revealed four deaths, all from the physical conditions the absence from which of clinical confirmation led to their symptoms being interpreted as neurotic.

A young male ataxic was found post mortem to have a glioma tracking selectively down the mid-brain. A woman with unexplained diarrhoea and weakness had a single small secondary in the liver, no primary discovered post mortem. An anxious man with recurrent invaliding chest pain died of a massive infarct. An intractable asthmatic died in an attack, no more helped by psychological than by physical methods.

However one looks at this dip from the barrel it is a reminder of how all too easy it is to allow universally latent psychopathology to fill a gap. The pragmatic actuary's target may be not the psychoneurotic patient but the tenuous nosology.

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Lyme Regis

Local corticosteroids in asthma

SIR,—Dr H M Brown (28 May, p 1408) blames you, to my mind unjustly, for altering your earlier, somewhat overoptimistic view of the advantages of steroid aerosols in asthma. Effective local steroid treatment of asthma started as early as 1955¹ with the insufflation of micronised corticosteroid from a powder blower, but it became popular only much later when given as an aerosol from a metered bottle. Replacing systemic by aerosolised steroids depends (a) on the severity of the case, as documented by the systemic maintenance dose, (b) on the accessibility of the surface of the bronchial mucosa. Most published studies show that patients on small maintenance doses (5.0–7.5 mg/day) can often be maintained on aerosol alone. If they require 10 mg/day or more and were given about 800 µg steroid aerosol in addition,^{2–8} this made it possible to reduce the oral dose by 5–8 mg/day. However, if the bronchial mucosa is covered, as is often the case, by tough mucus, this seems to obstruct the absorption of the aerosol, as might be expected.⁹ Unfortunately many authors have not reported how many of their patients had hypersecretion. Also, the prompt dilator effect of beta stimulants from aerosol bottles used by many asthmatics often creates typical conditional reflexes, which may also work after the steroid aerosol although it has no dilator action.

Three practical conclusions seem to follow: (1) Patients with bronchial hypersecretion (particularly those with persistent cough or regular nocturnal cough) are unlikely to benefit from steroid aerosols. (2) Patients with very mild dry asthma, mostly of allergic origin, who inhale bronchodilators not more often than twice daily, will probably benefit from steroid aerosols about 800 µg per day, or, alternatively, from an oral maintenance dose of 5–7.5 mg/day. If they are reasonably fit without either, neither systemic nor inhaled steroids are indicated. (3) Patients who have life-threatening attacks of asthma or are in danger of becoming invalids through asthma should in no circumstances be given a steroid aerosol but require high doses of a systemic steroid, beginning usually with 30 mg prednisone daily in the morning and tapering very slowly off as outlined elsewhere¹⁰ until the daily maintenance dose is found. Only then, and only if this maintenance dose is higher

than 7.5 mg/day, should gradual partial replacement of the systemic maintenance dose by steroid aerosol be attempted. During this process and afterwards continuous observation is necessary for spontaneous increases of the asthmatic obstruction by intercurrent infection or other factors, best noticeable from the increasing number of bronchodilator inhalations required. In such a case the systemic steroid must be doubled at once regardless of the steroid aerosol and, if necessary, other measures taken. In no case should the decision whether to increase the systemic steroid be left to the patient or, in the case of a child, to the parents. It is here that the danger of sudden death threatens, and it is here that I profoundly disagree with Dr H M Brown. I agree, however, in so far as the family doctor often is too reluctant to give high corticosteroid doses. This reluctance has caused, as some of our most experienced observers have shown,^{11,12} unnecessary deaths from asthma. I and my co-workers have observed during 25 years more than 2000 asthmatics requiring long-term steroids, but have seen surprisingly few deaths during this time, mostly in the aged and through non-asthmatic complications; none in children, of whom we have seen fewer.

In my experience steroid aerosols offer an advantage only to patients with moderately severe asthma who need systemic corticosteroids in a dosage of more than 7.5 mg per day. They will often be able to lower the maintenance dose by adding some steroid aerosol, thus perhaps reducing the risk of adrenal suppression.

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- ¹ Burger, J H, and Shaffer, J H, *Bulletin of the New York Academy of Sciences*, 1955, **61**, 56.
- ² Foulds, W S, et al, *Lancet*, 1955, **1**, 234.
- ³ Godfrey, M P, et al, *Lancet*, 1957, **1**, 767.
- ⁴ Stresemann, E, *Klinische Wochenschrift*, 1961, **39**, 198.
- ⁵ Cameron, S J, et al, *British Medical Journal*, 1973, **4**, 205.
- ⁶ Mygind, N, and Hansen, I B, *Acta Allergologica*, 1973, **28**, 211.
- ⁷ McAllen, M K, et al, *British Medical Journal*, 1974, **1**, 171.
- ⁸ Roscoe, P, et al, *British Journal of Diseases of the Chest*, 1975, **69**, 240.
- ⁹ Herxheimer, H, et al, *British Medical Journal*, 1958, **2**, 762.
- ¹⁰ Herxheimer, H, *A Guide to Bronchial Asthma*. London, New York, San Francisco, Academic Press, 1975.
- ¹¹ Macdonald, J B, et al, *British Medical Journal*, 1976, **1**, 1493.
- ¹² Macdonald, J B, et al, *British Medical Journal*, 1977, **2**, 721.

Reliable measuring of blood pressure

SIR,—We now have several effective anti-hypertensive drugs. We have proof that blood pressure reduction is beneficial in those with moderate or severe hypertension. What is the next goal? It would be interesting to know if drug treatment of mild hypertension is worth while, but I share the doubt expressed in your leading article (4 June, p 1429) about the likely result of the MRC trial. I do not think it will be decisive.

In my view probably the greatest need today is for some simple means of determining an individual's usual blood pressure as distinct from that which develops when he is confronted by a doctor (or nurse or technician) and subjected to the discomfort of sphygmomanometry. There is no doubt that this artificial environment adds a variable, unknown, and often large supplement to the ordinary pressure—a supplement which is considerably increased if the medical examina-

tion is considered to carry a threat of loss of livelihood. Under such circumstances I have recorded a pressure as high as 220/120 mm Hg in an otherwise normotensive subject.

It is frequently argued in favour of casual readings that in spite of their deficiencies they are the best guide we possess to prognosis and thus to the need for treatment. Although this is true in relation to large groups of people, casual readings are a poor guide to prognosis in individuals and inferior to basal readings.¹ Others argue in favour of casual readings that a rise in blood pressure with excitement indicates the existence of a state of "labile hypertension" and that this carries an adverse prognosis. Such an inference is completely unproved.

No, it would be an immense advantage if we could eliminate the artefact caused by sphygmomanometry. Blood pressure can be recorded accurately over long periods without the presence of a doctor or other medical worker, by means of an intra-arterial catheter, but so far no reliable means of doing this non-invasively has been devised. The next major advance in the management of hypertension will be the development of a reliable, inexpensive, non-invasive piece of equipment capable of recording the blood pressure repeatedly over a period of an hour or more with the patient in a state of relaxation. The first manufacturer to produce such equipment could expect to make a fortune.

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¹ Smirk, F H, in *Antihypertensive Therapy: Principles and Practice*, ed F Gorss, p 355. Berlin, Springer, 1966.

Bleeding in renal failure: a possible cause

SIR,—Following the report of Kazatchkine et al¹ that factor VIII—von Willebrand factor activity (VWFR) is decreased in the plasma of patients with chronic renal failure and may partly explain the haemorrhagic tendency in that condition, we have measured factor-VIII-related antigen (VIIIa), factor-VIII-procoagulant activity (VIIIc), and VWFR in a group of 20 patients undergoing long-term haemodialysis.

VIIIc was estimated by a standard two-stage assay,² VIIIa by unidirectional immunoelectrophoresis using the Laurell technique,³ and plasma VWFR by aggregation of formalin-fixed platelets in the presence of ristocetin.⁴

The results are as follows:

	Mean % ₀	Range % ₀	Reference range % ₀
VIIIc	267	122–404	50–200
VIIIa	219	93–400	50–170
VWFR	180	83–291	50–200

We confirmed the elevated levels of VIIIc and VIIIa found by Kazatchkine et al and others, but none of our patients had a depressed VWFR level. Indeed, the mean level was towards the upper limit of normal. VWFR levels did not differ significantly from VIIIa levels, but the difference between mean VIIIc and VWFR is highly significant (using two-way variance analysis, $t = 4.48$, $P < 0.001$) as is the difference between VIIIc and VIIIa ($t = 2.66$, $P < 0.05$).

We conclude, therefore, that our patients'

bleeding tendency cannot be explained on the basis of a lowered VWFR. The disproportionate increase in VIIIC compared with VIIIA and VWFR may represent a non-specific effect (*sic*) analogous to similar results seen after exercise.⁵ Nevertheless, in four patients the ratio VIIIA:VWFR was greater than 1.5, suggesting that the functional capacity of the factor VIII molecule (as assessed by ristocetin cofactor activity) may be impaired in some cases of renal failure.

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¹ Kazatchkine, M, *et al*, *British Medical Journal*, 1976, **2**, 612.

² Biggs, R, *Human Blood Coagulation, Haemostasis and Thrombosis*, 2nd edn, p 684. Oxford, Blackwell, 1976.

³ Laurell, C B, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1972, **29**, suppl 124, 21.

⁴ Macfarlane, D E, *et al*, *Thrombosis et Diathesis Haemorrhagica*, 1975, **34**, 306.

⁵ Stibbe, J, *Thrombosis Research*, 1977, **10**, 163.

Music in the hemispheres

SIR,—In referring to the recently published paper of some Japanese authors¹ Minerva suggests (4 June, p 1476) that "the right hemisphere may be dominant for singing" since "cases have been recorded of right-sided lesions causing loss of musical ability while leaving speech unimpaired." However, impairment of musical ability together with intact speech has also been noted with certain left-sided lesions.² None the less, there is good evidence for believing that singing is primarily subserved by the right cerebral hemisphere. In the rare cases of total left hemispherectomy performed on adults preservation of the ability to sing has been observed despite severe aphasia.³ In addition, intracarotid injection of sodium amytal on the right side has been found to impair singing to a greater extent than injection on the left.⁴

These findings for vocal musical expression are consistent with data from brain-damaged patients which indicate a superiority of the right hemisphere with regard to various receptive aspects of music. Furthermore, a technique known as dichotic listening has enabled these observations to be extended to normal subjects. Among right handers the simultaneous presentation of competing stimuli to the two ears may yield laterality effects related to the nature of the stimuli. Using verbal stimuli, significantly more correct responses are typically obtained in recognition of material at the right ear, while with non-verbal stimuli, particularly musical sounds, there is often an advantage for the left ear.⁵ Such findings are usually explained on the basis of suppression of the uncrossed by the crossed auditory projections to the cortex combined with a relative dominance of the left and right cerebral hemispheres for the perception of verbal and non-verbal stimuli respectively. It should be noted, however, that such effects may be related more to fundamental differences in the processing strategies employed by the two halves of the brain rather than to the intrinsic nature of the stimuli employed, for the same stimuli can give rise to opposite ear advantages depending on the task requirements.

Finally, in connection with the fact that singing may be preserved despite severe

aphasia it is of interest that one patient whose left hemisphere was removed at the age of 10 years was able to sing well only weeks after the operation, yet two years later was still unable, or unwilling, to repeat the lyrics in a normal speaking voice.⁶ This recalls to mind Hughlings Jackson's view that, while "propositional speech" is undertaken by the left hemisphere, the right side of the brain is responsible for "the automatic revival of words." Yamadori *et al* noted that all but five of their 21 aphasic patients required prompting by the examiner before singing as requested. These authors therefore suggested that the ability to initiate singing spontaneously is more related to the left hemisphere than to the right. Could it be that once primed, as it were, by the left hemisphere, or by explicit prompting, the right half of the brain can run on "automatically," this process being facilitated in some way by the availability of a familiar melody?

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¹ Yamadori, A, *et al*, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1977, **40**, 221.

² Wertheim, N, in *Handbook in Clinical Neurology*, ed P J Vinken and G W Bruyn, vol 4. Amsterdam, North Holland, 1969.

³ Smith, A, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1966, **29**, 467.

⁴ Gordon, H W, and Bogen, J E, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1974, **37**, 727.

⁵ Kimura, D, *Cortex*, 1967, **3**, 163.

⁶ Gordon, H W, in *Hemisphere Disconnection and Cerebral Function*, ed M Kinsbourne and W L Smith. Springfield, Thomas, 1974.

Hyperbaric oxygenation in paralytic ileus

SIR,—The gratifying results of this treatment, reported by Dr R E Loder (4 June, p 1448) have been observed by myself and others.¹ Beside the possible reasons for the improvement that he advances, a purely physical explanation could account for the spectacularly rapid recovery. Boyle's law indicates that at 2 atmospheres the volume of intestinal gas is reduced by 50%, while in the cylindrical form, which occurs in the lumen of the bowel, the diameter is reduced by 29%.² Because of the rapidity of the response it seems probable that the sudden relief of gaseous distension allows circulation in the bowel wall to be re-established and permits peristalsis to recommence.

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¹ Watanuki, T, *et al*, "Study on the effects of hyperbaric oxygenation upon intestinal paralysis," *Hyperbaric Medicine*, ed J Wada and T Iwa. Tokyo, Igaku Shoin, 1970.

² Brown, I W, *et al*, *Advances in Surgery*, 1965, **1**, 292.

Coronary artery spasm

SIR,—Your editorial on coronary artery spasm (7 May, p 1176) mentions facts probably relevant to the mechanism of death while shovelling snow. All five cases reported by Dr R M Whittington (26 February, p 577) had post-mortem evidence of considerable coronary artery atherosclerosis and therefore were liable to react to the cold pressor test of the environment by a rise in blood pressure accompanied by a decreased coronary blood flow from an increase in coronary vascular resistance.¹ The wind blowing on the day of the deaths, apart from increasing the chill factor, may also have caused a bradycardia.² These factors are possibly sufficient in themselves to cause death

without requiring the addition of unaccustomed, vigorous isotonic/isometric exercise or incriminating a stream of cold air down the trachea.³ In fact the heat exchange capability of the respiratory system is such that the inspired gases will be at body temperature by the time they reach the carina.

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¹ Mudge, G H, *et al*, *New England Journal of Medicine*, 1976, **295**, 1333.

² Le Blanc, J, in *Circumpolar Health*, ed R J Shephard and S Itoh, p 72. Toronto University Press, 1976.

³ Wells, C, *British Medical Journal*, 1977, **1**, 908.

⁴ Moritz, A R, *et al*, *American Journal of Pathology*, 1945, **21**, 311.

Management of rheumatoid arthritis

SIR,—It is a pity to see in your leading article (30 April, p 1120) emphasis on the treatment of rheumatoid arthritis (RA) yet again placed on a particular group of drugs—the non-steroid anti-inflammatory agents (NSAID)—and on "management by symptoms." Surely it is now generally accepted that all the group 1-3 drugs in Huskisson's¹ earlier classification have a temporary local effect but no influence on the course of the disease. Little effort need be spent in selecting which drug to use; the patient's preference and cost are what matter. "Management by symptoms" is appropriate only at this stage.

The more difficult problem, which should occupy a correspondingly greater proportion of any survey on this subject, is what to do next. The decision should be made on objective criteria. Serial measurements of serum acute-phase proteins (APR) and the ESR provide a guide.² These measurements are not influenced by NSAIDs, indicating the limitation of this class of drugs. Drugs which do lower APRs include gold and penicillamine, with their characteristically slow effect, and corticosteroids, with a rapid effect; although none of them has been clearly shown to halt disease progression, they probably delay it. Alternatively, progression of RA can be judged by tests of function or by x-rays; but each provides only retrospective information and is not as suitable as APR.

If NSAID do not adequately control symptoms and APR and ESR levels remain high, then disease progression will ensue; some additional treatment is indicated. "Management by symptoms" at this stage will not do; objective measurements are mandatory. Only such measurements can provide the information for efficient monitoring of drug effects and for assessing the relative merits of drugs that could affect disease progression. It may be necessary to resort to more than one such drug either serially or together. We have suggested elsewhere³ a policy, based on serial APR measurements, to cover most eventualities. So long as "management by symptoms" continues to be the goal we fear a proliferation of NSAID instead of the development of drugs with a more profound effect; we also fear ineffective, albeit relatively safe, management of RA.

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¹ Huskisson, E C, *Reports on Rheumatic Diseases*, No 54. London, Arthritis and Rheumatism Council, 1974.

² McConkey, B, *et al*, *Quarterly Journal of Medicine*, 1973, **NS 42**, 785.

³ Constable, T J, *et al*, *Lancet*, 1975, **1**, 1176.