thyrotrophin (TSH) responses in three cases are reminiscent of primary hypothyroidism rather than hypothalamic disease.

We have evaluated the growth and hormonal status of 14 children now aged 7-15 years who have been off leukaemia treatment for at least 1.1 years. In the year after stopping chemotherapy these children had a mean growth rate of 8 cm year (range 4.9-11.2 cm/year) and their linear growth has been maintained in all cases. We have not found any significant hormonal disturbance in those children who agreed to undergo a combined hypothalamic-anterior pituitary function test, and the older children are passing normally through puberty.

We agree that long-term careful surveillance of these children is mandatory but suggest that endocrine investigation is necessary only when their growth or development gives cause for concern.

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¹ Richards, G E, *et al*, *Journal of Pediatrics*, 1976, **89**, 553.

² Shalet, S M, *et al*, *Archives of Disease in Childhood*, 1976, **51**, 489.

³ Shalet, S M, *et al*, *Journal of Pediatrics*, 1977, **70**, 920.

Transmission of agent of Creutzfeldt-Jakob disease

SIR,—Your leading article "Creutzfeldt-Jakob under control" (25 February, p 463), raising the question of transmission of the spongiform encephalopathies and in particular the risk factors associated with medical and surgical techniques, prescribes "a close watch on all human-to-human transfers of material by artificial means." We have recently studied the possibility of such transmission by dental procedures, which may carry the risk of transfer between patients (or between patient and dentist) of gingival tissue contaminating dental burrs. Scrapie infection in mice reproduces many of the clinical features of Creutzfeldt-Jakob disease and has been used as an experimental model.

Adult C3H mice were infected with ME7 scrapie agent (kindly given to us by Dr A G Dickinson) and killed after 15 weeks (donors). Their gingival tissues were traumatised lightly with slowly rotating dental burrs, which were then used immediately (without cleaning) to traumatise the gingivae of healthy mice (recipients) under light ether anaesthesia. Controls were treated with burrs used previously on healthy donors. Twenty-four pairs of animals (experimental and control) were thus treated.

After 15 months the recipients were killed, coronal sections of brain and spinal cord cut, and the sections stained by Cajal's gold sublimate impregnation. None of the mice showed astrocytosis characteristic of scrapie infection. However, astrocytosis did develop in mice injected intraperitoneally with 5.0 (but not 0.5) mg infected gingival tissue, indicating the presence in the tissue of scrapie agent at a titre between $10^{2.5}$ and 10^3 infective doses per gram wet tissue. The amount of tissue contaminating the burr was found by weighing the burr before and after use to be 50-100 μ g; if all of this were transferred the probability of transmission of scrapie can be estimated at approximately 1 in 50.

If the agent of Creutzfeldt-Jakob disease is similarly distributed the findings suggest that a hazard of transmission of central nervous system (CNS) disorders of this type by dental procedures exists, although at a low level. If

so the prevalence of dental treatment indicates the need for caution in the dental management of patients with CNS disorders of known or suspected slow virus aetiology.¹ It would seem prudent that dentists, when treating such patients, should follow precautions such as those recommended for carriers of hepatitis B,^{2,3} in particular discarding steel burrs after treatments involving possible gingival trauma.

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¹ Adams, D H, and Bell, T M, *Slow Viruses*. Reading, Massachusetts, Addison Wesley, 1976.

² Adams, D, and Zwink, R, *British Dental Journal*, 1976, **141**, 341.

³ Nagington, J, and Varley, G W B, *British Dental Journal*, 1976, **141**, 337.

Cutaneous reactions to labetalol¹

SIR,—We have recently investigated a 64-year-old man who developed a widespread skin rash while taking labetalol as Trandate; the rash returned on rechallenge with pure labetalol.

Like the patient described by Dr R W Gange and Professor E Wilson Jones (1 April, p 816), our patient had been taking labetalol 400 mg twice daily for three months when his widespread itchy rash started to appear, and the challenge with pure labetalol resulted in recurrence of the rash also at two weeks. The eruption in our patient was not typical of lichen planus. When seen one month after the onset there was a symmetrical, widespread, scaly erythematous rash. On the extensors of the limbs and back of the hands there was follicular hyperkeratosis and erythema suggestive of pityriasis rubra pilaris. On the lumbar area the scales were heaped up as in psoriasis and on the flanks and sacral area the patches had a cyanotic tinge characteristic of lichen planus. Papules and bullae were absent and the genitalia were not involved.

Biopsy showed patchy basal liquefactive necrosis of the epidermis, intra-epidermal necrotic keratinocytes, and a dermal perivascular lymphocytic infiltrate; these changes are similar to those described by Dr Gange and Professor Wilson-Jones and are typical of beta-blocker cutaneous eruptions. Direct immunofluorescence showed fibrin deposition at the dermoepidermal junction, with cytooid bodies in a distribution compatible with lichen planus.

Our patient had no ocular or pulmonary abnormalities but had a weakly positive response to tests for antinuclear factor. The drug rechallenge was with "pure" labetalol 400 mg thrice daily supplied by Allen and Hanburys Research Ltd. The repeat cutaneous reaction to this challenge demonstrates that the labetalol is to blame and not the colouring or other constituents of Trandate.

We agree with Dr G M Levene and Dr Gange (25 March, p 784) that early reporting of cutaneous eruptions to new beta-blockers is essential and we hope to report this case in more detail in the near future. We wish to stress that both in our case and in that of Dr Gange and Professor Wilson-Jones the cutaneous eruption did not occur until the drug had been taken for three months, so that the link with labetalol may not be initially obvious. The interesting feature in our patient is that the eruption and histology were similar to those previously described in association with other beta-blockers—that is, although the histological appearances are compatible with lichen planus the eruption may resemble psoriasis, lichen planus, eczema, and pityriasis

rubra pilaris. The clinical picture in our case was, in fact, very similar to that occurring with oxprenolol.¹

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¹ Holt, P J A, and Waddington, E, *British Medical Journal*, 1975, **2**, 539.

SIR,—We read with interest the report by Dr R W Gange and Professor E Wilson Jones (1 April, p 816) of a patient who developed lichen planus on labetalol.

We have seen a 66-year-old female patient with essential hypertension who developed a lichenoid eruption after taking labetalol 300 mg thrice daily for 13 months. She first experienced a widespread pruritus and subsequently lesions appeared on her neck and spread to the trunk and limbs, sparing only the face. They were perifollicular, hyperkeratotic, and erythematous and in some areas became confluent. She also complained of a dry mouth and nose, although no lesions were seen on the mucous membranes.

Two biopsy samples showed several areas of hydropic degeneration of the epidermal basal layer; a few Civatte bodies and dyskeratotic cells were present. There was marked follicular hyperkeratosis, a prominent granular layer, and moderate dermal inflammatory infiltrate in relation to the hair follicles and the areas of degeneration. Bullous lesions were not seen. The overall appearances resembled those of lichen planopilaris. Immunofluorescence studies revealed several separate broad areas of linear basement membrane immunofluorescence with antifibrinogen. This band of fluorescence was similar to the findings of Barthelmes and Hausteil¹ in lichen planus, but globular deposits of IgG were not demonstrated.

No relevant autoantibodies were found in the serum. Labetalol treatment was stopped and the patient was given propranolol for hypertension but no specific treatment for her rash. After five weeks the rash cleared, apart from minimal discoloration. Two weeks later she was rechallenged by giving the same dose of labetalol and after a further 10 days the rash recurred with features and distribution similar to the original one. Since stopping the labetalol the second rash has also cleared.

We regard the positive rechallenge in both patients so far reported as evidence of a causal relationship between labetalol and the lichenoid eruptions. The significance of the immunofluorescent findings remains uncertain.

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¹ Barthelmes, von H, and Hausteil, V F, *Dermatologische Monatsschrift*, 1970, **156**, 85.

College of Anaesthetists

SIR,—It is popular these days to refer to the "Scottish Dimension" when discussing politics, oil, and industry. It seems all the more surprising therefore that none of your correspondents has observed that Scottish anaesthetists have three alternatives to choose from: (1) no change in the present arrangement; (2) an independent College of Anaesthetists in London; and (3) an independent College of Anaesthetists in Scotland.

A meeting to discuss the matter will be held in Edinburgh on 11 April. In a profession that