the instigation of their area review committee on non-accidental injury, to start pilot schemes along these lines.

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SIR,—We would like to take the opportunity of commenting on the important points made by two recent correspondents, Dr P C Corry and Mr G T Meredith (23 April, p 1084).

There is certainly a need to look at larger samples than we were able to include in our study (5 March, p 624). However, we should not be deterred from considering preventive action simply because the percentage of newborns "at risk" seems to be so large. In our experience intervention frequently does not have to be massive. Open recognition of the parents' difficulties in caring for the child can result in a more positive attitude towards existing services, which can often be adapted to provide the help the family needs.¹

Our data were collected at the maternity hospital. Thus most information, not unnaturally, was concerning the mother. This does not mean that all the children were battered by their mothers. We have found that both parents are often deeply involved in the abuse of their child, irrespective of who actually inflicts the injuries; it is not necessarily helpful to concentrate on "who did it." Sometimes the parent who is not the identified abuser in one incident subsequently batters the same child or marries another battering partner.

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¹ Beswick, K, Lynch, M A, and Roberts, J, *British Medical Journal*, 1976, 2, 800.

Icelandic disease (benign myalgic encephalomyelitis or Royal Free disease)

SIR,—We were interested to read your expert's reply to the question on the nature of Icelandic disease (9 April, p 965). We should like to present the following additional information:

(1) None of the names in common use is completely descriptive of this syndrome, which is not truly benign, is not always myalgic, and has no proved connection with hysteria or neurasthenia.¹

(2) The sufferers are usually parents of young children or members of the armed Forces or of the teaching, nursing, or medical professions. The classic illness has a biphasic pattern with an initial episode of gastrointestinal or upper respiratory tract infection, with or without a rash and lymphadenopathy, affecting either the patient or juvenile members of the family.

(3) The most characteristic presentation is profound fatigue and muscular weakness coming on during the day and increasing in severity with exercise—a diurnal rhythm contrary to that found with other forms of depression.

(4) Other symptoms that may accompany the initial illness or a relapse include muscular fasciculation, paraesthesiae, and disturbance of vision, with which nystagmus may be seen. Autonomic disturbances such as orthostatic tachycardia, vasomotor instability, and episodes of pallor are often prominent. Encephalitic disturbances include severe depression, emotional lability, and difficulty in concentration.

(5) Physical findings may include atypical lymphocytes in the peripheral blood, hepatitis, electromyographic evidence of myopathic and neuropathic disorders, and abnormal glucose tolerance curves.^{2,3}

(6) Relapses are a typical feature of this illness and may occur even after several years of good health.⁴

Last year a research group was formed to study the aetiology and epidemiology of this syndrome. Our investigations so far indicate that the illness may accompany the more common viral infections and that the unique fatigue pattern may be due to mitochondrial damage.

As objective manifestations of the disease can still be present over 30 years after the initial illness we should be glad to hear from former sufferers who were members of the medical and nursing staff of the Royal Free Hospital or other institutions which have experienced outbreaks. Communications should be sent to the honorary secretary of the group (JVD) at the address below.

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¹ Ramsay, A M, *Update*, 1976, 13, 539.

² Parish, J G, *IRCS Journal of International Research Communications*, 1974, 2, 22.

³ Leon-Sotomayor, L, *Epidemic Diencephalomyelitis*. New York, Pageant Press, 1969.

⁴ Marinacci, A A, and Von Hagen, K, *Electromyography*, 1965, 5, 241.

Mechanism of chloroquine induced involuntary movements

SIR,—I read with interest the report by Drs E M Umez-Eronini and Elspeth A Eronini on chloroquine induced involuntary movements (9 April, p 945). May I throw some light on the probable mechanism of these movements?

Chloroquine and phenothiazines combine avidly with melanin both in vitro and in vivo; this is believed to be based on a charge transfer reaction facilitated by the presence of electrons in the fused coplanar ring structures of both chloroquine and phenothiazines.¹ Melanin is a derivative of DOPA (phenylalanine → tyrosine → dihydroxyphenylalanine (DOPA) → DOPA-quinone → melanin). Chloroquine, a 4-aminoquinoline derivative, crosses the blood-brain barrier, and the brain and spinal cord contain 10-30 times the amount present in plasma.² It is quite logical to infer from the structure-activity relationship that chloroquine may also avidly combine with the dopaminergic receptors (like melanin) and thus by blocking those receptors (like phenothiazines, butyrophenones, metoclopramide, etc) in the nigrostriatal system it may produce involuntary movements. It is another example of drug-induced extrapyramidal disorders.

In the light of this it is better not to give patients with chloroquine induced involuntary movements phenothiazines like chlorpromazine, which may aggravate the situation. Anticholinergic anti-Parkinsonian drugs like bntropine, benzhexol, orphenadrine, ethopropazine, procyclidine, etc should be given in these cases as their action is not dependent on the dopaminergic receptors in the nigrostriatal system.

It needs to be mentioned that other members of 4-aminoquinoline family like amodiaquine, cycloquine, and hydroxychloroquine may also

produce involuntary movements in the same way as chloroquine.

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¹ Potts, A M, in *Physiological Pharmacology*, ed W S Root and F G Hofmann, vol II, part B, pp 329-397. New York, Academic Press, 1965.

² Rollo, I M, in *The Pharmacological Basis of Therapeutics*, ed L S Goodman, A Gilman, A G Gilman, and G B Koelle, 5th edn, p 1051. New York, Macmillan, 1975.

Insurance companies' attitude to psychiatric illness

SIR,—In recent issues you have printed letters from two psychiatrists expressing concern at the harsh attitude towards minor psychiatric illness taken by insurance companies, and the untoward experiences of five neurotic patients are mentioned. Dr J T Hutchinson (9 March, p 775) describes excessive loading against those who seek life insurance and Dr A B Sclare (16 April, p 1031) from his experience with employees of insurance companies becoming patients stresses the lack of confidentiality, punitive attitudes towards mental illness, and absence of discrimination between mild and serious psychiatric illness.

Although I would agree that the attitudes of the companies should be enlightened and informed, it is worth mentioning that the neuroses do carry a slightly increased risk of premature mortality as demonstrated in the studies by Babigian and Odoroff,¹ by Innes and Millar,² by Keehn *et al*,³ and by me.⁴ Further findings on the extent of this increased death risk will be published soon, but figures have generally been about 1.5 times those for the matched general population.

It would seem reasonable that psychiatrists should ask the insurance companies to take the psychiatric diagnosis into account in their assessment of weighting so that neuroses and other disorders can be differentially weighted. This would result in a slightly increased premium for neurosis which should by no means be prohibitive.

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¹ Babigian, H M, and Odoroff, C L, *American Journal of Psychiatry*, 1969, 126, 470.

² Innes, G, and Millar, W M, *Scottish Medical Journal*, 1970, 15, 143.

³ Keehn, R J, Goldberg, I D, and Beebe, G W, *Psychosomatic Medicine*, 1974, 36, 27.

⁴ Sims, A C P, *Lancet*, 1973, 2, 1072.

Maintenance digoxin

SIR,—Concerning Dr B J O'Driscoll's comments (16 April, p 1028) on our paper (19 March, p 749), comparison with pioneering studies is difficult because of historical emphasis on digitalisation rather than maintenance therapy, the fact that digitalis used to be pushed until cardiotoxicity occurred, and differences in concomitant therapy. Although Sir James Mackenzie¹ in 1910 obtained the best response in failure associated with "rapid" atrial fibrillation, he did not consider that decreasing the rate was the primary mechanism: "The good results obtained by the use of digitalis are doubtless due to the specific action of the drug on the function of tonicity." Windle² in 1917 demonstrated the value of digitalis in patients with pulsus alternans, while

Marvin³ in 1926 found it almost equally effective in sinus rhythm as in atrial fibrillation. Indeed Sir Thomas Lewis⁴ stated in 1946 that digitalis was generally recognised to be of value in failure with sinus rhythm.

In our study 16 of the 46 patients deteriorated clinically on placebo. In the remainder an increase in airways resistance, reversed by reintroduction of digoxin, was demonstrated. This reversible airways obstruction (asthma) may have progressed to overt pulmonary oedema had the placebo phase been extended. Digoxin also improved left ventricular function in a random sample from those in sinus rhythm who did not deteriorate clinically on placebo, as evidenced by shortening of left ventricular ejection time.

Thirteen of the patients studied were in atrial fibrillation, there being similar proportions among those who deteriorated clinically on placebo (4/16) and those who did not (9/30). All the patients in fibrillation had impaired atrioventricular conduction. Far from requiring digoxin to control their ventricular rate, six of these developed bradycardia at serum digoxin concentrations recommended for control of fibrillation. The study shows the value of maintenance digoxin after an episode of failure not only in patients in sinus rhythm but also in "slow fibrillators," in whom a lower serum digoxin concentration is recommended.

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¹ Mackenzie, J. *Diseases of the Heart*, p 282. Oxford, Oxford University Press, 1910.

² Windle, D. *Quarterly Journal of Medicine*, 1917, **10**, 274.

³ Marvin, H M. *Journal of Clinical Investigation*, 1926, **3**, 521.

⁴ Lewis, T. *Diseases of the Heart*, p 39. London, Macmillan, 1946.

Anonymous barbs

SIR,—I must deplore the editorial policy of allowing the author of Personal View (16 April, p 1026) to hide behind anonymity while firing his barbs into anaesthetists and nursing personnel. With respect to the former it is, of course, poor medical practice to omit a pre-operative visit, but such an omission is a little less than credible in this age of increased patient enlightenment. Nevertheless, I think that Personal View is an inappropriate forum for such remarks presented in this fashion. I hope that the author's practice of surgery would bear similar critical review by his colleagues, anonymously, of course.

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Adjunctive chemotherapy and breast carcinoma

SIR,—Premature reporting of the results of adjunctive chemotherapy in carcinoma of the breast has done untold damage to clinical trials in general and the management of carcinoma of the breast in particular.

When survival is the end point of a trial results should not be published for at least five years. With regard to adjunctive chemotherapy in carcinoma of the breast the idea is to prevent the colonisation of micrometastases. In view of the so-called doubling time of the malignant cell, then should patients die within the first three years it is obvious that bulk metastases were already present at the time of treatment. Our present methods of treatment are not sufficiently adequate to cure bulk metastases and therefore three-year survival rates are meaningless. It is probably unlikely that drugs can have much effect on malignant cells which may be in a resting phase, but as long as there is a slight possibility that results may be improved then the present trials must be allowed to continue.

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The thyroid and the psychiatrist

SIR,—You state in your leading article on this subject (9 April, p 931) that few psychiatrists would agree with Asher that psychotic states secondary to myxoedema are common and often missed. Asher's view may be correct, but only a few surveys of thyroid function in psychiatric patients have been reported.

We assessed thyroid function in 98 unselected female psychiatric admissions and found four cases of hypothyroidism, of which only one had been recognised clinically.¹ Routine screening for thyroid disease in women over the age of 40 presenting for the first time with a psychotic disorder might be well worth while.

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¹ Nicholson, G, Liebling, L I, and Hall, R A. *British Journal of Psychiatry*, 1976, **129**, 236.

Cost of ECG electrodes

SIR,—Disposable pre-gelled electrodes with a large adhesive surface are now commonly used in electrocardiographic monitoring. NHS expenditure on these electrodes cannot be insignificant and we consider that their cost and performance merit careful scrutiny.

We know of 12 brands of pre-gelled disposable electrode on the UK market. Two of these are British products and all but one of the remainder are manufactured in the USA. Although we estimate that the cost of raw materials is unlikely to exceed 10p, current prices range from 25 to 38p, with an average of 32p per electrode. On the important, but not necessarily valid, assumption that the electrodes remain in place the average cost of monitoring a patient with a three-lead system is thus 96p.

Comparisons on which those responsible for purchasing disposable electrodes could base a decision are needed but are not at present available. In a preliminary study of 12 pre-gelled electrodes we have found the performance of the majority to be broadly similar but have identified two electrodes which are inferior because of poor adhesion

or a tendency to produce frequent skin reactions.

At a time when the number of patients monitored is increasing methods of limiting NHS expenditure on ECG electrodes should be explored. We suggest that it should not be impossible to develop a reliable, high-performance, reusable or partially reusable monitoring electrode. In the short term the cost of disposable pre-gelled electrodes might be reduced if these were manufactured under contract to the NHS.

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Double-blind trials and the patient

SIR,—The double-blind trial of drugs is an established and widely used procedure. Difficulty may arise when an intelligent patient inquires what therapy is being used, and the experimenter must make his own ethical decision about the answer to be given. Sometimes, however, the new drugs may interact with other therapy to which the patient may be exposed elsewhere. It would seem, therefore, that whenever any patient is entered into any programme where this method is being used, provision should be made for full information to be available at any time from the trial centre on the drugs or placebo given to any individual involved or even for patients to be informed that they are part of such a trial. Although this may be inconvenient to researchers, the provision of a suitable card giving details of the centre and information source would seem a small price to pay for the safety it would help provide.

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Oestrogen-like effect of tamoxifen on vaginal epithelium

SIR,—Tamoxifen is an antioestrogenic compound used in breast malignancy. It is known for its binding to oestrogen receptors,^{2,3} is capable of some oestrogen-like or anti-oestrogen effects in experimental models,² and is probably effective also in antagonising prolactin secretion.⁴ The difference between oestrogen and tamoxifen stimulation of certain target cells seems to be the lack of replenishment of oestrogen receptors in tamoxifen-stimulated target cells.¹

In our unit 86 postmenopausal women with late breast malignancy have been treated with 30-40 mg of tamoxifen orally per day. All the patients had proved resistant to previous standard endocrine treatment and to multiple chemotherapy. All previous hormone treatment had been stopped at least two months before tamoxifen administration was started.

In 35 cases vaginal smears were taken just before and again after 30-45 days of tamoxifen treatment. From the smears the percentage of pyknotic cells (KPI), a good index of oestrogen activity, was calculated.⁵ In fertile normal women the index ranges in our experience from 40% to 80% during the proliferative phase of the menstrual cycle