of opacity all over the right and left lung fields. The asthmatic attack was relieved only after giving 100 mg of hydrocortisone sodium succinate intravenously.—We are, etc.,

Z. FARID

U.S. Naval Medical Research Unit No. 3,

S. BASSILY
A. HASSAN

Abbassia Government Fever Hospital,
Cairo, Egypt

¹ Farid, Z., et al., *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1972, **66**, 119.

Propranolol and the Hyperactive Carotid Sinus Reflex Syndrome

SIR,—The hyperactive carotid sinus reflex syndrome is a physiopathological condition in which syncope, originating in the carotid sinus and mediated through a cardiac and/or a peripheral vascular effect, develops on compression of the carotid sinus. The carotid sinus syndrome is an analogous physiopathological condition but of a higher grade as it manifests itself spontaneously.¹

The existence of a carotid sinus syndrome is a contraindication for the administration of beta-adrenergic blocking agents as these drugs inhibit sympathetic stimulation, important whenever vagal tone is increased.²

As the existence of a hyperactive carotid reflex syndrome might also be a contraindication for any therapy with beta-adrenergic blocking drugs, all the patients from our outpatient department who are to be put under treatment with propranolol are previously tested for a hyperactive carotid sinus reflex syndrome was diagnosed. A test dose Franke's procedure.^{3,4}

A 62-year-old man with grade III chronic coronary insufficiency was to be treated with propranolol in an initial daily dose of 120 mg. On compression of the right carotid sinus he was found to develop a brief syncope and marked bradycardia resulting from sinus arrest followed by junctional escapes (see fig., A). Thus a hyperactive carotid sinus reflex syndrome was diagnosed. A test dose of 2 mg of propranolol was administered intravenously as a bolus injection and 10 minutes later hyperextension of the head provoked a more prolonged syncope and a more marked bradycardia than previously. Thus the hyperactive carotid sinus reflex syndrome had been transformed into a carotid sinus syndrome after propranolol. Digital compression of the carotid sinus for a shorter period than previously provoked a much more lasting sinus arrest 15 minutes after propranolol (see fig., B).

Twenty minutes after propranolol 1 mg of atropine was injected intravenously; five minutes later the right carotid sinus was

massaged for several seconds. No effect was observed either on the electrical activity of the heart (see fig., C) or on the clinical condition of the patient. This last procedure and the corresponding result show the innocuity of our methods.

It is imperative to search for a hyperactive carotid sinus reflex syndrome in every patient who is to be treated with beta-adrenergic blocking drugs and this therapy avoided if the syndrome is diagnosed and the participation of a central cardiac mechanism in it demonstrated.—I am, etc.,

ARIEL J. REYES

Fundacion Procardias,
Durazno 2025,
Montevideo, Uruguay

- 1 Thomas, J. E., *Mayo Clinic Proceedings*, 1969, **44**, 127.
- 2 Isasi, E. J., Reyes, A. J., and de Bayarres, M. A., *Arquivos Brasileiros de Cardiologia*, 1969, **22**, 215.
- 3 Franke, H., *Deutsche medizinische Wochenschrift*, 1967, **92**, 1155.
- 4 Grand, A., and Lapicorey, G., *Coeur et Médecine Interne*, 1972, **11**, 265.

New Ideas on Vitamin D

SIR,—Professor Iain MacIntyre (14 April, p. 120) referred to our point of view regarding the role of parathyroid hormone in the regulation of 1,25 dihydroxycholecalciferol (1,25-(OH)₂D₃) biosynthesis. The statement which he attributed to me is at best only partially correct.

Except under the abnormal hypophosphataemic state, we believe that the parathyroid glands do play an important determining role in the regulation of 1,25-(OH)₂D₃ synthesis. Our experiments¹ have been completely verified by Fraser and Kodicek,² by Hill and Mawer,³ and by Rasmussen et al.⁴ If animals are made hypophosphataemic, the parathyroid hormone is no longer required to stimulate 1,25-(OH)₂D₃ synthesis.⁵ Of course we do not know the molecular events involved in the regulation, nor does anyone else to my knowledge. Though it is possible that the parathyroid hormone may stimulate 1,25-(OH)₂D₃ synthesis by changing ionic concentrations in the renal cell, the fact remains that under normal physiological circumstances (excluding hypophosphataemia), as far as we can presently surmise, the parathyroid hormone plays a major role in the stimulation of 1,25-(OH)₂D₃ synthesis. We know of no other points of view which have adequate experimental support.—I am, etc.,

H. F. DeLuca

Department of Biochemistry,
University of Wisconsin-Madison,
Madison, Wisconsin

- 1 Garabedian, M., Holich, M. F., DeLuca, H. F., and Boyle, I. T., *Proceedings of the National Academy of Sciences of the U.S.A.*, 1972, **69**, 1673.
- 2 Fraser, D. R., and Kodicek, E., *Nature New Biology*, 1973, **241**, 163.
- 3 Hill, L. F., and Mawer, E. B., *Clinical Science*, 1973, **44**, 4p.
- 4 Rasmussen, H., Wong, M., Bikle, D., and Goodman, D. B., *Journal of Clinical Investigation*, 1972, **51**, 2502.
- 5 Tanaka, Y., and DeLuca, H. F., *Archives of Biochemistry and Biophysics*, 1973, **154**, 566.

Malignancy of Bronchial Adenoma

SIR,—With reference to your leading article on this subject (19 May, p. 378), there must be others like myself who were surprised to read that bronchial adenomas are white. Possibly some are in some circumstances,

Electrocardiograms (lead II) from patient with hyperactive carotid sinus reflex syndrome. A. Right carotid sinus compression: sinus arrest and junctional escapes. B. Carotid sinus compression after propranolol: cardiac inhibition is enhanced. C. Carotid sinus massage after atropine: no effect on cardiac activity.

but personally, looking through the bronchoscope or at bronchotomy, I have never seen anything whiter than a light pink. The majority have been red, some very red, emphasizing their vascularity.

I would like to comment on one or two other points. The statement that the mass that projects into the bronchial lumen is only a small part of a more extensive tumour needs modification. It may be and usually is, and is manifestly so in large tumours, but in some cases the tumour does not extend through the whole thickness of the bronchial wall. I have on three occasions resected a tumour via a bronchotomy without excising the whole thickness of the bronchial wall. Two of the patients are free from recurrence 14 and 16 years later and the third was lost sight of after four years when he emigrated.

Finally, I am in no way qualified to express an opinion on the histology, but I have the impression that the boundary between bronchial adenoma and adenocarcinoma may be hazy and that pathologists do not always speak with the same voice. A tumour which some would classify as an adenoma may be classified as an adenocarcinoma by others. The histological report in the three cases mentioned above was "benign bronchial adenoma," and I see no reason to suspect that the reports were incorrect.

It seems to me that there is still need for further study before we can approach the treatment of bronchial tumour with complete confidence. If we regard all of them as malignant or potentially so we shall avoid the surgical error of treating a malignant lesion as though it were a benign one, but will we avoid the surgical misfortune of treating a benign lesion as though it were a malignant one?—I am, etc.,

VINCENT POWELL

Midhurst, Sussex

Haematology and Biochemistry of Ankylosing Spondylitis

SIR,—Dr. M. J. Kendal and others (28 April, p. 235) state that the relatively high values of haemoglobin and serum albumin in their patients were unexpected. It is, however, well known that patients with ankylosing spondylitis have much less tendency to anaemia than rheumatoid patients and that, when present, the degree of anaemia is seldom severe. For example, in their study of 212 patients Wilkinson and Bywaters¹ found mild anaemia in only 12. Admittedly, however, some authors (for example Lefkowitz and Thomas)² have noted a higher incidence. In practice a moderate degree of anaemia in spondylitis always warrants a search for complicating factors, especially gastrointestinal bleeding from drug therapy.

Slight elevations of serum alkaline phosphatase may occur in ankylosing spondylitis especially when radiological changes are advanced.³ However, it is not generally accepted that this can be the result of bony ankylosis, as is suggested. The elevations are always very slight, and indeed in the present series the mean level of alkaline phosphatase (13.33 units) is only at the upper limit of normal and (as is pointed out) does not differ significantly from the mean alkaline phosphatase (11.77 units) of the rheumatoid group.

While it is true that the E.S.R. does not

correlate with the degree of, and is not often a reliable guide to, disease activity, it is misleading to say that this investigation is "of little value" in ankylosing spondylitis. Even moderate elevations of the E.S.R. may be helpful in the diagnosis of the early case. Moreover, the authors give the normal range of the E.S.R. as 0-12 mm/1 hr. Most rheumatologists take a higher figure as the upper normal limit—up to 15 mm/1 hr in young males and 20 mm/1 hr in young females (even higher upper limits of normal are accepted in the elderly). Therefore the statement that "the E.S.R. was moderately raised in most patients" must be regarded with some reserve. In a few severe cases of ankylosing spondylitis the E.S.R. is very high and these patients do often have considerable pain; they are ill, wasted, and often respond poorly to conventional treatment with anti-inflammatory drugs or deep x-rays. A continued high E.S.R. can therefore be of some prognostic significance.

Regarding serum protein electrophoresis in spondylitis, it is worth adding that when immunoelectrophoresis is carried out in addition to conventional electrophoresis a much higher frequency of abnormalities is found. In 10 consecutive patients of mine paper electrophoresis showed abnormalities in only two, whereas immunoelectrophoresis showed abnormalities of one or more of IgA, IgG, and IgM immunoglobulins in half the group. From the point of view of early diagnosis this would seem to merit further study. When IgG antiglobulins are considered, elevated levels are found in the majority of patients as in other varieties of seronegative polyarthritis,⁴ but this is a more difficult investigation to carry out routinely.—I am, etc.,

D. N. GOLDING

Princess Alexandra Hospital,
Harlow, Essex

- 1 Wilkinson, M., and Bywaters, E. G. L., *Annals of the Rheumatic Diseases*, 1958, 17, 209.
- 2 Lefkowitz, A. M., and Thomas, J. R., *Annals of Internal Medicine*, 1958, 49, 89.
- 3 Mowbray, R., Latner, A. L., and Middlemiss, J. H., *Quarterly Journal of Medicine*, 1949, 18, 187.
- 4 Howell, F. A., Chamberlain, M. A., Perry, R. A., Torrigiani, G., and Roitt, I. M., *Annals of the Rheumatic Diseases*, 1972, 31, 129.

Amyloidosis and the Kidney

SIR,—It is a pity that your leading article on amyloidosis and the kidney (12 May, p. 322) conveyed the impression that the body organs are equally affected in primary and secondary amyloidosis, discounting the traditional view that this is not so. The assertions may be true for the kidney, heart, and alimentary tract but they certainly do not apply to skin.

Clinical involvement of the skin in secondary amyloidosis is rare, whereas it is common in the primary form and in association with myeloma. About a quarter of these patients have cutaneous lesions which are sufficiently characteristic to allow a firm clinical diagnosis in anticipation of biopsy confirmation. Translucent brown papules about the eyelids are often haemorrhagic. Sometimes larger but similar nodules appear on the face and lips. Diffuse infiltration of the fingers and hands (sometimes inducing haemorrhagic pseudobullae) leads to an appearance which may be mistaken for scleroderma.

These and other physical signs may lead

to recognition of the primary and myeloma-associated forms of amyloid by the dermatologist in patients with a variety of chronic systemic symptoms which have evaded previous diagnosis.—I am, etc.,

HARVEY BAKER

The London Hospital,
London E.1

Supporting Service for the Mentally Handicapped

SIR,—We wish to give our fullest support to Dr. E. B. McDowall (26 May, p. 481) in his demand for a single responsible body to provide properly co-ordinated services for the mentally handicapped.

This is what is done in most other countries which have organized provision for medical care. Unless we follow their example the present trend of fragmentation of the provision of services will lead to an overall decrease in care as the mentally handicapped take their place at the foot of the priorities in each group providing these services—whether social, educational, or medical.

Care for the mentally handicapped requires to be comprehensive and prolonged, and to ensure this a specific responsible authority is required.—We are, etc.,

R. C. MACGILLIVRAY
Chairman

Lennox Castle Hospital,
Lennoxtown, Glasgow

D. A. PRIMROSE
Secretary,

Western Regional Division of Mental Deficiency

The Royal Scottish National Hospital,
Larbert, Stirlingshire

Treatment of Status Asthmaticus

SIR,—I read with great interest your leading article (9 December, 1972, p. 563), on the treatment of status asthmaticus. Though the administration of hydrocortisone (as well as aminophylline) is essential for the treatment, its use results in some untoward effects, some of which have never before been reported.

I have now finished a study of 31 patients admitted in status asthmaticus and treated with intravenous hydrocortisone. The first group of 15 patients included patients who had previously been on steroid treatment for chronic asthmatic bronchitis, and the initial intravenous dose of 200 mg of hydrocortisone sodium phosphate did not give any side effects. The second group of 16 patients included patients who had never been on steroid treatment before, and the administration of 200 mg of hydrocortisone sodium phosphate induced side effects which included paraesthesiae,¹ macular rash, tremor of the arms and legs, and nausea and vomiting, as shown in the table. The duration

Reaction	No. of Patients*
Paraesthesiae	13
"Pins and needles"	10
Itching	5
Heat and chills	2
Numbness	10
Tightness	4
Formication	1
Tremor	5
Nausea and vomiting	3
Macular rash	1

*Most patients developed more than one symptom