The Committee established (or authorized) international standards or reference preparations for 26 different substances and 15 specific diagnostic antisera; a further 36 other substances are listed as proposed international preparations. The report condenses the information from some 940 pages of unpublished working documents considered by the Committee, and incorporates besides a full list of all existing international preparations. It is a valuable service to provide all this information together.

TRANSFUSION OF A FOETUS

The problems of haemolytic disease of the newborn due to incompatibility between maternal and foetal blood have been vigorously tackled in recent years. The introduction of exchange transfusion made such a change that kernicterus is now only rarely seen and haemolytic disease is less troublesome than formerly. But there remains a hard core of mothers who are strong producers of antibody and have husbands homozygous for the Rh factor. In these cases successive pregnancies almost inevitably lead to more and more severely affected infants and ultimately to foetal death *in utero* or abortion. It is this comparatively small group which is now attracting chief attention. The introduction of a safe method of obtaining a sample of liquor amnii for examination reported by D. C. A. Bevis,[1] and the subsequent follow-up of this work by A. H. C. Walker showing the importance of timing the paracentesis to between the thirty-second and thirty-fifth weeks, together with the wider use of serial estimations of antibody titre, have enabled obstetricians usually to make a reasoned evaluation of the degree to which the foetus is affected and to plan the time and method of delivery well in advance. The centralization of such cases in special units, where a team comprising obstetrician, paediatrician, and pathologist is constantly available and accustomed to the routine procedure, has helped greatly in lowering the mortality from haemolytic disease.

The search continues for a method of neutralizing the antibodies in the mother's blood, which would be the most logical way of preventing the disease, and the outcome is anxiously awaited. In the meantime it has become necessary to accept the fact that even very early delivery —for example, at 34 weeks—which usually necessitates caesarean section and certainly adds the hazards of prematurity and the risk of the hyperbilirubinaemia of prematurity to the danger of the haemolytic disease, will not save all affected babies. An ingenious and, in this instance, successful method of prolonging intrauterine life sufficiently to allow of the delivery of a viable infant is reported on page 1107 of the *Journal* this week by Dr. A. W. Liley, of Auckland, New Zealand. The procedures involved, however, bear so many hazards to mother and foetus that they can clearly have only a limited application. Even in the most skilled hands there are risks in amniocentesis, and these are sufficient to warrant limiting the number of times it is carried out in any individual case. The great value of Walker's work was in showing that, if the right gestation date was chosen, only one paracentesis was normally necessary. The case reported by Liley required several. The technical details are such that, though there must be occasions when the technique can save life, often it cannot be carried out because of anatomical difficulties. Furthermore, intraperitoneal transfusion is at best an inferior and unpredictable method of administering blood and, as Liley points out, cannot restore a foetus to normal. Nevertheless it is a remarkable achievement and one which calls for congratulations. It will also act as a spur to those whose present research is directed to finding a method of neutralizing the antibodies and so preventing the disease.

[1] Bevis, D. C. A., *J. Obstet. Gynac. Brit. Emp.*, 1956, **63**, 68.
[2] Walker, A. H. C., *Brit. med. J.*, 1957, **2**, 376.

MAPPING OF DISEASE

As a result of mapping the deaths from cholera in Soho in September, 1854, John Snow had the handle of the pump in Broad Street removed to stop the outbreak. Though Snow was far from being the first to use a map when studying the environmental causes of disease, the simplicity and effectiveness of his work set a striking example for later epidemiological research. Maps showing the distribution of cholera in London (1832), Leeds (1833), Exeter (1849), and the whole British Isles (1852) had preceded Snow's, and others were to follow. According to E. W. Gilbert,[1] who has published an interesting account of them, "the great outbreaks of cholera in the first half of the nineteenth century seem to have been the factor which first stimulated cartographic work of this kind"; and "the mapping of diseases began in England during those years, as did the mapping of the distribution of population."

Last week an important project was completed in the publication of a *National Atlas of Disease Mortality in the United Kingdom*.[2] It was prepared by Dr. G. Melvyn Howe from statistics published by the Registrars-General of the United Kingdom. The Royal Geographical Society sponsored its production through its Medical Geography Committee, which includes a number of distinguished medical men as well as geographers and had for its chairman Lord Nathan (who died last week). After preliminary maps showing the density of population in the United Kingdom there follow a series to illustrate the death rate (by means of the standard mortality ratio) for all causes of death, and then varieties of cancer, diseases of the cardiovascular system, of the respiratory system, of the digestive system, infant mortality, diabetes mellitus, accidents, and suicide. In addition to the maps, which are reproduced with admirable clarity, the author has provided an introduction and notes which will help in their interpretation. The reasons why death rates vary in different areas are apt to be exceedingly complex, especially when the cause as classified is a broad category such as "bronchitis" or "arteriolosclerotic heart disease, including coronary disease." But the atlas does admirably fulfil the author's aim of providing "the factual material on which future work may be based."

Perhaps the most remarkable instance in recent years of the value of mapping disease is to be seen in the studies carried out by E. T. Burkitt on the malignant lymphoma of children in Africa. The strict correlation of cases with certain limits of temperature and rainfall, and hence certain

[1] Gilbert, E. W., *Geograph. J.*, 1958, **124**, 172.
[2] Howe, G. M., *National Atlas of Disease Mortality in the United Kingdom*. London. Thomas Nelson and Sons. 1963. 35s. net.
[3] See *Brit. med. J.*, 1963, **1**, 1042.
[4] Stocks, P., in *Cancer*, ed. R. W. Raven, vol. 3, p. 154. London. 1958.
[5] Scott, E., *J. Coll. gen. Practit.*, 1960, **3**, 80.
[6] Payne, R. W., *Brit. med. J.*, 1961, **1**, 1809.

types of fauna and flora, has led to a search for a virus possibly carried by an insect vector subject to specified environmental restrictions.[3] Indeed the fact that many tropical diseases are transmitted by arthropodal or protozoal vectors has long made the mapping of cases a valuable part of aetiological studies. In Great Britain the geographical distribution of cases of cancer has excited interest, and Percy Stocks, among others, has published notable maps of it.[4] Likewise the incidence of pernicious anaemia has been effectively mapped,[5] as has a relationship between this disease and gastric cancer.[6] So long as the epidemiological study of diseases yields results will mapping be a part of it.

LINOLEIC ACID IN INFANT NUTRITION

The first half of this century saw a great surge of knowledge in the field of human nutrition. This included the diet of infants, and indeed the very safety and simplicity of artificial feeding contributed largely to the decline of breast-feeding throughout the Western world. However, the second half of the century is bringing with it an increasing realization that our knowledge of the dietary requirements during infancy is superficial. While we know the quantities and proportions of protein, fat, and carbohydrate which should go into a well-balanced diet, and something of the vitamin requirements, we are ignorant about the individual amino-acids and fatty acids. A practical example can be found in the nutritional problems which paediatricians have encountered during the long-term treatment of phenylketonuria with diets low in phenylalanine, one of the essential amino-acids.[1 2] It seems that a suboptimal intake of one essential amino-acid considerably distorts and increases the body's requirements for others. There is room for even more conjecture about the essential fatty acids and the possible consequences to the human organism when they are deficient.[3 4] Yet one of the important differences between human and cow's milk concerns the nature of the fat. The amount of linoleic acid, one of the essential fatty acids, is four to five times greater in human milk, and there is evidence that linoleic acid is an essential nutrient for infants.

The late A. E. Hansen and his colleagues[5] have recently reported the effects of feeding four groups, each of 100 infants, with four different milk preparations. Three contained variable amounts of linoleic acid in the same total amount of fat; the fourth contained only traces of linoleic acid. The results were striking. The most obvious clinical manifestation in the group fed a diet grossly deficient in linoleic acid was a persistently dry, scaly, and thickened skin. Another feature was perianal irritation. The growth rate of the linoleic-acid-deficient babies was also less than expected. When the diet was very low in linoleic acid the total fatty acids in the serum tended to be high, while the values for diene fatty acids were extremely low. On the other hand the level of trienoic acid in the serum varied inversely with that of the dienoic acid. The protein levels in the serum were uninfluenced by these variations in the intake of linoleic acid. Thus it is apparent that human infants do not thrive when given a diet deficient in linoleic acid. The surest method of providing a well-balanced diet is still breast-feeding.

[1] Report to the Medical Research Council of the Conference on Phenylketonuria, *Brit. med. J.*, 1963, 1, 1691.
[2] See also ibid., 1963, 1, 1686.
[3] James, A. T., and Lovelock, J. E., *Brit. med. Bull.*, 1958, 14, 262.
[4] Sinclair, H. M., *Lancet*, 1959, 1, 252.
[5] Hansen, A. E., Wiese, H. F., Boelsche, A. N., Haggard, M. E., Adam, D. J. D., and Davis, H., *Pediatrics*, 1963, 31, Suppl. No. 1, 171.

CATCH-UP GROWTH

A good gain in height and weight in a child is a sign of health. Conversely during periods of illness or undernourishment growth slows down. What happens to growth during recovery? A. Prader, J. M. Tanner, and G. A. von Harnack[1] noted acceleration of growth in five children during and after recovery, and they coin the term "catch-up" growth. As might have been expected, they found that during the catch-up phase gain in weight was accelerated more than gain in height and in one child exceeded four times the average rate for the chronological age. Yet acceleration of gain in height was also remarkable: a boy with hypothyroidism, on being given thyroid, gained in height at a rate four times the average for his age. In the other children gain in height exceeded the average for age by two to three times. Skeletal maturation also showed this catch-up phenomenon but to a lesser degree than did linear growth. When the boy with hypothyroidism was given thyroid, the bone age advanced at three times the expected rate, whereas in the other children it advanced at only twice this rate.

Children grow at the greatest rate during the first two years of life. Prader and his colleagues suggest that it is also during these early years that maximum velocity of growth can occur in the catch-up phase, and that ultimate adult stature is then unlikely to be significantly impaired. But when illness or malnutrition slows down growth during the later years of childhood, and especially during the years of puberty, compensatory growth during recovery may not be sufficient for the child to reach the adult stature he would otherwise have achieved.

One of their patients suffered from an adrenal tumour with Cushing's syndrome; the excess steroid secretion had stunted growth. At the age of 4 years the tumour was removed and catch-up growth was remarkable. This case provides indirect evidence for the view that the ultimate height reached by children treated with steroids before puberty is not significantly affected unless treatment has to be continued for more than a few years; only then need the use of a protein anabolizer be considered to counteract the action of cortisone in retarding growth.

This important study, which on the practical level is a reminder of the importance of regular and accurate determinations of children's weight and height, raises also theoretical questions of fundamental biological importance to which we do not yet know the answers. What are the mechanisms responsible for catch-up growth? Even more mysterious, why does the catch-up phase come to an end and growth slow down again to the normal rate for the child's age at the very time when the child has regained his original growth channel?

We record with regret the death on October 26 of Sir William Kelsey Fry, formerly dean of the Faculty of Dental Surgery of the Royal College of Surgeons.

[1] Prader, A., Tanner, J. M., and von Harnack, G. A., *J. Pediat.*, 1963, 62, 646.