Miss Round.² We await the estimations of vitamin D levels to be completed on random samples from children in our survey. Maybe we shall be shown to be wrong, but in view of the marked difference between the heights and weights of our treated children and the control groups and the correlation of vitamin D levels with serum alkaline phosphatase found in Asians by Dr. O'Riordan and his colleagues³ we doubt it. A full report on the effects of treatment and on alkaline phosphatase levels will be submitted for publication shortly.—We are, etc.,

W. T. COOKE
P. ASQUITH

- Holmes A. M., Enoch, B. A., Taylor, J. L., and Jones M. E., *Quarterly Journal of Medicine*, 1973, 42, 125.
- Round, J. M., *British Medical Journal*, 1972, 3, 114.
- Preece, M. A., et al., *Lancet*, 1973, 1, 907.

Erysipelothrix Septicaemia

SIR,—In answer to the question put by Drs. W. D. Alexander and C. S. Goodwin (31 March, p. 804) our patient never received steroids for her psoriasis and was never on any form of immunosuppressive drugs. She remains well and there is no obvious predisposing factor that we can discover.

We agree that we would perhaps have been wiser to be less dogmatic and to report that there was "no clinical evidence of endocarditis," but in the cases previously reported the endocarditis has been gross, with severe valve damage in every case, and we felt that endocardial involvement was unlikely in our patients.—We are, etc.,

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Thrombotic Thrombocytopenic Purpura after Influenza Vaccination

SIR,—We wish to report a case of thrombotic thrombocytopenic purpura following influenza vaccination.

A 23-year-old Sikh nurse was vaccinated with Flenzavax (Wellcome). No immediate reaction was noted, but 14 days later she developed the first of numerous spontaneous bruises, and after a further seven days increasing pallor prompted a blood count, after which she was admitted to hospital. Examination revealed anaemia, numerous bruises, a positive Hess's test, and a blood pressure of 180/95 mm Hg, but no other abnormalities.

Investigations showed: haemoglobin 9.2 g/100 ml, reticulocytes 9%, white blood count 8,200/mm³, platelet count 39,000/mm³, and peripheral blood film showing the typical features of a microangiopathic haemolytic anaemia with numerous schistocytes and microspherocytes. Direct Coombs test negative. Bone marrow showed hyperplastic erythropoiesis, normal leucopoiesis, and normal numbers of mature megakaryocytes but with little platelet budding visible. Fibrinogen titre normal. Fibrinogen degradation products not increased. L.E. cells absent. Blood urea 34 mg/100 ml. Midstream urine contained few red cells, no white cells or casts; sterile. Total serum bilirubin 4.7 mg/100 ml. Serum electrolytes, serum alanine aminotransferase, alkaline phosphatase normal. Immunoglobulins: IgA 133 mg/100 ml, IgG 2,800 mg/100 ml, IgM 55 mg/100 ml, anti-nuclear factor, thyroid, mitochondrial, and smooth muscle antibodies negative. Pregnoticon

test negative. A chest x-ray and barium meal showed no abnormalities.

The clinical course is shown in the figure.

Despite several days of intravenous heparin the haemoglobin and platelet levels continued to fall, the red cell abnormalities became more striking, and the blood urea level rose to 68 mg/100 ml. On the eighth day the patient became stuporose incontinent with marked neck stiffness, but without focal neurological signs. Heparin was discontinued and prednisolone 100 mg daily commenced. Over the next three weeks the platelet count rose and the evidence of red cell damage on the blood film lessened. The blood urea returned to normal and all neurological abnormalities disappeared within one week of starting prednisolone. At follow-up the blood film, platelet count, and blood urea are normal and prednisolone has been discontinued. She is normotensive, and there are no clinical findings to suggest a collagen disorder or disseminated malignant disease.

The aetiology of thrombotic thrombocytopenic purpura and the related condition of the haemolytic-uraemic syndrome of childhood are unknown. One current view^{1,2} is that in certain individuals circulating soluble antigen-antibody complexes might be formed, possibly due to impaired responsiveness, following antigenic stimuli such as virus infections or vaccinations. These complexes can trigger platelet aggregation, disseminated intravascular coagulation, and possibly vascular endothelial damage, with consequent thrombocytopenia and "microangiopathic" haemolysis. The development of thrombotic thrombocytopenic purpura after influenza vaccination in our case, and after triple-antigen and T.A.B. vaccination in another,³ might be relevant to this hypothesis. Similarly, cases of the haemolytic-uraemic syndrome have been reported after triple, polio, measles, and smallpox vaccinations and viral infections.^{1,4}—We are, etc.,

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- Brain, M. C., *Seminars in Hematology*, 1969, 6, 162.
- Pitney, W. R., *Seminars in Hematology*, 1971, 8, 65.
- Frick, P. G., and Hitzig, W. H., *Lancet*, 1960, 2, 1401.
- Davison, A. M., Thompson, D., and Robson, J. S., *British Medical Journal*, 1973, 1, 654.

Curarizing Substance in Myasthenia Gravis

SIR,—Dr. Mary B. Walker (7 April, p. 42) recalls experiments carried out in the 1930s which strongly suggested that a curarizing substance produced in forearm muscles during contraction to the point of fatigue will increase the weakness of proximal muscles when the blood from the forearm is allowed to re-enter the circulation by deflating the cuffs previously constricting the arms. She mentions that these experiments "have been confirmed, though not by all observers." I have demonstrated this elegant experiment of Dr. Walker's on many occasions. The accompanying photographs show the dramatic increase of weakness in facial muscles and upper lids one minute after deflation of the arm cuffs in one of my patients. My experience confirms Dr. Walker's opinion that failure might be due to attempting the experiment on too mild a myasthenic or on one under the influence of neostigmine.

An observation very much in line with Dr. Walker's, although less neat, was made in 1929 at the Salpêtrière by Pierre Bourgeois. In his Paris thesis on myasthenia¹ he reproduces two photographs to illustrate what he calls "*l'expérience du ptosis*"

FIG. 1—Patient looking up before inflation of cuffs.

FIG. 2—Patient looking up one minute after release of cuffs.

provoqué." His patient, a middle-aged man, was asked to flex the fingers of his right hand repeatedly to the point of exhaustion. As fatigue came on the eyelids drooped progressively, the right eye developed a slight external squint, and the face assumed the myasthenic mask.—I am, etc.,

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¹ Bourgeois, P., *La Myasthénie*, Paris, N. Maloine, 1929.

Increased Dosage of Disodium Cromoglycate

SIR,—Observations on the safety of disodium cromoglycate in the long-term use in children failed to show evidence of significant toxic or allergic damage.¹ In the course of the study it was, however, noted that 13.4%

of patients using four capsules (each containing 20 mg) per day had no disodium cromoglycate in a random urine sample taken at a suitable interval after they stated they had inhaled a capsule of the drug, and a further 16% had very small amounts in the urine, suggesting that very little of the drug had been absorbed. In most cases the inhalation of a capsule under supervision produced appreciable amounts in a subsequent urine specimen, but in some cases the children appeared to be unable to inhale enough disodium cromoglycate from a single capsule to give appreciable absorption of the drug. It seemed possible that the use of eight capsules a day instead of three or four might lead to a better therapeutic result.

Eleven patients were chosen who all suffered from chronic perennial asthma which had not responded well to either three or four capsules of disodium cromoglycate daily. The average age of the group was 13.2 years and they had suffered from asthma for an average of 9.5 years. After an observation period of two weeks they were asked to take eight capsules (without isoprenaline) daily for three months. Their progress was assessed by clinical examination, ventilatory tests, and symptom record cards. The results are summarized in the table.

	Month 1	Month 2	Month 3
Responded	6	6	6
Did not respond	5	4	—

Those who failed to respond dropped out of the study before it was completed, but about 50% did do better on eight capsules a day. No toxic effects were encountered, but one patient complained of increased tightness in the chest temporarily after using the capsules. From the symptom records the most significant effect was decrease in asthma at night, noted by the end of the first month ($P > 0.05$), and this effect continued throughout.

It seems worth while, in some cases in which response to the standard dose is poor, to try the effect of an increased dose. There is no reason to suppose that it is not safe to do so.—I am, etc.,

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1 Smith, J. M., and Pizarro, Y. A., *Clinical Allergy*, 1972, 2, 143.

Sickle-Cell Anaemia

SIR,—I read with interest Colonel H. Gall's letter (24 February, p. 488) seeking information on the early history of sickle-cell anaemia. Although Herrick¹ specifically mentioned the "sickle-shaped red blood corpuscles" which he observed in the peripheral blood film of his patient, the disease was thereafter referred to at first as "Herrick's anaemia."² It was Mason³ in 1922, not Emmel⁴ in 1917 as suggested by Linde,⁵ who introduced the term "sickle-cell anaemia" which survived modifications² and qualifications^{6,7} to remain in popular usage since then.

A review article by Margolies² refers to two descriptions of sickle-shaped red cells in human blood before Herrick's publication. In 1902 Dresbach encountered a healthy 22-year-old mulatto student in Ohio whose peripheral

blood contained numerous elliptical red cells.⁸ This man died young from cardiac failure preceded by an attack of tonsillitis, and it was argued that since he was in good health when Dresbach made his haematological observation, the student could not have had the disease described by Herrick. Now that we know that, in sickle-cell disease, anaemia is not the essential sign and not its most dangerous component, and the susceptibility of patients to bacterial infections and the risk of sudden death from cardiac complications make it probable that Dresbach's patient, after all, had sickle-cell disease. Sergeant and Sergeant⁹ in 1905 described "demi-lune" erythrocytes in some Algerian Negroes who had malaria. Since malaria and sickle-cell disease can coexist in a patient, these French writers retain their place, albeit tenuous, in the early history of sickle-cell anaemia.

This haemoglobinopathy is an old disease in West Africa, where "long before Herrick described sickle-cell anaemia . . . Ghanaian recognised the disease as a dangerous hereditary syndrome called by different names in different tribes . . . and known to be very serious especially in the rainy season and during pregnancy . . . Some elderly men could trace back several generations relations who had died young from the disease."¹⁰ The earliest description of this disease that I know of, however, was given by Africanus Horton in 1874 in his monograph *The Diseases of Tropical Climates and Their Treatment*,¹¹ which Colonel Gall will find in the Royal Army Medical College library at Millbank. Horton's elegant description anticipated by decades some of the features of sickle-cell disease that were later recognized: the premonitory fever of crises; the rheumatism which shifted from joint to joint and which "metalized" to internal organs (heart, abdominal viscera) to cause severe, sometimes fatal complications; and the remarkable observation that the sufferers had enlarged bones. The disease was characterized by "long continuance and frequent recurrence of symptoms," which seldom terminated fatally unless the internal organs were involved, when death might be rapid as the disease "may suddenly seize on the muscular coat of the heart," as was later exemplified by Dresbach's patient. Horton found that there was constantly an abnormality in the blood and mentioned the peculiar constitutional tendency to the disease among "natives of the tropics . . . who suffer dreadfully from this disease in the rainy season."

If it is correct that in prehistory sickle-cell anaemia was brought to Africa by nomadic bearded "tall men" of Asia,¹² even earlier descriptions of this disease may exist somewhere. It cannot be said of the anaemia which Herrick described in 1910 that "See, this is new."¹³—I am, etc.,

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2 Margolies, M. P., *Medicine*, 1951, 30, 357.

3 Mason, V. R., *Journal of the American Medical Association*, 1922, 79, 1318.

4 Emmel, V. E., *Archives of Internal Medicine*, 1917, 20, 586.

5 Linde, S. M., *Sickle Cell; A complete guide to prevention and treatment*. New York, Pavilion Publishing Company, 1972.

6 Hahn, E. V., *American Journal of the Medical Sciences*, 1928, 175, 206.

7 Graham, G. S., and McCarty, S. H., *Southern*

Medical Journal 1930, 23, 598.

8 Bishop, F. W., *Archives of Internal Medicine*, 1914, 14, 388.

9 Sergeant, E., and Sergeant, E., *Comptes Rendus Hebdomadaires des Séances et mémoires de la Société de Biologie*, 1905, 58-59, 51.

10 Konotey-Ahulu, F. I. D., *Ghana Medical Journal*, 1968, 7, 118.

11 Horton, J. A. B., *The Diseases of Tropical Climates and Their Treatment*. London, Churchill, 1874.

12 Lehmann, H., and Cutbush, M., *British Medical Journal*, 1952, 1, 404.

13 *Ecclesiastes*, ch. 1, v. 9-10.

Dangerous Pleasures

SIR,—In your leading article "Full Strength to Extra Mild" (21 April, p. 134) you have one sentence concerning cigarette smoking which must be challenged.

You say, "No other product carrying such a risk of ill health yet with so few restrictions on its sale is allowed to be advertised and sold to the public." What, in heaven's name, about alcohol? Although many people enjoy and may be helped by occasional small doses, surely it is the direct cause of more deaths from disease, and, don't forget, road accidents and suicides, than any cigarette smoking. Also compare the "social" illnesses—poverty, wives and families with nervous complaints, crime, industrial accidents.

I do not advocate the "prohibition" of either alcohol or cigarette smoking, but if you are to be fair, if the present "Health Warning" has to be printed on cigarette packets, then it would be logical to print on every bottle of beer, whisky, etc.: "Drinking may be a danger to your health and welfare and the health and welfare of others." And to a much lesser degree what about the "danger to health" of refined sugar, sweets, etc.? The whole thing is out of balance and your article is no help . . . perhaps editors too, don't smoke, but "like a drink (in moderation, of course)."—I am, etc.,

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Psychiatric Inpatients from Urban Communities

SIR,—Dr. T. Fryers's paper (14 April, p. 76) raises almost as many questions as it answers. For instance, in table IV it is shown that on 31 December 1958 Birmingham had only 196.8 beds/100,000 population occupied by patients of more than two years' length of stay, whereas 13 years later, despite a very active community-based service, Salford had 255.3 such beds. A reasonable deduction would seem to be that a community-based service led to an increase in long-stay patients, as no one in Birmingham would claim, I think, that the mental hospital service was community-based in 1958. The truth is that before 1948 the City of Birmingham had an appalling record for boarding out its long-stay patients. At Powich Hospital, Worcester (of which I was formerly Medical Superintendent) alone on 5 July 1948 there were over 400 boarded-out patients from Birmingham. Facts like this, along with changes in catchment areas, often vitiate extrapolations from epidemiological studies.

Where, however, a catchment area has remained static for a number of years retrospective studies can be of value. Taking 1 January 1960 as zero date, I calculated the