schizophrenia can learn a great deal from these families, and the efforts of organisations such as the National Schizophrenia Fellowship to promote the welfare of patients and their families deserve professional encouragement and collaboration.

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Disturbed behaviour induced by high-dose antipsychotic drugs

SIR,—The account by Drs Thomas R E Barnes and Paul K Bridges (26 July, p 274) of disturbed behaviour related to high-dose antipsychotics raises some interesting questions. The suggestion that increasing anticholinergic activity is shown with increased neuroleptic doses receives support from some open studies of high-dose versus low-dose treatment,^{1,2} in which at very high doses extrapyramidal effects diminished or disappeared but were present when dosage was in the standard range. This could be regarded as being due to a continuing increase of anticholinergic activity after basal ganglia dopamine receptors had been blocked. However, several double-blind studies^{3,4} have failed to show this effect and increasing dosage merely resulted in increased extrapyramidal side effects.

The issue might have been partly resolved if it had been shown that the form of disturbance described was that which might be expected with anticholinergic toxicity. However, other than pointing out that both their patients and those reported by MacVicar⁵ became excited and aggressive the authors give no further information. The "toxic psychosis" to which they refer would presumably include disorientation in time and place together with a greater likelihood of visual hallucination than in non-toxic states. In addition, anticholinergic poisoning may cause blurred vision, dry palms, and flushed skin *inter alia*,⁶ none of which are mentioned.

The distinction is important, for if the change in the patients' behaviour was due to neuroleptics acting as dopamine agonists it is interesting that the form of the illness changed to one atypical for the patient. If it was due to anticholinergic activity of neuroleptics then we might expect to see some of the changes outlined above. If, on the other hand, increasing dosages merely increase extrapyramidal effects, then akathisia, a physical and mental restlessness which is a side-effect of neuroleptics, might have contributed to the excitement and agitation described.

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¹ Ayd FJ. *Proc R Soc Lond* 1976;**69**, suppl 1:14-22.

² Rifkin A, Quitkin F, Carrillo C, et al. *Arch Gen Psychiatry* 1971;**25**:398-403.

³ Quitkin F, Rifkin A, Klein DF. *Arch Gen Psychiatry* 1975;**32**:1276-81.

⁴ Carscallen HB, Rochman H, Lovegrove TD. *Canad Psychiat Assoc J* 1968;**13**:459-61.

⁵ MacVicar K. *Am J Psychiatry* 1977;**134**:809-11.

⁶ Laurence DR. *Clinical pharmacology*. 4th edn. Edinburgh: Churchill Livingstone, 1973:16.

Prostaglandin E₁ in affective disorders and alcoholism

SIR,—In support of the theory of ethanol enhancement of prostaglandin (PG)_E synthesis

followed by a reduction in its synthesis, put forward by Drs D F Horrobin and M S Manku (7 June, p 1363), I report remission of severe hangovers in two patients whom I treated with safflower oil, a PGE₁ precursor.

Case 1—A 56-year-old man with chronic depression experienced debilitating hangovers characterised by dysphoria and lethargy following an evening's consumption of 170-227 ml (6-8 oz) of spirits. Isocarboxazid, 50 mg a day, remitted the depression but did not affect the hangovers. I introduced linoleic acid in the form of safflower oil, 4 g a day, and within a few days he was entirely free of hangovers. This benefit has continued during eight months of linoleic acid therapy.

Case 2—A 48-year-old man took lithium in an attempt to halt a 20-year history of episodic excessive drinking. Drinking 114-170 ml (4-6 oz) of vodka was followed by a tachyarrhythmia and an incapacitating hangover. After taking lithium 150 mg twice daily for two days he had a precipitous onset of anxiety, dysphoria, and polyuria, and an irregular pulse. He took 3 g of linoleic acid in the form of safflower oil and within 20 minutes these symptoms abated. Lithium was stopped and he continued to take linoleic acid, 5 g a day. The alcohol-precipitated arrhythmia and the hangovers have remitted on this regimen.

Ethanol temporarily abolishes familial tremor and the tremor associated with alcoholism but after drinking stops the tremor intensifies.¹ The mechanism for this, as discussed by Drs Horrobin and Manku, could be an initial increase in PGE₁ synthesis, which abolishes the tremor, followed by a reduction in PGE₁ synthesis secondary to depletion of dihomogammalinolenic (DGLA) stores. Lithium inhibits the mobilisation of DGLA and its conversion to PGE₁² and in some patients linoleic acid appears to be an effective remedy for the tremor and other neurological manifestations of lithium toxicity.³

The time-honoured belief that eating an oily meal before heavy drinking mitigates intoxication and hangover may have had substance. Linoleic acid and other prostaglandin precursors may be of benefit in some alcohol withdrawal states.

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¹ Critchley M. *Brain* 1949;**72**:113-39.

² Horrobin DF. In: Johnson FN, Johnson S, eds. *Lithium in medical practice*. Baltimore: University Park Press, 1978.

³ Lieb J. *Prostaglandins and Medicine* 1980;**4**:275-9.

Physical training and coronary risk factors

SIR,—It is a pity that exercise, as a possible preventive measure against coronary disease, should get an apparent let-down in the paper by Mr Antony W Sedgwick (5 July, p 7) before the possible benefits have had a chance to come to us across the Atlantic.

Fortunately, the authors admit that, firstly, they were looking at risk factors rather than the actual incidence of heart disease and, secondly, their criteria for the intensity of exercise may not have been stringent enough. On the first point, the quoted paper by Morris *et al*¹ uses far larger numbers, and reports the actual onset of coronary symptoms or death. Their figures indicate the protective effect of violent exercise. On the second point, Cooper, also quoted, gives us precise criteria for adequate exercise. His *Aerobics*,² a book for the public, advises the weekly acquisition of 30 "aerobic" points. This can be done cycling or swimming; but, as an example, a two-mile

jog in 16 minutes every Monday, Wednesday, and Friday is just adequate. And for those of us who are initially unfit he has a carefully graded programme for the first 16 weeks.

I understand that some ex-marathon runners have wide coronary arteries when examined post mortem, and there is also the suggestion that they only rarely die prematurely from infarction. As this specialty is taken up by the athlete late in his career, the implication emerges that wide coronaries can be acquired in the otherwise mature male—not a new idea, I'm sure, but surely good news if we all got our exercise just right?

Meanwhile would Minerva (28 June, p 1626) kindly stop knocking joggers? Of course, we look miserable—try looking happy with your jaw maximally open for air intake.

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¹ Morris JN, Chave SPN, Adam C, Sirey C, Epstein L, Sheehan D. *Lancet* 1973;**i**:333-9.

² Cooper K. *Aerobics*. London: Bantam, 1972.

Right bundle-branch block

SIR,—I was most interested to read your leading article on right bundle-branch block (14 June, p 1392). In 1948, aged 30 years, while teaching undergraduates I suddenly developed typical symptoms of coronary thrombosis unassociated with hypertension, previous coronary, vascular, or congenital heart disease, pulmonary embolism, or cardiomyopathy. Various cardiac symptoms and signs occurred during the succeeding two months, after which time I returned to normal hospital and university duties, eventually becoming a first-class life insurance risk. Details of this illness were published in 1971.¹

In 1977 I developed symptoms and signs of mild-to-moderate hypertension, which are well controlled by the effective treatment of colleagues. Since 1948 the currently accepted electrocardiographic criteria of right bundle-branch block have persisted.

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¹ Blackburn EK. In: Greene R, ed. *Sick doctors*. London: Heinemann Medical Books, 1971:63-4.

Propranolol and thyroid hormones

SIR,—We have read with interest the report of Dr Paul Heyma and his colleagues (5 July, p 24) in which they describe giving propranolol (DL-propranolol) and D-propranolol to six euthyroid subjects receiving L-thyroxine (T₄), and giving D-propranolol to six hypothyroid patients receiving T₄ replacement.

They conclude that the effect of DL-propranolol on T₄ to triiodothyronine (T₃) conversion is unrelated to its β -adrenergic-blocking activity and is related to its "membrane-stabilising activity". The lack of effect of atenolol, a cardioselective β -adrenergic-blocking drug devoid of membrane-stabilising activity, that we (unpublished observations) and others¹ have observed would seem to support this suggestion. We have also studied, however, the effect of oxprenolol, a non-cardioselective drug with membrane-stabilising activity, and acebutolol, a cardioselective drug with membrane-stabilising activity, on circulating thyroid hormones in

hyperthyroid patients and observed no change in serum T3 concentrations.² We realise that these β -adrenergic blocking drugs are less active than propranolol as membrane-stabilising agents, both as a local anaesthetic and in their action on intracellular cardiac potentials,^{3,4} but we would have expected to see a fall in serum T3 levels if the mechanism proposed by Dr Heyma and others is correct. Further information on this point, in particular from the study of hyperthyroid patients, is obviously required.

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¹ Nilsson OR, Karlberg BE, Kagedal B, Tegler L, Almquist S. *Acta Med Scand* 1979;206:21-5.

² Jones MK, John R, Jones GR. *Clin Endocrinol* (in press).

³ Vaughan-Williams EM, Papp JG. *Postgrad Med J* 1970;suppl:22-32.

⁴ Basil B, Jordan R, Loveless AH, Maxwell DR. *Br J Pharmacol* 1973;48:198-211.

Febrile seizures

SIR,—The "consensus statement" of The National Institutes of Health (NIH) about febrile seizures (26 July, p 277) is remarkable among writings on this subject because of its clarity. Nevertheless in their answer to the question "Which children should be considered for prophylaxis?" the authors appear to be guilty of muddled reasoning.

They list as reasons for anticonvulsant prophylaxis those conditions which might presage the later development of epilepsy—that is, abnormal neurological findings, prolonged or focal convulsions, or a family history of epilepsy in a first-degree relative. This seems at odds with their statement (in italics) that "There is no evidence to support the concept that prolonged therapy with anticonvulsants prevents the development of epilepsy or significant neurological deficits." If, as they say, anticonvulsant prophylaxis prevents only subsequent febrile convulsions then surely the indications for such treatment should be those factors which are associated with a high risk of recurrent febrile convulsions (such as age less than 18 months) and not those associated with a higher risk of later developing epilepsy (all of which are unalterable by the time the decision about prophylaxis comes to be made). Most articles of the past 10-15 years on the use of anticonvulsant prophylaxis after febrile convulsions have emphasised the risk of subsequent epilepsy or neurological damage. It now seems, however, that such risk is small and unlikely to be greatly influenced by giving anticonvulsants.¹

The equation to be balanced is now, therefore, much simpler: on the one side the likelihood and undesirability of further febrile convulsions, and on the other the risks of long-term prophylaxis as outlined by the NIH panel. In most instances the right-hand side of this equation might be felt to be the more weighty but on occasions, such as with a very young child or when parental anxiety is unusually high, the risks of therapy might be thought to be worth while.

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¹ Nelson KB, Ellenberg JH. *Pediatrics* 1978;61:720-7.

Convulsions associated with campylobacter enteritis

SIR,—The occurrence of convulsions in several children during an epidemic of campylobacter enteritis reported by Dr S Havalad and others (5 April, p 984) prompts us to report two further cases admitted to a general paediatric ward in the last two years.

A 14-month-old boy with no previous history of fits had a generalised convulsion lasting 20 minutes. He had felt hot the day before and on admission his temperature was 40°C. There was slight rhinorrhoea but no other clinical abnormality. A cerebrospinal fluid examination showed normal biochemical values, no cells, and no bacterial growth. Symptomatic treatment with phenobarbitone, paracetamol, and cooling was commenced. Twelve hours later bulky and offensive stools, without blood or mucus, were passed and these and a rectal swab taken on admission yielded *Campylobacter jejuni*-coli. There was no vomiting and he recovered within four days with no additional therapy.

A 4-year-old girl was admitted following a generalised convulsion lasting 10 minutes, which was associated with several episodes of vomiting and diarrhoea. She had never had a fit before. Her temperature was 37.7°C and there was still some twitching of the limbs on admission. A cerebrospinal fluid examination was normal but *C jejuni*-coli was isolated from a rectal swab. Like the previous child she recovered within four days with symptomatic treatment. *C jejuni*-coli was subsequently isolated from faeces of the patient's 6-year-old sister, who had no symptoms.

In the last two years *C jejuni*-coli was found in only two other children (one with croup and one with vomiting) from a total of approximately 1300 who had a routine rectal swab examined on admission. About a quarter of these were admitted following a fit, so in this small series the association between fits and admission to hospital with campylobacter enteritis was no greater than expected by chance.

Campylobacter infection appears to be an uncommon cause of febrile convulsions but the experience of Dr Havalad and his colleagues and our own reported here indicate that it should be considered as a possible cause in children whose convulsion is associated with diarrhoea.

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Aminocaproic acid myopathy

SIR,—The report by Dr C K Biswas and others (12 July, p 115) of an acute necrotising myopathy occurring during treatment with aminocaproic acid, together with other reports of this complication,¹ raises doubts about the safety of this form of treatment in patients with subarachnoid bleeding and in other conditions.

We have now had experience of two cases. In both recovery was complete when the drug was withdrawn. The pathogenesis of the disorder is uncertain, but our studies suggested that microvascular thrombosis may play a part.¹ Attempts, however, to induce the myopathy experimentally in the rat failed, even when doses several times larger than those given to patients were used. The myopathy seems to occur in patients in whom the drug has been given for longer than about a month, and in

most cases the interval between starting the drug and the development of myopathy has been longer than this. The optimal duration of therapy in patients with subarachnoid bleeding is uncertain, but experience with this complication suggests that other fibrinolytic agents, such as tranexamic acid, may perhaps be free of this serious complication.

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¹ Kennard C, Swash M, Henson RA. Myopathy due to amino caproic acid. *Muscle and Nerve* 1980;3:202-6.

Adverse reactions to D-penicillamine after gold toxicity

SIR,—Dr M J Dodd and others (21 June, p 1498) provided two explanations for the findings in their interesting paper. They suggested that patients who develop side effects from D-penicillamine after demonstrating toxicity to gold salts may do so either because the former drug results in mobilisation of gold from tissue stores or because patients develop cross-reactivity to the thiol component common to both drugs. A third possibility should be considered: susceptibility to drug toxicity may relate to genetic status¹⁻³ and thus patients who develop side effects from one drug may be at risk from another.

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¹ Panayi GS, Wooley P, Batchelor JR. *Br Med J* 1978;ii:1326-8.

² Bell CL, Schur PH. *Arthritis Rheum* 1979;22:592.

³ Batchelor JR, Welsh KI, Tinoco RM, et al. *Lance* 1980;i:1107-9.

Following up patients with rheumatoid arthritis

SIR,—Your recent leading article (12 July, p 97) on the continuing care of people with rheumatoid arthritis makes dismal reading. The rheumatologist will contribute his expertise. He cannot, however, offer much in the way of personal support, except at moment of crisis. His junior staff and ancillary workers are bound, in the nature of things, to change at fairly frequent intervals with consequent loss of continuity.

The general practitioner must necessarily be involved, and the care of the chronic sick is one of his acknowledged responsibilities. You mention epidemiological evidence of the prevalence of this disease. It follows that general practitioners do, in fact, gain considerable familiarity with both its manifestations and its treatment.

Could we not co-operate more? The rheumatologist may know that certain practices are more ready than others to shoulder this particular responsibility. If he is in doubt, could he not ask? It is important also that in providing intensive involvement early in the course of the disease hospitals do not undermine confidence in the patient's doctor. Lastly, there is a great need for vocational trainees to acquire experience in rheumatology.

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