the hyperkeratotic aspect, with few residual squamous lesions; the inflammatory component disappeared after 14 days. The second patient, affected by a nummular type of psoriasis with large and thick plaques, has been followed up for only 7 days, but the results have been good.

Correlations between skin and H_2 receptors have been described.[1-3] Our observations seem to confirm these findings, suggesting new lines of research into the cause of psoriasis and into its treatment.

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NON-ACCIDENTAL BARBITURATE POISONING OF CHILDREN

SIR,—Dr Lorber (Aug. 26, p. 472) described unexplained episodes of coma in a two-year-old child. He asked whether anyone has had a similar experience and postulated that it might be a case of encephalitis lethargica.

I have had a similar experience. This was a child of the same age or a little older, who also came in with many unexplained episodes of coma, during which multiple investigations were done, even going as far as a brain biopsy. No abnormalities were detected. Several of the episodes occurred while the child was in hospital. Eventually the child was discharged undiagnosed only to turn up at another hospital elsewhere a few months later. There again similar episodes occurred. However, fortunately, the parent of a child in the next bed happened to notice the mother giving the child some tablets and asked what they were. The story then came out that the mother had been feeding the child barbiturates in large amounts unknown to anyone. At first she strenuously denied it, but, when confronted with the evidence, she admitted that she had been doing it over a long period of time. The mother required psychiatric help. I should mention in conclusion that this case occurred before the days of efficient drug screening of blood and urine and possibly, therefore, is not the explanation in Lorber's case. Nevertheless, the fact that the child seen in Sheffield had a rash when the periods of unconsciousness occurred makes one wonder whether this was a drug sensitivity.

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⁂As Dr Lorber subsequently reported (Sept. 23, p. 680) the Sheffield case was one of non-accidental barbiturate poisoning.—ED. L.

THE DOG IT WAS THAT DIED

SIR,—Dr Blaser and colleagues (Nov. 4, p. 979) describe five cases of campylobacter enteritis aasociated with young dogs with diarrhœa. We have seen a campylobacter infection concerning a dog with rather different circumstances.

A 19-year-old student nurse had diarrhœa and vomiting with pyrexia and abdominal pain on July 13, 1978. *Campylobacter* sp. was isolated from her stools and she recovered during a course of erythromycin stearate. She had eaten hospital food at work and the same food as her family at home, except for some pork luncheon meat the previous day which had been obtained from a local butcher. No other food eaten the previous week is suspect but none of the luncheon meat, the most obvious source, was available for examination. Her sister, who was also offered the pork luncheon meat, did not like it after having tasted it and gave her share to their dog. The dog, a previously well 8-year-old alsatian, became ill 4 days after eating the luncheon meat and collapsed and died after 36 h. Necropsy revealed a large quantity of blood-stained fluid in the dog's abdominal cavity, severe enteritis, with the mucous membrane a uniform dull red colour throughout its length, and bloodstaining of the contents. The liver was enlarged and mottled. The heart was engorged with blood. *Campylobacter* sp. was isolated from the dog's blood, fæces and tissues. Dr M. B. Skirrow (Worcester Royal Infirmary), who kindly examined the isolates for us, found those from the girl and the dog to be indistinguishable and fairly similar to a control strain (N.C.T.C.11168) and unlike most pig strains.

We thank Mr Alan Slee for the dog necropsy report and his cooperation.

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CHOLESTEROL AND IMMUNE RESPONSE TO INFLUENZA ANTIGENS

SIR,—Immunisation can alter blood lipids in animals.[1,2] Lipoproteins may have immunoregulatory properties in both animal and human systems,[3,4] and lipid abnormalities have been described in human disorders with immunological features such as minimal lesion nephrotic syndrome,[5] rejecting organ allografts,[6] and systemic lupus erythematosus.[7] Because of our interest in immunological mechanisms in vascular disease,[8] we tested the hypothesis that immunological stimulation can affect lipids in man; to do this we looked for changes in lipid levels after prophylactic immunisation with influenza vaccine.

Influenza virus subunit vaccines (Commonwealth Serum Laboratories) were purified by zonal ultracentrifugation.[9] 28 volunteers aged 18–26 were studied at an airforce academy; 12 were immunised by subcutaneous injections of 1 ml of a trivalent vaccine containing 250 I.U. of each of strains A/Texas/1/77, A/USSR90/77, and B/Hong Kong/8/73; 16 received monovalent vaccine containing 500 I.U. of B/Hong Kong/8/77. Paired sera (pre-immunisation and one month post-immunisation) were stored at −20°C, subsequently treated to remove non-specific inhibitors,[9,10] and assayed for specific influenza antibodies by hæmagglutination inhibition.[10] Total cholesterol, triglycerides, and high-density-lipoprotein (H.D.L.) cholesterol were measured by conventional methods.[11]

As summarised in the table, immunisation was followed by a significant *increase* in mean level of total cholesterol and by a *decrease* in mean level of H.D.L.-cholesterol. The variation in H.D.L.-cholesterol associated with immunisation (mean square =0·062 on 1 d.f.) and the variation between individuals (mean square =0·116 on 27 d.f.) were both much greater than the error mean square (0·006 on 27 d.f.). The lipid changes associated with immunisation were more striking in subjects

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MEAN (S.E.M.) LIPID LEVELS (mmol/l) AND ANTIBODY RESPONSES (LOG HAEMAGGLUTINATION TITRE) BEFORE (S1) AND AFTER (S2) INFLUENZA IN 28 VOLUNTEERS

	Cholesterol		Triglycerides	Mean $\log_e$
	Total	H.D.L.-C		
S1	5·82 (0·15)	1·31 (0·05)	1·28 (0·10)	1·53 (0·15)
S2	6·02 (0·15)	1·25 (0·05)	1·57 (0·19)	3·68 (0·23)
S2-S1	0·198 (0·087)	−0·068 (0·021)	0·293 (0·151)	2·15 (0·24)
t	2·27	3·24	1·94	9·0
P	0·04	0·005	0·10	highly significant

receiving the trivalent vaccine than in those receiving the monovalent vaccine.

The mean log titre for B/Hong Kong influenza antibody increased considerably after immunisation (table), but there was variation from subject to subject. The antibody response was greatest in subjects showing the greatest fall in H.D.L.-cholesterol after immunisation (r=−0·55; P=0·002), in subjects with high intitial levels of total cholesterol (r=0·48; P=0·01), and in those with higher levels of specific antibody before immunisation (r=0·37; P<0·05). In a multiple regression analysis, these three variables accounted for 52% of the variation in log antibody titre after immunisation (P=0·001).

Thus immunisation with influenza vaccine appears to be followed by an increase in total cholesterol and by a decrease in H.D.L.-cholesterol levels; furthermore, influenza antibody production appears to be greater in subjects with higher levels of total cholesterol before immunisation and in subjects in whom H.D.L.-cholesterol levels fall most after immunisation. An obvious interpretation is that the lipid changes are partly caused by immunisation, and that lipids can also affect the response to immunisation. To establish this, controlled studies are needed to exclude the possibility that the lipid changes are due to coincidental changes in diet or season; in vitro experiments are needed to exclude the possibility that lipids can modify the hæmagglutination inhibition assay for influenza antibody (as has been described for rubella virus assays).[12]

If such artefacts can be excluded, these observations suggest firstly that variation in lipid levels might explain some of the variation in immunological responses, and secondly, that immunisation or natural infection with viral antigens might contribute to variation in lipid levels in man.

J. D. M. was supported by the National Health and Medical Research Council of Australia. We thank Dr D. Campbell and Ms D. Miles for the biochemical assays.

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VITAMIN B_6 IN MANAGEMENT OF GYRATE ATROPHY OF CHOROID AND RETINA

SIR,—In 1973 Simell and Takki reported hyperornithinæmia in patients with gyrate atrophy of the choroid and retina, a progressive genetic disorder leading to blindness by age 40–50.[1] Senger et al.[2] reported deficient activity of ornithine ketoacid aminotransferase (O.K.T.) in cultured skin fibroblasts in this condition, a finding which has been confirmed by several groups, including ours.[3–7] Several investigators have tried large oral doses of vitamin B_6 without clinical or biochemical improvement[2 8–10] However, Shih et al. reported an increase in O.K.T. activity in cultured skin fibroblasts from one of their five patients when increasing amounts of pyridoxal phosphate were added to the assay medium.[10]

We have demonstrated O.K.T. deficiency in cultured skin fibroblasts from four patients with gyrate atrophy. We report here the results of studies on the response to vitamin B_6 in vivo and in vitro.

Three of our four patients (patients 1–3) showed a highly significant biochemical response to oral vitamin B_6, manifest by a decrease in serum-ornithine (0·64±0·14 mmol/l, n=12, to 0·34±0·08 mmol/l, n=20; P<0·0005) and return to normal in the depressed serum-lysine (0·074±0·015 mmol/l, n=12, to 0·103±0·021 mmol/l, n=20; P<0·0005) on high-dose therapy (600–750 mg/day). The serum ornithine:lysine ratio seemed to be an even better index of B_6-induced response than did either aminoacid alone, the ratio falling from 9·3±1·6 (n=11) to 3·2±0·8 (n=16) on high-dose treatment (P<0·0005). Surprisingly, low doses of vitamin B_6 (18–30 mg/day) produced as great a response in these patients as did the high doses.

In-vitro response to pyridoxal phosphate was examined by measurement of O.K.T. activity in cultured skin fibroblasts from all four patients. All demonstrated increased enzyme activity with increasing pyridoxal phosphate in the assay medium. Although cells from patient 4 had the lowest O.K.T. activity with all concentrations of pyridoxal phosphate used, these cells also responded, suggesting that this test may not always indicate a vitamin B_6 response in vivo.

To evaluate further the in-vivo response to oral vitamin B_6, repeated *Ganzfeld* electroretinography, which measures the action potential of the photoreceptors and bipolar cells of the retina, and electro-oculography which measures the light-induced rise of the resting potential of the eye, were done over several months on patients 1 and 3. With high-dose vitamin-B_6 therapy both patients showed significant improvement in the electroretinogram, manifest by an increase in the b-wave amplitude of 103% for patient 1 and 14% for patient 3 (P<0·0005 for both; paired or correlative *t* test). Conversely, the b-wave amplitude decreased by 21 and 7%, respectively, in the two patients when pyridoxine was reduced (P=0·005). A-wave amplitudes also improved with vitamin-B_6 therapy, increasing by 126% in patient 1 (P=0·007) and by 7% in patient 3 (P=0·03). B-wave implicit times likewise showed improvement, decreasing by 11% in patient 1 (P=0·004) and 9% in patient 3 (P=0·001). Electro-oculographic response and dark adaptometry showed mild improvement.

These findings are preliminary, but we wanted to encourage others encountering patients with gyrate atrophy of the choroid and retina to evaluate their patients for vitamin-B_6 responsiveness. Long-term trials will be necessary to determine whether, in certain individuals, vitamin B_6 slows or halts the progression of this disease.

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