of the specialized tissue. He felt that for inhibition to occur it should be shown that the vagus nerve innervated the entire ventricular specialized network, and that acetylcholine should be shown to suppress spontaneous activity of ventricular Purkinje fibres. It would seem that these two conditions also require to be met with regard to verapamil and the human heart before the claims of Drs. Livesley and Oram can be justified.—I am, etc.,

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¹ Vassalle, M., *American Journal of Cardiology*, 1971, 28, 245.

Epidemic Ataxia in Western Nigeria

SIR,—Dr. B. O. Osuntokun (3 June, p. 589) states, "I have found no evidence of viral infection as an aetiological factor [of epidemic ataxia]." It is true that efforts to isolate a virus have so far been unsuccessful, and Dr. Osuntokun is undoubtedly referring to the work of the Virus Research Laboratory of the Faculty of Medicine, University of Ibadan, although he did not say so. In collaboration with the Wesley Guild Hospital, Ilesha, Western Nigeria, we have been investigating the possible viral aetiology of this condition, and the first report is at the moment being prepared for publication. Experience dictates that we should not close our minds to the possibility of viral aetiology, as it is a known fact that in the developing countries, where laboratory facilities are relatively limited, a negative result does not permit one to pronounce a categorical verdict. A "no find" may well be due to a "no extensive" or "no exhaustive" examination. A classical example is the case of dengue viruses in Africa. Physicians and indeed scientists have for a long time concluded that the continent of Africa was a dengue-free zone. But in 1970 from our laboratory dengue viruses were isolated and fully documented.¹

In clinical virology, while there is the danger to look upon viruses as a diagnostic dump heap, there is also the equally dangerous risk of returning a negative verdict too early in the operation. An open mind will help open prospects for future closer examination.—I am, etc.,

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¹ Carey, D. E., Causey, O. R., Reddy, S., and Cooke, A. R., *Lancet*, 1971, 1, 105.

Dressler's Syndrome

SIR,—Dr. M. S. T. A. Lawrence and Professor Ralph Wright (11 March, p. 665) report a case of Dressler's syndrome complicated by tamponade unassociated with haemorrhage into the pericardial space. I would like to report a further case.

A 62-year-old man originally presented in May 1971 with an acute myocardial infarction. At follow-up two months after the first attack he was complaining of tiredness, dyspnoea, and shoulder and back pain. His chest x-ray showed an enlarged cardiac shadow with no sign of pulmonary con-

gestion. He was treated with diuretics and practolol without symptomatic or clinical benefit.

In November 1971 he was first seen at this hospital. At this time his jugular veins were filled to his ears, liver edge palpated 5 cm below the costal margin, 15 mm Hg arterial paradox, but no sign of fluid in his lungs. His chest x-ray showed a large globular heart shadow but no pulmonary oedema. He was admitted for further investigations, which, apart from Hb 12.3 g/100 ml and E.S.R. of 43 mm, were unremarkable.

The diagnosis seemed clear: post-myocardial infarction (Dressler's) syndrome, complicated by tamponade. An attempt was made to aspirate the pericardial fluid but was unsuccessful. He was started on prednisolone 60 mg a day with a brisk improvement in his condition. His jugular venous pressure fell to normal, and his cardiac shadow returned to a normal size and shape. Steroids were reduced to a maintenance dose of 10 mg a day. He has now been well for six months, apart from one episode of pericardial pain and a friction rub occurring a month after discharge, which responded to a brief increase in his steroid dosage. His steroids have now been tailed off.

This man seems a typical example of a postmyocardial infarction syndrome presenting two months after the initial infarct with tiredness, anaemia, a raised E.S.R., and signs of pericardial disease. He had physical signs of cardiac tamponade with x-ray confirmation. It seems unlikely that this could have been due to haemorrhage as he was not on anticoagulants and because he responded so well to steroid therapy. It seems likely that this situation can be complicated by pericardial effusion, severe enough to give tamponade and which responds very well to steroid therapy.

I would like to thank Dr. Turner for his permission to report his case.

—I am, etc.,

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Food and Cyanide

SIR,—I would like to comment on two specific aspects raised in your leading article (27 May, p. 481) which have been of particular interest to me since our original studies on the aetiology of tobacco amblyopia¹ and retrobulbar neuritis in pernicious anaemia.²

Firstly, it is certainly important to remember that, besides being present in tobacco smoke and alcohol, cyanide is widely distributed in the plant kingdom. In this connexion, I contended that retrobulbar neuritis in patients with vitamin B₁₂ deficiency who are non-smokers is the result of exposure to cyanide from some other source than tobacco.³ Abnormally raised plasma-cyanocobalamin levels have been found in some patients with the so-called "West Indian amblyopia"⁴ and in Nigerian patients with tropical amblyopia and ataxic neuropathy.⁵ The ophthalmic findings, as reported, are consistent with the strict criteria we specified and adopted in the diagnosis of tobacco-amblyopia visual fields,¹ and add further support to the hypothesis that exposure to cyanide from the dietary source

of cassava, or other roots or vegetables containing cyanogenic glycosides, contributes to the pathogenesis of tropical amblyopia.

If the indiscriminate dumping of industrial cyanide waste continues unchecked, with the inherent risk of pollution of soil and water supplies, there may well come the time when more widespread chronic cyanide neurotoxicity occurs from a dietary source in persons with a genetic or acquired error of cyanide or vitamin B₁₂ metabolism.

Secondly, I consider that your statement that "although it has been suggested that vitamin B₁₂ has a primary role in the detoxification of cyanide, this is not finally proved" is open to misinterpretation. It is certainly well recognized that cyanide is also converted to thiocyanate by an independent pathway via the enzyme rhodanese, which is present in vivo in high concentration in the liver.⁶ Clinical studies from many centres have shown conclusively that hydroxocobalamin, but not cyanocobalamin, is a powerful cyanide antagonist. Because confusion is likely to persist in the profession over the differences between various forms of vitamin B₁₂ commercially available, we have drawn attention to the superiority of hydroxocobalamin, and the possible adverse effect of cyanocobalamin in neuro-ophthalmological disorders, and submitted a case for the complete withdrawal of cyanocobalamin in favour of hydroxocobalamin for therapeutic use.⁷ In our view, the only indication for the continued availability of cyanocobalamin is its use in the performance of the Schilling test of vitamin B₁₂ absorption.

Looking to the future, it is possible that other cyanide antagonists may become available for our therapeutic use with the obvious advantage of oral administration. In such circumstances, I would strongly urge that all patients with proved tobacco amblyopia and patients with optic atrophy, myelopathy, or neuropathy of obscure origin should be very carefully screened for evidence of vitamin B₁₂ deficiency before embarking on any therapy other than hydroxocobalamin.—I am, etc.,

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- 1 Heaton, J. M., McCormick, A. J. A., and Freeman, A. G., *Lancet*, 1958, 2, 286.
- 2 Freeman, A. G., and Heaton, J. M., *Lancet*, 1961, 1, 908.
- 3 Freeman, A. G., *Lancet*, 1959, 2, 963.
- 4 Wilson, J., Linnell, J. C., and Matthews, D. M., *Lancet*, 1971, 1, 259.
- 5 Osuntokun, B. O., and Osuntokun, O., *American Journal of Ophthalmology*, 1971, 72, 708.
- 6 Smith, A. D. M., *Lancet*, 1961, 1, 1001.
- 7 Foulds, W. S., Freeman, A. G., Phillips, C. I., and Wilson, J., *Lancet*, 1970, 1, 35.

Neuromuscular Involvement in Pituitary Gigantism

SIR,—Dr. P. D. Lewis (27 May, p. 499) describes two cases of pituitary gigantism with neuromuscular involvement. I would like to report a case of similar neuromuscular involvement in a man aged 69 with acromegaly of at least eight years duration.

This man first presented in a Dublin hospital in 1964 with left foot drop; acromegaly was noted for the first time. The acromegaly has not apparently progressed since then, and clinical indices of activity have been negative over the past two years. His feet, however, have got steadily worse.

He shows evidence of severe peripheral neuritis affecting both legs with marked wasting of the calves and absent sensation to pin-prick and cotton wool over the feet and legs. Plantar flexion and dorsiflexion at the left ankle are completely lost, and the interphalangeal joint of the left great toe is destroyed by neuropathic arthropathy. His feet are extremely painful and he has troublesome trophic ulcers. In addition he has gross impairment of muscle power in the proximal muscle groups of the lower limbs.¹

This case would appear to be a further example of peripheral neuropathy and myopathy associated with pituitary growth hormone excess.—I am, etc.,

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¹ Mastalgia, F. L., Barwick, D. D., and Hall, R., *Lancet*, 1970, 2, 907.

Amantadine-induced Aggressiveness

SIR.—The antiparkinsonian effect of amantadine was shown in 1969 by Schwab¹ and since then confirmed by several other authors.² The behavioural and biochemical effects of this drug in experimental animals³ suggested to Vale *et al.*⁴ the possibility of using it as an antidepressant; a positive effect was claimed by them in depressed patients.

On the basis of this finding, we have treated four aged depressed patients with amantadine for at least three weeks. The dose regimen was started with 100 mg/day and then slowly increased to 300 mg/day within 10 days.

We did not observe any positive effect on mood but, conversely, noticed a progressive increase of motor restlessness, anxiety, and sudden bursts of violent, aggressive behaviour, with hostile attacks upon the ward's staff. The hostility and aggressiveness became evident usually after 10-15 days of treatment, when amantadine plasma levels were about 800 ng/ml, and tended to disappear within 4-6 days after discontinuation of treatment. A detailed description of these results will be published later.

Since we could not find any data in the literature on amantadine-induced aggressive behaviour in depressed patients during observations have been made by others.

The appearance of aggressive and hostile behaviour in depressed patients during amantadine treatment is also of particular interest in view of a similar phenomenon recently observed by Goodwin *et al.*⁵ in depressed patients treated with high doses of L-dopa. The same authors suggest that the aggressiveness seen in humans after L-dopa may be related to an increased catecholamine synthesis. Considering the similarity between the antiparkinsonian and pharmacological effects of L-dopa and amantadine, it is possible to hypothesize the existence of an analogous mechanism to explain the clinical results obtained with our patients.—We are, etc.,

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¹ Schwab, R. S., England, A. C. Jr., Poskanzer, D. C., and Young, R. R., *Journal of the American Medical Association*, 1969, 208, 1168.
² Parkes, J. D., Zilkha, K. J., Calver, D. M., and Knill-Jones, R. P., *Lancet*, 1970, 1, 259.

³ Fibiger, H. C., Fox, M., McGeer, E. G., and McGeer, P. L., *Journal of Pharmacology and Pharmacology*, 1971, 23, 724.
⁴ Vale, S., Espeiel, M. A., and Dominguez, J. C., *Lancet*, 1971, 2, 437.
⁵ Goodwin, F. K., Murphy, D. L., Brodie, H. K., and Bunney, W. E., *Biological Psychiatry*, 1970, 2, 341.

Varieties of Smoke

SIR.—I recently re-read your leading article (18 September 1971, p. 656) which questions the value of tar assays. The views expressed were somewhat disturbing and persuade me to raise several points.

(1) Measurement of the tar delivered at the proximal end of the butt by a particular brand of cigarette is a simple, reliable procedure.¹ It is used in America, Canada, and Australia—at least by the tobacco industry and by private or public health organizations. Interpretation is also simple—a cigarette delivers so many milligrams of tar to the smoker's lips if smoked in standard fashion. From tests performed in the chemistry department at Monash University a smoker's "tar table" has been produced, and from it a comparison between brands is possible.

As you say, smoking habits vary, but a packet of Australian cigarettes near the top of this table delivers 100 mg of tar and 6 mg of nicotine; a packet of cigarettes from the bottom of the table delivers 520 mg of tar and 32 mg of nicotine. These are gross differences. The fact that more frequent puffing may occur could hardly make up a five-fold difference in tar and nicotine delivery.

(2) The smoking dogs of Hammond and Auerbach² demonstrated that lung damage is related quite directly to regular tar intake. Mortality rates in filter smokers, as recorded by Bross,³ suggest the same.

If low-tar cigarettes were available on the British market (you will only find them by testing), some smokers who used them would notice diminution of cough and return of taste (personal observation).

(3) The people who are going to die soon from smoking are the addicts of 20, 30, or 40 years. If they cannot give up, they can smoke pipes, cigars or low-tar cigarettes and thereby lower their risk. We should not abandon the present generation of bread-winners. None of this suggests low-tar cigarettes are "safe," they are merely less risky.

(4) It is not difficult to differentiate between relative risks in a public campaign. It has been done in the U.S.A. and Canada, and our own experience in the State of Victoria is also of some interest.

We can reasonably claim to have generated a demand for low-tar cigarettes among addicted smokers over the past three years. Since per capita cigarette consumption has not changed much, this is presumed to be at the expense of high-tar brands. We have seen no signs that this campaign has encouraged or unduly reassured smokers, although some have worked down the ladder and eventually given up. Two low-tar brands are now among the more heavily promoted brands in this State. (The tobacco industry is not notably responsive to pressure of public health opinion, but is acutely sensitive to the demands of the market). I think this campaign is a useful gesture to the smoker with a high and immediate risk. It need not detract from the overall anti-smoking message.

If your editorial advice is taken, you will never see low-tar cigarettes on the market, never discover the benefit of this to the coughing, tasteless smoker, and never gain material for the necessary epidemiological study which is needed to determine just how much a lower daily tar intake lowers smoking risk.—I am, etc.,

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¹ Moore, G. E., Bross, I., Shamberger, R., and Bock, F. G., *Cancer*, 1967, 20, 323.
² Hammond, E. C., *et al.*, *Archives of Environmental Health*, 1970, 21, 740.
³ Bross, I. D. J., and Gibson, R., *American Journal of Public Health*, 1968, 58, 1396.

Presenile Dementia

SIR.—Unfortunately, the facts presented in our paper (29 April, p. 249) do not help to answer many of the questions posed by your correspondents.

The mean age of the 106 patients investigated for presumed dementia was 61 years; the youngest was aged 34, and the oldest was aged 78. The outcome of investigation in relation to the age at which it was carried out is shown below.

Age	<50	50-59	60-69	70+
No. of patients ..	8	40	43	15
Not demented (uncertain in parentheses)	3 (2)	7 (3)	3 (2)	2
Diagnosis of Dementia				
Space occupying mass		2	5	1
Arteriosclerotic ..		1	5	2
Alcoholic		4	2	
Normal pressure hydrocephalus ..		1	3	1
Creutzfeldt - Jakob disease		1	1	1
Huntington's chorea	2	1		
Post - traumatic cerebral atrophy ..		1		
Postsubarachnoid haemorrhage ..	1			
Limbic encephalitis			1	
Cerebral atrophy ..		19	21	8

Our data do not help define "an age criterion" for selection of demented patients for full investigation asked for by Dr. P. K. Bridges (20 May, p. 465). This decision remains a matter of judgement in which chronological age is one of many factors taken into consideration. For this reason the term "presenile" (which has no age definition) was used for it conveys the same concept of biological age as does the indefinable term adult life.

To answer Dr. H. M. Hodgkinson (13 May, p. 404) on "the value of neurological investigation at any given age in middle life" would require a much larger number of patients, and to complete the picture one would wish to know the cause of dementia in those elderly patients who are not fully investigated in life.

Dr. Hodgkinson also asks for further information on those patients who were judged to be amenable to (that is, capable of) treatment. We felt it would be useful to give some conservative estimate, and the 15% figure quoted included the three patients with benign intracranial tumours,