

which Dr Coope and her colleagues based their statistics are not available and may, in fact, not differ markedly from the range of normal for their laboratory. For example, although they comment on raised levels of factor X, there is no significant difference in this parameter between their oestrogen-treated and placebo groups. The thromboelastogram also showed no significant change. The clinical significance of their reported changes cannot, therefore, be defined.

The main indication for long-term oestrogen replacement therapy is to prevent certain menopausal-related conditions such as osteoporosis. By following patients for more than one year one can frequently detect a biphasic effect in which, for example, disturbed carbohydrate balance is followed by normalization of tolerance.² The same may also be true of the coagulation mechanism. Thus von Kualla *et al*³ concluded that conjugated oestrogens produced a shift toward hypercoagulability as evidenced by a shift of the parameters of the thromboelastogram (in contrast to the findings of Dr Coope and her colleagues) and the detection of fibrin monomers. However, the latter test became positive more frequently after five than after 21 tablets. As far as I am aware, our study is the only long-term evaluation of the effect of natural oestrogens on coagulation.

Finally, it is commonly observed that certain women appear to have an increased sensitivity or idiosyncrasy to oestrogens (including conjugated oestrogens) and react by developing (among other side effects) hyperglycaemia,¹ hyperlipaemia,⁵ and hypertension.⁶ It is therefore essential that greater consideration be given to individual response and that judgment should not be based solely on the reaction of a study group. Although formal long-term epidemiological surveys have not yet been conducted, it is pertinent to note that the conjugated oestrogens have been available for 30 years without any significant clinical association between their use (in the usual dose recommended for oestrogen replacement therapy) and the development of thrombotic sequelae etc, as was reported following the relatively brief exposure to the synthetic oestrogens in the birth control pill.

MORRIS NOTELOVITZ

Department of Obstetrics and Gynecology,
University of Florida College of Medicine,
Gainesville, Florida

- 1 Notelovitz, M. and Grieg, H B W, *South African Medical Journal*, 1975, **49**, 101.
- 2 Di Paola, G, Robin, M. and Nicholson, R, *American Journal of Obstetrics and Gynecology*, 1970, **107**, 124.
- 3 von Kualla, E, Droegemueller, W. and von Kualla, K N, *American Journal of Obstetrics and Gynecology*, 1975, **122**, 688.
- 4 Notelovitz, M, *South African Medical Journal*, 1974, **48**, 2599.
- 5 Notelovitz, M. and Southwood, B, *South African Medical Journal*, 1974, **48**, 2552.
- 6 Notelovitz, M, *South African Medical Journal*. In press.

Information contained in drug advertisements

SIR,—Dr G V Stimson (29 November, p 508) concludes that the low level of information currently presented in drug advertisements, particularly the omission of approved names and prescribing information, may be related to the reliance of companies on supporting data sheets, which the Medicines Act 1968 now requires to be circulated. A comparison with previous advertising practice

is, however, available¹ and suggests that this conclusion may not be correct. Patterns of advertising prior to the Act were not substantially different from those of the present.

In this four-week study of communications received by one general practitioner in direct mail advertisements and those contained in periodicals and magazines there were 697 advertisements relating to 267 drugs. Approved names were omitted in 3.4% of advertisements. Of the drugs advertised, 55.8% were classified by the Standing Joint Committee on the Classification of Proprietary Preparations (Proplist) according to the therapeutic efficiency and acceptability and 6.7% were classified in group B—that is, unacceptable drugs. Only 19.8% of advertisements were supported by reference to journals. Pictorial content was 65.8% and was particularly high in relation to drugs acting on the nervous system, which had the largest number of advertisements (147). The frequency of inclusion of prescribing information was not specifically recorded.

Apart from the requirement for data sheet circulation, it was hoped that the provision of the Act would reduce the quantity and improve the quality of advertising material by ensuring inclusion of the approved name(s) of the active constituent(s), rejecting advertisements with strong emotional orientation, and encouraging a rational scientific basis. With Dr Stimson's confirmatory conclusion on the insufficiency of information in current drug advertisements in periodicals we may possibly see improvements in drug advertising in the near future.

KENNETH S WILSON

Royal Infirmary,
Edinburgh

- 1 Wilson, K S, *Health Bulletin*, 1969, **27**, 40.

What are haemorrhoids?

SIR,—In your leading article (15 November, p 365) the impression is given that I do not consider venous congestion to be important in piles. Such is not the case and I would be grateful for the opportunity of putting the record straight.

My main thesis, certainly, is that the anal canal is lined by discrete cushions of specialised submucosal tissue whose purpose is to assist in continence (incidentally, the three main ones may be subdivided to a greater or lesser extent so that the anal lumen, although usually closing to a more or less triradiate slit, may appear stellate) and that piles are merely the result of their downward displacement. However, in the article to which you refer¹ and elsewhere^{2,3} I have argued that their displacement may be attributable to straining, causing venous congestion and therefore swelling of the cushions, making their expulsion more likely.

Other possibilities exist. First, hard stools may be more likely to push them out or "sticky" ones to drag them. Secondly, a rigid, narrow anal ring might predispose to piles; there would be less likelihood of the cushions flattening when the circumference of the anal canal cannot be much increased on defaecation. Thirdly, irritation of the anal lining (as in diarrhoea) may cause the cushions to swell and thereby be extruded.

Another question on which I would like to comment concerns the bleeding seen in the absence of piles. It is perfectly possible

that in some people only the upper (mucosa-covered) part of the cushion prolapses; this highly vascular tissue may then be nipped between its firm anchorage at the pectinate line and the stool.

HAMISH THOMSON

Gloucestershire Royal Hospital,
Gloucester

- 1 Thomson, W H F, *British Journal of Surgery*, 1975, **62**, 542.
- 2 Thomson, W H F, *Lancet*, 1975, **2**, 494.
- 3 Thomson, W H F, *Proceedings of the Royal Society of Medicine*, 1975, **68**, 574.

Whooping-cough vaccination

SIR,—Apropos the letter from Professor N R Grist (29 November, p 519) it may be worth pointing out that it is common knowledge among experienced paediatricians that phenobarbitone in relatively high dosage is a very effective symptomatic treatment for whooping cough in young infants and will control the spasms without producing untoward side effects.

We have seen a small epidemic of 10-15 cases in young infants at Booth Hall Hospital over the past year and in every case in my care, some of them with alarming symptoms characterised by apnoea and bradycardia, phenobarbitone was rapidly effective, although some babies relapsed when it was discontinued.

If this is general experience, as I suspect, it weakens the argument for exposing older infants to the rashes and discomforts of whooping-cough vaccination in order to reduce the risk of younger and more vulnerable babies becoming infected; it may also cast some light on the mechanism of paroxysmal coughing.

JOHN A DAVIS

University Department of Child Health,
St Mary's Hospital,
Manchester

Acute rhabdomyolysis and renal failure after injection of peanut oil

SIR,—It is difficult to understand what made Dr K L Lynn (15 November, p 385) choose peanut oil as the causative agent of rhabdomyolysis and acute renal failure in a drug addict who had taken seven other drugs at the same time, including alcohol and narcotics, and was brought unconscious to hospital.

Heroin addiction and coma are two well-documented causes of rhabdomyolysis and acute renal failure.¹⁻³ However, the case report contains clues that point to another interpretation. Swollen, painful, and tender muscles with rapid onset of muscle wasting and weakness involving predominantly the lower limbs shortly after a binge and recovering with abstinence is the classical picture of acute alcoholic myopathy. This uncommon but well-defined syndrome is usually accompanied by myoglobinuria and occasionally by acute renal failure.⁴⁻⁸

Dr Lynn describes "a flaccid paraplegia with loss of pain and tactile sensation below L2 with sacral sparing" without comment or diagnosis. This either means a coincidental incomplete transverse myelitis (known to occur in drug addicts⁹) at an unusual level with inexplicable sacral sparing and unexpected preservation of the sphincter function or, alternatively, an attempt to describe in neurological terms myopathic

weakness in a poorly co-operative addict in the withdrawal stage. Tenderness and pain could well make bedside examination of sensory function impossible. Alcoholic peripheral neuropathy should also be considered as a possible cause of the sensory loss.

The case for peanut oil has certainly not been proved and it would be premature to add this substance to the long list of causes of rhabdomyolysis. In this context it is of interest that peanut butter in the melted form has been reported to be used intravenously by addicts in Los Angeles, though there is no known "high" effect.¹⁰

PETR SKRABANEK

Department of Neurology,
St Laurence's Hospital,
Dublin

- 1 Richter, R W, *et al*, *Journal of the American Medical Association*, 1971, **216**, 1172.
- 2 Penn, A S, Rowland, L P, and Fraser, D W, *Archives of Neurology*, 1972, **26**, 336.
- 3 Rowland, L P, and Penn, A S, *Medical Clinics of North America*, 1972, **56**, 1233.
- 4 Perloff, G T, Hardy, P, and Velez-Garcia, E, *New England Journal of Medicine*, 1966, **274**, 1277.
- 5 Hed, R, Larsson, H, and Wahlgren, F, *Acta Medica Scandinavica*, 1955, **152**, 459.
- 6 Fahlgren, H, Hed, R, and Lundmark, C, *Acta Medica Scandinavica*, 1957, **158**, 405.
- 7 Hed, R, *et al*, *Acta Medica Scandinavica*, 1962, **171**, 585.
- 8 Schneider, R, *Southern Medical Journal*, 1970, **63**, 485.
- 9 Richter, R W, and Rosenberg, R N, *Journal of the American Medical Association*, 1968, **206**, 1255.
- 10 Landy, E E, *The Underground Dictionary*, p 147. London, MacGibbon and Kee, 1971.

Localised plasmacytoma in a patient with α -chain disease in remission

SIR,—We read with great interest the letter from Dr J Rogé and others (25 October, p 225) about their unique case of α -chain disease which remains in complete remission six years after treatment with antibiotics only. This case and our own case, to which they refer (25 May 1974, p 409) represent benign examples of α -chain disease that respond to treatment, remain in remission for long periods of time, and are possibly cured. At the other end of the scale is the fulminant type which shows poor response to treatment and fast deterioration and death from generalisation of the disease.¹⁻³

We should like to take this opportunity to report the further history of our case, which may be of interest. This patient had been symptom-free and in complete immunological and histological remission for 20 months after stopping all treatment when he developed a plasmacytoma involving the ileocaecal area. During this phase of his illness there was no evidence of reactivation of α -chain disease. The tumour was resected and the patient, nearly two years after the operation, remains symptom-free on a weekly maintenance dose of 200 mg of cyclophosphamide intravenously. It appears that the plasmacytic tumour of the ileocaecal area originated from a new abnormal clone and that the patient's α -chain disease is still in remission.

O N MANOUSOS
J C ECONOMIDOU

Second Department of Medicine,
University of Athens,
Hippokraton General Hospital,
Athens

- 1 Seligmann, M, *et al*, *Annals of the New York Academy of Sciences*, 1971, **190**, 487.

- 2 Economidou, J C, *et al*, *American Journal of Digestive Diseases*. In press.
- 3 Manousos, O N, in *Topics in Gastroenterology*: 3, ed C S Truelove and M J Goodman, p 259. Blackwell, Oxford, 1975.

Salt overdosage

SIR,—The report of a case of salt overdosage (15 November, p 386) and subsequent correspondence raise questions of practical importance in managing hyperosmolar states. Dr R C M McGouran, in discussing his report, recommends rapid lowering of the plasma sodium to limit the duration of damaging osmotic shrinkage of brain tissue. Dr Carol Fitzpatrick (29 November, p 517) feels that the standard practice of slow rehydration of hypernatraemic infants should be extended to adult cases to prevent brain damage due to a rebound cellular overhydration with cerebral oedema and convulsions.

In animal experiments Holliday *et al*¹ have shown that saline infusions producing constant hypernatraemia lead to shrinkage of brain cells over the first few hours followed by a gradual resumption of normal cell volume, which is complete within a few days and is accompanied by an increase in cell potassium. This increase falls short of the calculated requirement to restore normal cell volumes at the raised osmolality and they concluded that, in addition to the uptake of potassium ions, the cell substrate itself could generate, by molecular rearrangement, so called "ideogenic osmoles" to protect against a hyperosmolar extracellular milieu.

Consequently in treatment of a hyperosmolar patient, once normal cell volumes have been attained, if this augmented intracellular osmole quota (both potassium and ideogenic) cannot be jettisoned at a parallel rate with the fall in extracellular osmolality, further water may enter the cells and over-expansion of the intracellular space ensue. It could aid rational management if it were possible to detect clinically the point at which the initially contracted intracellular space had regained its normal size and was in imminent danger of over-expansion. Holliday's work suggests that at this point the avidity for potassium of the contracted cell should have declined to zero and potassium ions should begin to pass back into the extracellular fluid. This occurrence should be clinically recognisable. Dr McGouran's case demonstrates the initial phase of cellular potassium avidity, with a plasma potassium of 3.1 mmol/l in the absence of any stated reason for potassium depletion.

In a personal case of acute hypernatraemia without dehydration the initial plasma sodium level was 186 mmol/l and the patient deeply comatose. Treatment with one litre of 5% dextrose infused every eight hours and no diuretics produced a steady fall to normal sodium levels by the fifth day. No convulsions occurred, but consciousness took three weeks to return and recovery of the central nervous system was insufficient to allow the patient to return to an independent existence. The initial potassium level was 2.9 mmol/l and ECG changes of hypokalaemia were marked. As the plasma sodium declined to normal levels the potassium rose to 4.6 mmol/l and the ECG became normal. Once plasma potassium had risen within the normal range, on the third day, urinary potassium increased and over the subsequent four days there was a net body loss of over 400 mmol before a balance was reached.

This case illustrates how the considerable movements of potassium that occur in these gravely ill patients may be observed by simple estimations of plasma and urinary electrolytes supplemented by ECG traces.

With further experience I feel they will be increasingly useful in deciding the point at which the rapid initial lowering of osmolality, which some might deem advisable, must be abated to perhaps that which a functioning pair of kidneys and a normal fluid intake might attain.

R S MACDONALD

London W4

- 1 Holliday, M A, *et al*, *Journal of Clinical Investigation*, 1968, **47**, 1916.

Continuous positive airway pressure by facemask in newborn infants

SIR,—We should like to thank Mr L P Allen and his colleagues at University College Hospital for their timely article (18 October, p 137) on continuous positive airway pressure (CPAP) by Bennett facemask. Timely for us because on the day of publication we had an infant with severe respiratory distress syndrome who was rapidly deteriorating.

We had not previously attempted the use of CPAP because the many problems associated with head enclosure (Gregory box, Barrie's bag) and endotracheal tubes were too great, we felt, with insufficient and inexperienced staff. However, the use of the face mask seemed attractively simple. We did not have a Bennett mask and so we used a black rubber oxygen funnel (commonly used for administering oxygen during resuscitation following delivery and found on most resuscitation trolleys), and this produced an excellent seal.

When CPAP was first applied the infant was deteriorating and in 100% oxygen had a P_{aO_2} of 6.1 kPa (46 mm Hg). After two hours of CPAP at 8 cm H_2O the P_{aO_2} had risen to 10.2 kPa (77 mm Hg) and after three hours to 24.7 kPa (186 mm Hg).

The method proved to be simple, safe, and effective and could be easily managed by nursing staff unfamiliar with intensive neonatal care.

D G BANNISTER
C I HAINES

Bromsgrove General Hospital,
Bromsgrove, Worcs

Fluoride and bones

SIR,—Drs Jenifer Jowsey and B L Riggs (27 September, p 766) make a number of comments on our paper concerning prophylactic fluoride treatment and aged bones (12 July, p 73). Their letter includes a few points which we cannot fully understand.

With regard to calcium intake, as we mentioned in our discussion, the amount of milk our patients consumed daily was on average one litre. This contains 1200 mg of calcium, which according to all standards is more than needed. Drs Jowsey and Riggs consider "the lack of accompanying calcium" to have had a deleterious effect on our patients. We, however, think that it is the total amount of calcium consumed which counts and not whether this is taken in tablets or from natural sources. Of course it is important to examine the literature, but many studies done on test animals are in contradiction to the optimistic view of Drs Jowsey and Riggs as to the beneficial effect of fluoride on the strength of bones. And, again, no results from theoretical studies