ACETAZOLAMIDE IN THE TREATMENT OF SICKLE-CELL ANAEMIA

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Sickle-cell anaemia, together with other genetically determined haemoglobinopathies, is becoming an increasingly important cause of childhood mortality in the tropics as deaths from other tropical diseases steadily decrease in number. So far no treatment has been of any avail, and the only supportive measure of any real value during a crisis has been blood transfusion. Recently, however, it has been suggested that acetazolamide ("diamox") might be a valuable therapeutic agent, since it acts as a carbonic anhydrase inhibitor and was shown in one case to diminish intravascular sickling (Hilkovitz, 1957). We would therefore like to record our experiences of the use of this drug in three children with sickle-cell anaemia admitted to King George VI Hospital, Nairobi.

Case Reports

Case 1.—A child age 3 months was admitted with a chest infection and diarrhoea. The haemoglobin was 6.1 g./100 ml. and the spleen was enlarged to one fingerbreadth below the costal margin. Evidence of a haemolytic anaemia with a positive sickling test, an S+F pattern of the haemoglobin on paper electrophoresis, and the presence of the sickle-cell trait in both parents established the diagnosis. A transfusion was necessary because of the general clinical condition, and 100 ml. of blood was given intraperitoneally. Two days later a further transfusion of 200 ml. was given, after which the haemoglobin was 8.6 g./100 ml. Acetazolamide in a dosage of 10 mg. six-hourly was started. Though the picture was now slightly confused by the presence of the intraperitoneal blood, it was felt that acetazolamide, if of any value, should at least prevent the haemoglobin falling back to its original pre-transfusion level. Acetazolamide was continued for 35 days, after which time the haemoglobin was 7.7 g./100 ml. It was then stopped as the parents were refusing to keep the child in hospital any longer, but it seemed that the haemoglobin was slowly falling despite treatment.

Case 2.—A child aged 2½ years had been diagnosed previously as a case of sickle-cell anaemia and was admitted for investigation of a possible congenital heart lesion. The haemoglobin was 7.9 g./100 ml. On the 21st day after starting acetazolamide in a dosage of 21 mg. six-hourly, the child developed Koplik's spots and the haemoglobin had dropped to 5.4 g./100 ml. On the 23rd day the haemoglobin had further dropped to 4.2 g./100 ml. and the development of measles appeared to have coincided with a haemolytic crisis. This drop in haemoglobin had occurred despite continued treatment with acetazolamide.

Case 3.—A child aged 4 years was admitted with kwashiorkor and found incidentally to have sickle-cell anaemia (diagnosis being based on the same criteria as Case 1). Dietary treatment was instituted, and the child's nutritional condition had greatly improved when the development of a pyrexia, a dactylitis of the foot, and an increasing icterus indicated an incipient haemolytic crisis. The haemoglobin at this stage was 6.7 g./100 ml. and acetazolamide, 21 mg. six-hourly, was started to see if the development of the crisis would be in any way prevented or modified. However, despite treatment the haemoglobin fell

dramatically, and six days later was only 3.5 g./100 ml. Diarrhoea then developed, so the acetazolamide was stopped and an intravenous blood transfusion was given. Acetazolamide appeared to have no effect, since the haemoglobin could scarcely have fallen more rapidly as the crisis developed.

Comment

The dosage of acetazolamide was based on Hilkovitz's suggestion of 7 mg. per kg. per day in four divided doses. At this level of dosage little effect on diuretic function was to be expected, and in fact no diuresis was observed. In any case, if an undetected diuresis had occurred the haemoglobin would have been expected to rise from haemoconcentration. In fact, none of the cases showed a rise in haemoglobin. In Case 1 it fell slowly, as would have been expected after transfusion. Case 2 actually went into crisis during treatment with acetazolamide, the crisis coinciding with the onset of measles. In Case 3 the development of the crisis appeared to be in no way influenced by the acetazolamide.

As the criterion of efficacy for any treatment of sickle-cell anaemia rests ultimately on its ability to prevent or decrease haemolysis, it appears that acetazolamide has failed in this respect, and its value as a therapeutic measure is open to doubt.

REFERENCE

Hilkovitz, G. (1957). *Brit. med. J.*, **2**, 266.

INOCULATION RECORDING BY TATTOOING

BY

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With an increase in the immunization programmes of infants and children against many diseases the need for some method of indelibly recording the event in a readily available manner is receiving much attention. The use of cards for this purpose is by no means ideal, since they fairly rapidly become undecipherable if carried on the person and are often mislaid or discarded after a time. Dr. Parish (1959) has advised the use of engraved metal disks which would be carried on the person. These, however, although more permanent than the cards, are nevertheless subject to the disadvantage that they may be mislaid, and certainly in the course of time would very likely be discarded as a nuisance, perhaps when the information was most urgently required. Furthermore, the actual engraving would require special arrangements to be made in all hospitals and even in doctor's surgeries.

Importance of Tattooing

It must be recognized that both cards and disks allow a large amount of information to be recorded, not only of inoculations but also of other medical details. The importance, however, of having a permanently available record is not equal for all types of inoculation; for instance, whooping-cough and diphtheria are most likely to occur in the early years of life when any inoculations are still fresh in the memory of both doctor and parents, and there has been little time for card records to be mislaid or obliterated. In the case of tetanus, on the

FIG. 1.—The complete instrument.

other hand, the circumstances are different for three main reasons: (1) many years may have elapsed since the inoculation, which in any case, if performed in infancy, is outside the patient's memory; (2) the patient may be unconscious; and (3) it is routine practice in many hospital receiving-rooms to give A.T.S. for all types of injury, even minor ones, in which the skin is penetrated. In the case of tetanus inoculation, therefore, it is exceedingly important that the record should be really permanent and on the person of the individual; the only way of satisfying these requirements is by tattooing.

To overcome the difficulty which tattooing involves of recording several inoculations given simultaneously it

FIG. 2.—Component parts

would be possible to adopt some form of standardized coding recognizable by all concerned, whereby a single letter or design could be used to cover these several immunities. Even this would not overcome the difficulty of recording subsequent inoculations, and clearly the number of letters which might be tattooed is for aesthetic reasons limited. For the important tetanus inoculation, however, the single letter T would be sufficient. It has been suggested that to use tattooing for this purpose is facetious, but perhaps this is one of those facetiae which deserve serious attention, for, as will appear, the process can be done easily and instantaneously at the time of the inoculation.

The desirable characteristics of such a tattoo are that it must be obvious when looked for and yet not conspicuous, and this immediately raises the question of position, for the site should be standardized, hidden, and yet easily available for inspection. The lateral aspect of the great toe, the inside of the lip, under cover of the ear over the mastoid, over the hip just below the iliac crest have all been canvassed as possible sites, but the latter position seems on the whole the most suitable. Clearly, if the method is adopted the site and side of the mark would have to be established at a national or perhaps even international level.

The Tattooing Instrument

For performing the tattoo I have devised and made the instrument shown in the photographs. It is about the size of a fountain pen and is in effect a spring gun which on being released drives a "bullet" (g) having needle points arranged in the form of a letter T through

a paste of dye for a predetermined distance into the skin. The best dye for this purpose is ordinary commercial lamp black mixed to a paste with a little water and sterilized by heat. The "bullet" itself, the needle-points of which alone penetrate the skin, can be sterilized by boiling or chemically by immersion in "dettol" in spirit. A little of the paste is applied to the cleaned skin of the area; the "bullet" is inserted into the muzzle of the gun (a), where it is held by a light spring (b), and the plunger (f) is withdrawn to its full extent. The gun is now applied firmly to the skin and the trigger (c) pressed. The tattooing is instantaneous and practically painless. Depth of penetration (usually 2-3 mm.) is controlled by adjustment of the screwed cap (d) and depends upon the thickness of the skin at the selected site and on the age of the patient. Extra bullets (with other designs if necessary) can be accommodated in the hollow head of the plunger (e). I have found that needle-points prepared from stainless piano wire by grinding give a better tattoo than the very highly polished and smooth commercial article.

FIG. 3.—Enlarged view of "bullet."

The tattoo, of course, consists of a series of dots arranged in the form of a T; is easily identifiable but not conspicuous, and, like all tattoos, is permanent. It is probable that a tattoo performed in infancy will stretch with the growth of the child, but, although sufficient time has not elapsed to observe if this is so, it seems unlikely that it will be enough to render the mark unrecognizable.

For the photographs I am indebted to Miss Turnbull, of the photographic department, Charing Cross Hospital.

REFERENCE

Parish, H. J. (1959). *Brit. med. J.*, 1, 640.

Medical Memoranda

Further Evidence of the Association between Mercury and Pink Disease

Warkany and Hubbard (1953) have presented impressive evidence of the association between pink disease and mercury. They have examined this problem from many aspects and quote a total of 97 references in the world literature. Despite this a considerable amount of scepticism exists (Naish, 1955; Farquhar *et al.*, 1956), mainly because a number of cases occur in which there is no evidence of mercury ingestion as judged by the