

even if they are not entirely original. Some years ago a similar red light was flashed by Kathleen Jones.¹¹ "Only in Britain", she said, "has 'progress' taken the form of denying that the mental hospital has a useful function and planning for its abolition".

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- ⁴ Ministry of Health, *A Hospital Plan for England and Wales* (Cmd. 1604). London, H.M.S.O., 1962.
- ⁵ *British Medical Journal*, 1971, 2, 62.
- ⁶ Early, D. F., and Magnus, R. V., *British Journal of Psychiatry*, 1966, 112, 595.
- ⁷ Hailey, A. M., *Psychological Medicine*, 1971, 1, 128.
- ⁸ *Lancet*, 1971, 1, 438.
- ⁹ *Local Authority Hostels for the Mentally Ill: A survey of Thirty-one Hostels*. London, Ministry of Health, 1966.
- ¹⁰ Durkin, E., *Hostels for the Mentally Disordered*. London, Fabian Society, 1971.
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Henoch-Schönlein Purpura and the Kidneys

In its usual form Henoch-Schönlein purpura is a disease of childhood, with a peak incidence between the ages of 2 and 5 years. The clinical manifestations are legion but most characteristic are a typical rash, fever, arthritis, gastrointestinal symptoms, and renal disease.¹ Boys are affected more often than girls, and most patients recover completely within a month.

The nature of the condition is obscure but the basic pathological lesion is an inflammation of small blood vessels, sometimes associated with fibrinoid necrosis of their walls. Hypersensitivity to various allergens, including infecting organisms,² food,³ and drugs,⁴ has been implicated but why some individuals should respond in this way is still not known.

The incidence of renal involvement is high and has varied in different series between 12 and 49%.⁵ W. Osler⁶ reported that five of his seven fatal cases died in renal failure and this has led to perhaps unjustified pessimism about the prognosis of the patient with haematuria. It is now clear^{5 7 8} that the usual lesion is a focal proliferative glomerulonephritis. The more severe examples may show striking cell necrosis within some of the glomerular lobules, with capsular adhesions and localized crescent formation. Such patients have haematuria with a varying amount of proteinuria, which is often sufficiently heavy to produce a nephrotic syndrome. Their prognosis is generally good. S. R. Meadow and his colleagues⁹ have followed 43 children with Henoch-Schönlein purpura and focal renal lesions for an average of three years (range 1-15 years) and shown that two-thirds recover completely. The remainder, though left with persistent haematuria and sometimes proteinuria, have remained well with stable or improving renal function. By contrast, occasional patients show a florid diffuse proliferative glomerulonephritis with extensive crescent formation, which may be associated with a necrotizing arteritis affecting afferent arterioles and interlobular arteries. The clinical course is stormy and may end with death in renal failure within a few weeks or months, though, again, complete recovery may occur.

Allen and his colleagues noted that their older patients tended to have a more serious illness than the younger ones, with a higher incidence of severe gastrointestinal and renal disease and a higher rate of recurrence of the other manifestations.¹ Meadow has found the same and it appears that this tendency may apply to the rare adults who develop this

condition. H. S. Ballard and his colleagues¹⁰ have recently described 14 patients aged 29 to 89 years who had Henoch-Schönlein purpura with renal involvement. Most were studied in retrospect and in only half was renal histology available. Ten patients recovered but four—all of whom had extensive epithelial crescent formation in the kidneys—died from renal failure within five months of the start of the illness.

In another series,¹¹ of 38 adults with Henoch-Schönlein purpura with evidence of renal involvement, three patients ultimately died—one in the acute phase with extensive crescent formation and the others at two and a half and five years with respectively progressive focal proliferative disease and hypertension. This relatively high mortality rate is in strong contrast to the situation found in children; only two of Meadow's 87 cases with renal disease died. The difference may partly be due to the inclusion among the adults of cases of the microscopic form of polyarteritis nodosa.¹² This illness, which may produce a clinical picture remarkably like that of anaphylactoid purpura (except that it has a more sinister prognosis), serves to emphasize the overlap that may occur between the different diseases causing vasculitis.

It is difficult to assess the results of treatment of any condition that has such a varied course. The detection and elimination of infectious or other sensitizing agents are logical steps. Allen and his colleagues had little doubt that steroid therapy was useful in treating the articular and gastrointestinal manifestations but were not impressed by its effect on either the skin or the kidneys. This view is shared by Meadow and his colleagues, who no longer prescribe steroids for patients with minor renal lesions. These authors have given cyclophosphamide with and without steroids to several of their more severely affected children (including 12 with extensive crescent formation) and have recorded several striking successes. Nevertheless, this therapy has not been controlled and its justification must be established by clinical trials.

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- ⁶ Osler, W., *American Journal of Medical Sciences*, 1904, 127, 1.
- ⁷ Heptinstall, R. H., and Joeles, A. M., *Proceedings of the Royal Society of Medicine*, 1959, 52, 211.
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Standardization in Haematology

The safe and effective use of biological materials used in therapeutics calls for preparations of known activity which can be used as national or international standards or as reference preparations with which to compare them. It is of vital importance that all therapeutic preparations of insulin, for instance, should be comparable in terms of activity.

The World Health Organization has provided this essential service by the creation of international laboratories for

biological standards. Two are in Britain at the National Institute of Medical Research and at the Central Veterinary Laboratory, Weybridge. The work of these institutes is characteristic of the fundamental support which W.H.O. provides for modern medicine. The preparations available cover a wide range, including blood typing sera, enzymes and hormone preparations, plasma protein fractions such as coagulation factors, antibiotics, immune sera, vaccines, and many others. The principle is to provide preserved materials of measured stability whose activity is ascertained in recognized centres by biological or microbiological assay. It is not often possible to describe the activity of such preparations in absolute terms, and the empirical approach of agreed international units of activity has proved its worth in practice.

More recently the need for standard reference preparations has extended through the rapid expansion of laboratory medicine and of clinical chemistry in particular. A number of independent bodies, such as the International Federation of Clinical Chemists, have convened committees on standards. Progress has been slow, and the interrelation of assay methods and standardization has emerged as a field for investigation which has so far received little attention. Techniques for the validation of assay methods are still comparatively crude. A further need for standardization arises from international survey work on such matters as nutritional status in different communities, and here substances such as iron, vitamin B₁₂, and folate are important. Two main approaches have been used. The first is essentially empirical and consists in the distribution of preserved specimens, usually of sera, to a number of laboratories, whose results are statistically analysed. The common experience of a group of laboratories is used as a measure of the precision of each. The second approach is the production of standard reference preparations in which the active component is described in absolute units.

The International Committee for Standardization in Haematology (I.C.S.H.) performed a notable service to medicine when it succeeded in obtaining widespread agreement for the specification of a standard haemoglobin preparation now in worldwide use.¹ We may now with some confidence compare results of haemoglobinometry from reputable laboratories no matter where they may be. It is a measure of the problems of standardization that this agreement took many years to achieve in spite of the fact that the concentration of haemoglobin in blood is high and measured in grammes per 100 ml, that its molecular weight and structure are known with some accuracy, and the absorption characteristics of its derived pigments are well characterized. No other single substance in blood occurs in such concentration. The problems are multiplied when dealing with concentrations measured in milligrams per 100 ml and even more so with the trace substances measured in micrograms.

However, encouraged by this success the International Committee enlarged the range of its activities and convened a number of panels for specific problems. Recently its Expert Panel on Iron, set up in 1966, has made a first report recommending a provisional specification for a standard serum iron preparation.² The recommendations are based on investigations undertaken by the panel which were described in a symposium at the Thirteenth Congress of the International Society of Haematology in Munich in 1970.³

It might be expected that substances which can be prepared in highly purified form would lend themselves to simple standards of pure substance. It is indeed not difficult to prepare highly accurate standard aqueous solutions of

many substances, including iron, commonly assayed in clinical chemistry. But problems arise from differences between organic media and aqueous solutions, in some cases from the instability of the pure substance, from binding or partial binding with proteins, from changes in fluid volume which occur on protein precipitation or dialysis, from the reconstitution of freeze-dried material to original volume, and from the presence of interfering substances—e.g., haemoglobin in iron assay. Attempts to define standards in absolute terms must take such problems of technique into account.

An interesting feature of the present provisional recommendations for iron assay is that the standard preparation should consist of two specimens with a difference in concentration of the variable—in this case the concentration of iron—of an accurate pre-determinable amount. When biochemical assays involve substances which can be prepared with known chemical purity, this approach to standardization offers the possibility of assay standards of a high order of accuracy. It may be applicable to many clinical biochemical assays and deserves careful study.

It is apparent from the report of the Expert Panel on Iron that the I.C.S.H., as well as seeking international agreement in its field of interest, is successfully promoting joint international research to achieve its objective. But clearly the various bodies now exploring standardization procedures should be brought together to co-ordinate their efforts, and the W.H.O. would seem to be the natural agency to undertake this.

¹ *British Journal of Haematology*, 1967, Supplement 13, p. 71.

² *British Journal of Haematology*, 1971, 20, 451.

³ To be published shortly.

Science on Show

In one of those reflective moments that come to young and old alike the question is sometimes posed: What is science? And the answer often boils down in the end to some version of: It is what scientists do. Though not very helpful to the logician that lurks in all of us, this conclusion does have the merit of emphasizing the personal responsibility of men for their conduct. Science comprises certain activities of people making decisions in play or earnest. Something of the imagination and ingenious thought that go into scientific research appears on stage periodically at the Royal Society's conversaciones, of which one was held last week to entertain the Fellows and their guests.

Among the exhibits displayed in the society's rooms at Carlton House Terrace was one by Dr. R. F. Hellon, of the National Institute for Medical Research, on the thermostat that keeps the body's temperature so remarkably constant. It consists of cells in the hypothalamus that are specially sensitive to their own temperature and also responsive to nervous impulses from receptors in the skin. Receiving information from inside and outside the body, it then controls the reactions of shivering, sweating, and so on to maintain a constant temperature. Drs. P. Pearson and M. Bobrow, of the M.R.C.'s Population Genetics Unit at Oxford, showed how fluorescent staining of human chromosomes with quinacrine dihydrochloride could distinguish each one individually. The technique was pioneered at the Karolinska Institute in Stockholm. Bands of fluorescence make a characteristic pattern on each chromosome, and for some unknown reason the Y chromosome always shows much brighter