91 nmol/l (0.82 ng/ml), normal range 11.3-47.8 nmol (3.14-13.37 ng/ml). The serum luteinising hormone (LH) level was low normal (7.6 IU/l, normal range 7-16 IU/l) and serum FSH was undetectable.

Urinary gonadotrophin excretion was low (< 10 mouse units/24 h). A luteinising hormone-releasing hormone (LHRH) test showed a sub-normal LH response (ΔLH maximum 14 IU/l, normal range 27-160 IU/l) and a normal FSH response (3.6 IU/l, normal range 0.3-5.9 IU/l).

Thus, in contrast to the findings of Dr Carter and his colleagues, our patient with Klinefelter's syndrome showed the combination of defective pituitary LH and TSH reserve, whereas basal levels of FSH were undetectable with intact pituitary FSH reserve, indicated by the response to LHRH. This patient was the first case of hypogonadotrophic hypogonadism with Klinefelter's syndrome in our similarly documented series of 40 patients with hypergonadotrophic Klinefelter's syndrome.

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¹ Rabinowitz, D., et al., *American Journal of Medicine*, 1975, 58, 584.

ROSE system for treatment of cholera dehydration

SIR,—Cholera remains endemic in Indonesia and sometimes occurs in epidemics. Mortality rates in childhood cholera remain high in some reported series although improvements have occurred recently with the introduction of successful forms of oral therapy.^{1,2} We have recently found a form of simultaneous oral and intravenous rehydration to be very effective.

Ninety-five children aged 6 months to 13 years with severe dehydration and shock presented over a 9-day period in February 1976 after severe floods in Jakarta. The clinical diagnosis of cholera was supported by the passage of copious rice-water stools. Stools from 25 out of 31 patients examined microbiologically contained *Vibrio cholerae* El Tor Inaba type. A similar epidemic involving 70 patients aged 8 months to 13 years occurred over a six-day period in May 1976. *V. cholerae* type Ogawa was grown from 23 out of 32 stool specimens examined. Of the total of 165 patients, 15 were less than 12 months of age, 73 were aged 1-6 years, and the other 77 were aged 6-13 years. Patients were rehydrated by simultaneous oral and intravenous fluid administration. Ringer's lactate was given intravenously at 30 ml/kg body weight for the first hour and at 10 ml/kg/h for the next seven hours. An isotonic glucose-electrolyte mixture was given orally ad libitum; this mixture contains 85 mmol Na⁺/l, 70 mmol Cl⁻/l, 30 mmol HCO₃⁻/l, 15 mmol K⁺/l and 120 mmol glucose/l. Breast-fed children remained on breast-feeding throughout the period of treatment. Most children were discharged at the end of the eight hours' treatment; all were checked clinically three days after discharge. There were no deaths and no significant complications.

This indicates that childhood cholera can be successfully managed in a busy, inadequate, and understaffed hospital ward using a standard method of simultaneous oral and intravenous rehydration. In Indonesia this is known as the "ROSE" method, the explanation

being R for rehydration, O for oral fluid replacement, S for simultaneous intravenous rehydration, and E for education of mothers about diarrhoea and dehydration. This is very important and in large Indonesian cities a child's admission to hospital is often one of the few opportunities for this educational process to occur. This ROSE method is now being used on a nation-wide basis.

These results represent a marked improvement over recent years. In 1963 the mortality rate from childhood cholera in Jakarta was 46%, when glucose-saline was given intravenously. In 1973 the mortality rate dropped to 10%, when sodium bicarbonate was added to the intravenous fluid, in 1974 it dropped even further to 3.5%, when Ringer's lactate was given intravenously followed by glucose-electrolyte solution orally. This simple ROSE system could be used in large hospitals where facilities for intravenous therapy are available. Minor modifications, such as the substitution of sucrose for glucose, in the oral fluid should not adversely affect the results. Sucrose is much more readily available and much cheaper and has been shown to be very useful in the oral treatment of this disease.^{3,4}

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² Pierce, N F, *et al*, *Annals of Internal Medicine*, 1969, **70**, 1173.

³ Nalin, D R, *Lancet*, 1975, **1**, 1400.

⁴ Moenginah, P A, *et al*, *Lancet*, 1975, **2**, 323.

A case of reticulosis

SIR,—Dr Stuart Carne and Dr J M Whitehouse's article (19 February, p 492) seems to me to confuse doctors' anxiety and patients' anxiety. All doctors believe that the greatest sin they can commit is to miss an early case of malignant disease in spite of the fact that there is very little hard evidence that finding malignant disease early improves the prognosis. So when the nurse-mother mentions the possibility of Hodgkin's disease up goes the doctor's level of anxiety and off he goes on the medical pursuit trail—eventually passing his anxiety on to the consultant, who promptly amplifies it.

I was positively sweating by the time I got to the end of the article, but none of the doctors gave me the feeling that they really believed that this child had Hodgkin's disease—they were too busy rationalising their own anxiety into "treating the mother's anxiety." But from the beginning I was expecting to be informed as to why the mother was anxious. Had she just had nursing experience of Hodgkin's disease or had she had some much closer experience in her own family or in a close family friend? If you are going to treat the mother's anxiety, then surely the first thing to do is to try to trace it back to its roots. If she had had a personal experience of this disease, then compare the onset in the case she had in mind with that of her healthy son. That might relieve her anxiety forthwith. Alternatively, if it was just nursing experience,

she might have accepted the general practitioner's diagnosis—especially if this were reinforced with a simple blood test and two weeks on cephalixin. I am not surprised that this child developed postoperative complications.

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Rising incidence of childhood diabetes

SIR,—While the frequency of childhood diabetes in Glasgow may indeed be on the increase, this cannot possibly be concluded from the data presented by Dr J O Craig and his colleagues (5 March, p 639). Although their figures do, as they state, represent incidence (new cases per unit time) at the Royal Hospital for Sick Children, it is, of course, changes in incidence per unit population which are required if a change in frequency is to be demonstrated.

If the (rather shaky) assumptions are made that all new cases of childhood diabetes present at hospital and that the RHSC has a catchment population which has been consistent over time both in its size and in the comparability of its age structure to that of the City of Glasgow, then estimates of the child population of Glasgow may be applied to the data in order to show changes in frequency. If the Registrar General's decennial census figures for the 0-14-year age group in the City of Glasgow are employed as mid-decade estimates (interpolating for 1941) the numbers of cases to be expected relative to the 1933-6 incidence and population figures and the trend in the frequency of cases are as follows:

Period	No of cases		O : E
	Observed (O)	Expected (E)	
1933-6	27	27	1
1937-40	41	25.8	1.6
1941-4	17	25.8	0.7
1945-8	25	24.5	1.0
1949-52	19	24.5	0.8
1953-6	25	24.5	1.0
1957-60	39	25.1	1.6
1961-4	62	25.1	2.5
1965-8	48	21.2	2.3
1969-72	66	21.2	3.1
1973-6	113	21.2	5.3

That these figures do in general reflect the trends described by Dr Craig and his colleagues in no way justifies their description of their raw data as demonstrating a "true increase of morbidity" and it is similarly to be hoped that others will consider sceptically their suggestion that "conversations with colleagues" provide an adequate substitute for hard data in relation to this question at national level.

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Fatal oxprenolol poisoning

SIR,—We were interested in the account by Drs A Khan and J M Muscat-Baron of the death of a 57-year-old woman following an overdose of oxprenolol (26 February, p 552). It is somewhat surprising that loss of consciousness was one of the earliest manifestations of overdose with this drug. We wonder whether the salt emetic administered by the patient's husband could have contributed to her death. It is now well accepted that saline

emetics can be dangerous¹ and that their administration may lead to the rapid development of coma.^{2,3} Hypernatraemia, cerebral oedema, and congestion of the gastrointestinal mucosa are characteristic of salt poisoning. It is important to establish that these features were absent in the case described before accepting that the neurological findings were entirely due to oxprenolol.

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¹ Lawson, A A H, *British Journal of Hospital Medicine*, 1976, **16**, 333.

² Roberts, C J C, and Noakes, M J, *Postgraduate Medical Journal*, 1974, **50**, 513.

³ Goodbody, R A, *et al*, *Medicine, Science, and the Law*, 1975, **15**, 261.

Wound sepsis in colonic surgery

SIR,—Dr A T Willis and his colleagues (5 March, p 607) are to be congratulated on the elimination of bacteroides sepsis with prophylactic metronidazole in 27 patients undergoing elective colonic surgery in whom no oral antibiotic bowel preparation was used.

Using Leigh's¹ techniques of transport and culture, we have examined swabs or fragments of the incised colon and subcutaneous tissues as well as pus from any subsequent wound sepsis in 103 consecutive patients undergoing emergency or elective ileocolorectal surgery studied prospectively in two trials of antibiotic prophylaxis of wound sepsis. Sixty-one of these patients received oral antibacterial (as well as mechanical) bowel preparation, usually with a combination of phthalylsulphathiazole, neomycin, and tetracycline.

The wound sepsis rate when the bowel was prepared and the patient also protected by a single dose of 1 g of cephaloridine intracutaneously before skin closure was 3 out of 31 (9.7%). When the bowel was prepared but ampicillin, saline irrigation, or povidone-iodine was used in the incision 10 patients out of 30 (33.3%) suffered wound sepsis. These figures are comparable with the 4 (all aerobic) septic wounds out of 27 (14.8%) in patients prepared with metronidazole in the series reported by Dr Willis and his colleagues. When no antibiotic preparation was used the corresponding rates with and without cephaloridine were 6 out of 15 (40%) and 18 out of 27 (66.7%) compared with 12 out of 19 (63.2%) in Dr Willis's unprepared patients.

Bacteroides spp were isolated from only one patient (in organ, subcutaneous tissue, and pus) out of 61 who had had routine preparation compared with 9 out of 42 (21.4%) from bowel specimens, 4 out of 42 (9.5%) from subcutaneous tissue, and 12 out of 24 (50%) from pus in patients who had had no antibacterial bowel preparation.

It would appear that long-established methods of bowel preparation are not inferior to metronidazole in the prevention of sepsis after colonic surgery. The rationale for a seven-day course of metronidazole after operation, when it is established that the main cause of wound sepsis is bacterial contamination of the abdominal wall during surgery, eludes us.

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¹ Leigh, D A, *British Medical Journal*, 1974, **3**, 225.