Tuberculosis in Immigrants

SIR,—Your leading article (30 January, p. 247) on "New-style Cold Abscesses" is valuable in drawing attention to two recent papers in the *British Journal of Surgery*^{1,2} which describe a clinical manifestation of tuberculosis relatively much more common in the immigrant section of our population. These subcutaneous cold abscesses, which are quite often multiple, are a form of tuberculous disease well recognized in many developing countries. But one cannot allow the statement with which the leading article begins to go unchallenged. It is simply not true that "most tuberculosis seen in Britain today is in the immigrant population," though it is possible that most of the tuberculosis seen by the surgeons in Bradford and Birmingham, who wrote the two articles in question, is in immigrants.

A survey carried out by the British Tuberculosis Association in 1965 showed that an undue proportion (actually 16.5%) of all tuberculosis occurred in immigrants, mainly those from Commonwealth countries of Asia.³ The survey is being repeated this year. There has been only a modest influx of immigrants since 1965. Experience in Bradford and other cities shows that immigrants continue to experience a relatively high incidence of tuberculous disease for several years after coming to this country.⁴ So there may be rather more cases in immigrants in 1971 than in 1965. At the same time, cases of tuberculosis in the indigenous population have been declining by about 10% per annum,⁵ so there will be considerably fewer cases in this group. Nevertheless, one can confidently predict that in 1971 there will be at least twice as many cases of tuberculosis in the indigenous British population as in the immigrant population.—I am, etc.,

J. R. LAUCKNER

Newcastle General Hospital,
Newcastle upon Tyne

¹ Shaw, N. M., and Basu, A. K., *British Journal of Surgery*, 1970, 57, 418.

² Ward, A. S., *British Journal of Surgery*, in press.

³ British Tuberculosis Association, *Tubercle*, 1966, 47, 145.

⁴ Aspin, J., *British Medical Journal*, 1962, 1, 1386.

⁵ Department of Health and Social Security, *Annual Report of the Chief Medical Officer for 1969*, London, H.M.S.O., 1970.

Gynaecologists' Views on Amphetamines

SIR,—In his article on dysmenorrhoea (6 February, p. 329) Dr. V. R. Tindall rightly draws attention to the desirability of avoiding the use of amphetamine-containing substances in the treatment of this condition, giving alternative preparations of value.

I am therefore particularly concerned at the recommendation of Professor Philip Rhodes¹ for the use of Drinamyl (dexamphetamine plus amylobarbitone) and Edrisal (acetylsalicylic acid plus phenacetin plus amphetamine) in dysmenorrhoea with the express intention of producing an elevated mood by reason of their amphetamine content. It is now widely agreed that virtually the only condition for which amphetamine might be considered of value is narcolepsy, and its use as a pep pill is universally condemned.

It is disturbing enough that Professor

Rhodes should recommend Edrisal for its mood elevating qualities, but positively alarming that he should advocate the prescription of "purple hearts" for anything.

Might I express the hope that both he and other gynaecologists will search their consciences to see whether they cannot in good faith now join the large band of qualified men who are operating a voluntary ban on these substances?—I am, etc.,

A. LEWIS

London W.9

¹ Rhodes, P., *Update*, 1970, 2, 1501.

Antidiuretic and Hypoglycaemic Activity

SIR,—Vasopressin, chlorpropamide, paracetamol, and aminopyrine have a number of structural features in common, which might explain why these drugs may all have antidiuretic activity.¹ The common features are a phenyl group, usually *para*-substituted, associated with an amide or amide-like group terminated by a relatively hydrophobic group. Vasopressin includes the sequence tyrosine-phenylalanine (Fig. 1).

Folate Deficiency and the Pill

SIR,—Attention has been drawn recently to the development of folate deficient megaloblastic anaemia in women on oral contraceptive therapy.¹ No biochemical or radiological evidence of malabsorption was obtained in these patients, but the results of small intestinal biopsies were not reported. We have recently had the opportunity of studying a patient who developed a severe folate deficient anaemia while on oral contraceptives, in whom initially there were small intestinal changes which reverted towards normality on stopping oral contraceptives and giving folic acid supplements.

A 21-year-old housewife, who had had two previously normal pregnancies, presented two years ago with a severe anaemia. Her diet had been satisfactory and she has never

Antidiuretic activity tends to be preserved if the tyrosyl hydroxyl group is modified.² The calculated lowest energy conformations of vasopressin³ show this sequence exposed and available for interaction with receptor sites. Of the other drugs, the common features are most easily seen in the structure of chlorpropamide (Fig. 2), but they can

also be discerned in the structures of paracetamol and aminopyrine. Metformin has none of these structural features. It is a strongly basic derivative of guanidine, and might interact with a receptor site specific for the arginyl residue of vasopressin, which is essential for the antidiuretic activity of the hormone.²

If this structural analysis is correct, then chlorpropamide and metformin should show synergism with respect to both antidiuretic and hypoglycaemic activity.—I am, etc.,

A. J. KNELL

King's College Hospital Medical School,
London S.E.5

¹ *British Medical Journal*, 1971, 1, 302.

² Schröder, E., and Lübke, K., "The Peptides," vol. 2, p. 365. New York, Academic Press, 1966.

³ Gibson, K. D., and Scheraga, H. A., *Proceedings of the National Academy of Sciences of the United States of America*, 1967, 58, 1317.

a convoluted pattern on dissecting microscope examination. On section there was a dense inflammatory infiltration of plasma cells and lymphocytes in the lamina propria and the surface cells of the villi were low columnar with a poor brush border towards the tips of the villi. The villous length to crypt depth ratio was approximately equal.

During the last year, during which she has had a further pregnancy, this patient has remained well on a normal diet. Further investigations show: haemoglobin 14.0 g/100 ml, red cells normal; serum folate 8.0 ng/100 ml; faecal fat excretion 3.3 g/24 hr. Xylose excretion was again low at 1.4 g. in 5 hrs. A tritium labelled folic acid (H^3FA) absorption test was carried out using an oral dose of 40 μ g/kg. body weight of H^3FA . Thirty-two per cent was excreted in the urine which is within normal limits.² A second small intestinal biopsy (Fig. 2) showed a mixed pattern of leaves and ridges under the dissecting microscope. The villous height to crypt depth ratio was 2 to 1. The villi showed a normal tall columnar surface epithelium with a normal brush border. The lamina propria contained scanty plasma cells and some lymphocytes.

Though there is clearly an association between folate deficiency and oral contraceptive therapy we feel that this case raises a number of problems in the assessment of such patients. Streiff has clearly shown that in healthy women on oral contraceptive therapy there is a defect of absorption of dietary polyglutamates but no defect in absorption of monoglutamate.³ He has postu-

lated an inhibition of folate conjugase activity in the hydrolysis of dietary polyglutamate to more readily absorbable monoglutamate forms. However, small intestinal biopsy appearances in his patients who became anaemic were not described, and it is possible that these patients could have had occult coeliac syndromes in which folate deficiency was precipitated by contraceptives. The failure of complete reversal to normality of the intestinal mucosa in our case and the continued abnormality of xylose excretion point to this possibility. In addition, the direct effect of the drug on the small intestinal mucosa cannot be discounted as there was definite improvement after stopping contraceptives and prolonged treatment with folic acid. Certainly folate deficiency per se as in nutritional or puerperal states has not been associated with mucosal changes.^{4 5} Other reports suggest that folate deficiency in women on oral contraceptives is by no means uncommon, and further descriptions of the small intestinal biopsy appearances would be of interest.—We are, etc.

P. J. TOGHILL
P. G. SMITH

General Hospital,
Nottingham

- 1 Streiff, R. R., *Journal of the American Medical Association*, 1970, 214, 105.
- 2 Klipstein, F. A., *Blood*, 1963, 21, 626.
- 3 Streiff, R. R., *Clinical Research*, 1969, 17, 345.
- 4 Gough, K. R., Read, A. E., McCarthy, C. F., and Waters, A. H., *Quarterly Journal of Medicine*, 1963, 32, 243.
- 5 Veeger, W., Ten Thije, O. J., Hellemans, N., Mandema, E., and Niewig, H. O., *Acta Medica Scandinavica*, 1965, 177, 493.

Dehydration and Fat Babies

SIR,—Your recent leading article (16 January, p. 125) on the dangers of hypernatraemic dehydration in obese infants prompts us to draw attention to a related topic. It was shown five years ago in the United States that once weaning started the American baby was likely to have his sodium intake doubled and soon trebled, as he gulped down increasing amounts of the proprietary strained foods so eagerly proffered him by his mother.¹ This seems to have evoked little attention in Britain, yet our estimates of the sodium and chloride content of three generally available and popular brands of similar food on sale in our shops make it unlikely that things are different here. The figures are as follows:

		Na ⁺ Cl ⁻ (mEq)	
		Na ⁺	Cl ⁻
Brand A 4½ oz (120g) tin ..	Beef broth	12	14
	Chicken and vegetable broth	11	12
Brand B Powder equivalent to 4½ oz (120g) tin ..	Vegetable, chicken, and tomato	21	18
Brand C 4½ oz (120g) jar ..	Vegetable and chicken	18	18

The majority of infants are now artificially fed (cow's milk containing nearly three times as much sodium chloride as human milk) and it is not at all unusual to

find solids added to the diet within a few weeks of birth.² During the second six months of life, if not earlier, an infant may consume more than one of the above brand tins, jars, or packs daily in addition to his cow's milk which alone supplies him with more than enough sodium and chloride for his needs.

Young rats, of a strain known to develop hypertension, did so earlier than controls when they were given a high salt intake (American infants' weaning diet) at weaning.³ Hypertension had earlier been shown to persist in similar rats after an excessive salt intake was stopped.⁴ Though there is no certainty as to whether there is a relationship between excessive salt intake and essential hypertension in humans,⁵ population studies attempting to answer this question have considered only the adult salt intake. We have reason to suppose that obesity in adult life is sometimes related to obesity—and by implication overfeeding—in infancy.

Perhaps we should be looking much more critically at feeding practices in the first year of the first decade where hypertension as well as obesity are concerned. It is often difficult to change established feeding patterns later, but Fomon⁶ has shown that young infants will readily accept unsalted weaning foods, which may be unpalatable to their mothers.—We are, etc.,

PAMELA A. DAVIES
ELIZABETH A. HUGHES

Hammersmith Hospital,
London W.12

- 1 Puyau, F. A., and Hampton, L. P., *American Journal of Diseases of Children*, 1966, 111, 370.
- 2 Arneil, G. C., *Dietary Study of 4,365 Scottish Infants—1965*, No. 6. Edinburgh, Scottish Home and Health Department, 1967.
- 3 Dahl, L. K., Heine, M. and Tassinari, L., *Nature*, 1963, 198, 1204.
- 4 Dahl, L. K., *Journal of Experimental Medicine*, 1961, 114, 231.
- 5 Pickering, G., *Hypertension, Causes, Consequences and Management*. London, J. & A. Churchill, 1970.
- 6 Fomon, S. J., Thomas, L. N., and Filer, L. J., *Journal of Pediatrics*, 1970, 76, 242.

Renal Tubular Necrosis after Gastroenteritis in Infants

SIR,—Dr. A. R. Chrispin and others (14 February 1970, p. 410) report that in the case of three infants who had gastroenteritis accompanied by severe dehydration the presence of renal tubular necrosis and renal insufficiency could be demonstrated. Having described the characteristic features of excretion urographic studies they recommend a method suitable in practice for the demonstration of change. The specific nature of the radiological differences was confirmed in experimental nephropathic studies in a more recent paper.¹ It was stressed that the cases would not have been recognized merely from clinical symptoms, and it was suggested that renal tubular damage is a relatively frequent complication in shock conditions in infants.

We should like to draw attention to our own observations, which provide a further basis for the supposition that renal tubular damage in the above diagnosis is more frequent than previously thought. In addition, our data suggest that the renal damage is initiated by urate nephropathy. In our first observations² we found that in severe