cell count can be treated by the transfusion of leucocyte concentrates, barrier nursing, and the judicious use of antibiotics. It might appear a comparatively simple matter to maintain the red-cell count artificially, but in many species, including man, haemorrhages are very important in the genesis of the anaemia. Changes in various haemostatic mechanisms have been reported, but the most important factor is the decrease in the numbers of platelets.[10] The thrombocytopenia follows a decrease in the numbers of megakaryocytes, and this, it has been concluded, is in its turn due to a block in the cellular division of the stem cell preceding the megakaryoblast.[11 12] Simple transfusions of whole blood have been of little value in experimental animals, though concentrates of platelets were found to correct defects in haemostasis.[13-15] Recent work on the subject[16] suggests, however, that though fresh platelets will control post-irradiation haemorrhage in rats the more convenient preparation of lyophilized platelet material is of no use for this purpose. Preparations derived by a new method,[17] which dispenses with lyophilization and preserves the platelets intact, may possibly be of use in the treatment of radiation disease. The method is complicated and entails a new principle of "closed-system centrifugation" during which the platelets are freed from plasma proteins.[18] They are eventually stored in gelatin and will keep for many months. Such preparations have been used in cases of marrow aplasia and thrombocytopenia caused by cancer chemotherapy, a condition somewhat similar to radiation aplasia.[17]

Platelet transfusions can act only as replacement therapy; they cannot stimulate an aplastic marrow to produce more platelets. Consequently repeated transfusions are necessary for the whole of the period when a dangerous thrombocytopenia is present. It is also possible that other factors besides thrombocytopenia are important in the haemorrhagic diathesis. A heparin-like anticoagulant, at one time thought to be important, may now be discounted,[2] but possible defects in the endothelial lining of the capillaries cannot be ruled out. Evidence for increased permeability of capillaries has been found in man 24 hours after as little as 100 r of local irradiation,[19] and various capillary changes have been reported in rats well before the time when thrombocytopenia would be expected.[20] Curious intravascular globules, which appear to contain a polysaccharide, have been found in some animal experiments,[21 22] and the degree of haemorrhage in individual animals was correlated with the size and amount of these globules. It was suggested that this material, acting as emboli and inducing endothelial damage, might, in the presence of a thrombocytopenia, cause haemorrhages. But it does not seem likely that such material is important in all species, for while it was plentiful in dogs and swine it was rarely seen in guinea-pigs, even though all three species are equally liable to post-irradiation haemorrhage.

A ROYAL EVENT

Despite the crowds outside Buckingham Palace, the television cameras, and the newscasters' words crackling round the world, the Royal Birth was just as much a family crisis and, when all was safely over, an occasion for family rejoicing as the birth of a child in any other household. True, the crisis was not quite of the nature of the emergency when last a reigning monarch gave birth to a baby. Then, so the *British Medical Journal* of April 15, 1857, informs us, Queen Victoria "was taken so suddenly with the pains of labour that a common hackney cab had to be despatched for Dr. Locock." Things were managed better in 1960, and for the Queen's medical attendants—Mr. J. H. Peel, Dr. V. F. Hall, Sir John Weir, and Lord Evans—there were no such undignified journeys as Dr. Locock had to suffer.

With the birth of the new Prince the Royal Family is strengthened not only in numbers but in all sorts of ways which may be intangible but which a strongly knit family can always make manifest. We can assure our Patron, the Queen, and our President, Prince Philip, Duke of Edinburgh, that this very happy Royal event will be a cause of great rejoicing among members of the British Medical Association.

GENETIC CLUES TO HISTORY

Soon after it had been shown that the blood groups are inherited as simple Mendelian characters, L. and H. Hirschfeld[1] observed in Salonika, where soldiers of the first world war and refugees from many parts of the world had been congregating, that different nations and different races showed different frequencies of the ABO genes. The B group is now known to be most frequent in India and in Central Asia, and the further people live from these parts the lower will be the frequency of the B gene. Thus in Europe the Basques have the lowest frequency of the B gene and the Russians the highest.[2 3] The MN system shows differences in gene frequencies in the Pacific area, where the ratio M to N is about 1 in the Chinese and Japanese, well above 1 in the American Indians, and well below in the Melanesians, Micronesians, and Australian aborigines.[3 4] Likewise Rhesus gene combinations are

variously distributed,[3 5-7] and the relatively high frequency of Rh-negative among the Brahmins in India, for instance, serves to emphasize their relationship with Europeans.[8]

The anthropological value of these characters depends much on whether they are stable from one generation to the next. Until recently the ABO blood groups were considered to be "neutral" characters—neutral, that is, in relation to the probability of their perpetuation from parent to child and, as such, anthropological markers *par excellence*. However, in 1953 I. Aird, H. H. Bentall, and J. A. Fraser Roberts[9] showed that the incidence of cancer of the stomach was greater in persons of blood-group A than in those of Group O. It is now known that the incidence of duodenal ulcer is about 40% higher in persons of blood-group O than in those belonging to groups A. B, and AB. Many other conditions have been investigated, and perhaps the most interesting association is that between pernicious anaemia and blood-group A.

In 1954 A. E. Mourant, director of the Medical Research Council's Blood Group Reference Laboratory, published his encyclopaedic survey of the distribution of the human blood groups.[3] He stressed that for practical purposes two classes of characters should be distinguished, those like the MN groups and, surprisingly, the Rhesus groups, which are fairly uniform over large areas and therefore seem to be stable systems suitable for tracing distant anthropological history, and those like the ABO groups, which show considerable differences even within otherwise uniform populations and can therefore possibly be used to trace relatively recent anthropological events. Even in Britain the ABO frequencies vary considerably. Their distribution reflects the Danish and Anglo-Saxon influence south and east, and the predominance of early British (or "Celtic") blood north and west. H. J. Fleure has remarked that the higher O incidence in the Glasgow area than in the rest of Scotland may be due to the many urbanized Highlanders there (from the West Highlands) and West Irish.[10] On the other hand a high A incidence in the region of Furness would reflect the many links with the Dano-Norse city of Dublin. Blood-group A is still very frequent in north-west Germany, Schleswig-Holstein, and Frisia, from where the Anglo-Saxons came. The frequencies of group A in Great Britain are expected to be higher where the Anglo-Saxons came with their wives as settlers rather than as military conquerors, because villages founded by them would be to a great extent endogamous. Very early cemeteries indicate the existence of such villages in the East Riding of Yorkshire, Norfolk, Cambridgeshire, north Northamptonshire, and Leicestershire, where the frequency of A is in fact high.[10] For the Solent and Hampshire, on the other hand, there are many indications of warlike invasion and struggle. Warrior bands would predominantly be male and take native girls; this might explain the stronger persistence of the O group in those parts of England.

Mourant's book, despite its completeness otherwise, did not tabulate the vast mass of data to be derived from the transfusion services. Now, under the auspices of the Nuffield Blood Group Centre, which is administered by the Royal Anthropological Institute, Mourant, Kopec, and Domaniewska-Sobczak have published exhaustive tables of all known ABO data and up-to-date maps of their distribution.[11] This monumental work surveys the outcome of just under 6 million blood-group estimations. It is a veritable treasure-house of information, of immense value for research.

Though a gene devoid of adaptive value may be an illusion, there is no need to assume that the ABO blood-groups have therefore lost their interest for the anthropologist.[12] While it is true that deductions covering very long periods will have to be made with caution, it is still possible to use the ABO groups in terms of human history over 2,000–3,000 years (rather than 20,000 years). The blood groups of old human remains have been determined since 1934, when W. G. and L. G. Boyd[13] first tested tissues from American and Egyptian mummies. Later, tests were carried out on ground bone.[14] A fascinating report of a Ciba Foundation Symposium[15] shows how the investigation of blood-group frequencies in certain areas of present-day Italy, combined with a knowledge of the distribution of blood groups in ancient times, may help to show where the Etruscans originally came from. In an Appendix K. Oakley and Madeleine Smith state the requirements of the British Museum (Natural History) for determining the blood groups in human bones from current and future excavations at Etruscan and Roman sites.

[1] Hirschfeld, L., and Hirschfeld, H., *Lancet*, 1919, 2, 675.
[2] Boyd, W. C., *Tabul. biol. ('s-Grav.)*, 1939, 17, 113.
[3] Mourant, A. E., *The Distribution of the Human Blood Groups*, 1954, Oxford.
[4] Birdsell, J. B., and Boyd, W. C., *Amer. J. phys. Anthrop.*, 1940, 27, 69
[5] Wiener, A. S., Sonn, E. B., and Belkin, R. B., *Proc. Soc. exp. Biol.*, 1943, 54, 238.
[6] Etcheverry, M. A., *Dia méd.*, 1945, 17, 1237.
[7] Mourant, A. E., *Nature (Lond.)*, 1947, 160, 505.
[8] Sanghvi, L. D., and Khanolkar, V. R., *Ann. Eugen. (Lond.)*, 1950–51, 15, 52.
[9] Aird, I., Bentall, H. H., and Roberts, J. A. F., *Brit. med. J.*, 1953, 1, 799.
[10] Fleure, H. J., in Kopec, A., *Advanc. Sci.*, 1956, 51, 200.
[11] Mourant, A. E., Kopec, A. C., and Domaniewska-Sobczak, K., *The ABO Blood Groups*, 1958. Oxford. (Blackwell Scientific Publications, 42s.).
[12] Roberts, J. A. F., *J. roy. anthrop. Inst.*, 1958, 88, 115.
[13] Boyd, W. G., and Boyd, L. G., *Proc. Soc. exp. Biol.*, 1934, 31, 671.
[14] Candela, P. B., *Amer. J. phys. Anthrop.*, 1936, 21, 429.
[15] *Ciba Foundation Symposium on Medical Biology and Etruscan Origins*, ed. G. E. W. Wolstenholme, and C. M. O'Connor, 1958, London (J. & A. Churchill, 45s.).

TRIAL OF LIVE POLIOMYELITIS VACCINE

The evidence is mounting that oral poliomyelitis vaccine may give a stronger and more lasting immunity than vaccines of the Salk type. Some months ago we published the results of the important Singapore trial[1] of Sabin's Type II vaccines, and a few weeks ago we reviewed[2] recent reports from other parts of the world. Now, as the Minister of Health announced in Parliament last week, the Medical Research Council is to

[1] Hale, J. H., Doraisingham, M., Kanagaratnam, K., Lee, L. H., Leong, K. W., and Monteiro, E. S., *Brit. med. J.*, 1959, 1, 1541.
[2] Ibid., 1959, 2, 624.

carry out small-scale trials of the Sabin vaccine in selected areas of Britain.

In the absence of epidemics of poliomyelitis, the only way of assessing the degree of protection given by a vaccine is to estimate the neutralizing antibodies in the serum and to find out whether or not the attenuated viruses of which the vaccines are made establish themselves in the intestine. Even the proposed small trials will therefore necessitate much laboratory work, and probably not more than 300 or 400 children will take part in this investigation. With the advice of the family doctors concerned medical officers of health of the areas where the trials are to take place will select the children, in groups of 20 or so, from among those whose parents agree to their receiving the vaccine. The children will be 6–9 months of age and, of course, they will not have already received any injections of Salk vaccine. Some parents may not feel inclined to agree to their children entering this trial, and others will probably wish to obtain the views of their family doctor before agreeing. Since the trial is designed to find out the best system of dosage of oral vaccines against poliomyelitis no guarantee can be given that the dose of vaccine taken by any particular child will produce a lasting immunity, but it will be helpful for parents to know that the Sabin vaccine which is to be used has already been widely tested and found to be safe and convenient. Further essential information about the vaccine can be obtained only by carefully conducted trials such as that now to be undertaken by the Medical Research Council.

ALCOHOLIC CARDIOMYOPATHY

Excessive consumption of alcohol may result in myocardial disease.[1-3] The clinical manifestations may vary from the type of cardiac failure with higher than normal output found in beriberi heart disease, which responds to thiamine, to the low-output type of cardiac failure associated with hypertrophy and fibrosis of the myocardium and not or scarcely responding to thiamine.[4-6] It is the latter type that is more commonly seen in the Western Hemisphere and may easily be overlooked, because clinically it resembles other forms of cardiomyopathy or coronary arterial disease.

W. Brigden[5] in 1957 described 13 cases of heart disease in patients who were heavy drinkers and had no other apparent cause for the myocardial failure. The patients' ages ranged from 41 to 69; all but one were men; seven drank nothing but beer, with an average consumption of 10 pints (5.7 l.) a day for 10 to 40 years. The six other patients drank one or more bottles of spirits a day for 10 to 20 years. Symptoms and signs appeared earlier and were more severe in those who drank spirits. Nutrition was uniformly good and it was often difficult to elicit the true history of alcoholic habits. All presented with dyspnoea on exertion, and in several this was accompanied by palpitation. None had chest pain or syncope. Cardiac failure soon appeared after the onset of symptoms, with generalized enlargement of the heart. Tachycardia was usual and irregularity from extrasystoles or atrial fibrillation common. The pulse tended to be small, without evidence of hypertension. Triple rhythm associated with myocardial failure was common. The electrocardiogram confirmed the arrhythmia due to atrial fibrillation in five cases. In sinus rhythm the P waves tended to show slight right atrial preponderance. The QRS–T complexes showed various degrees of myocardial damage. The T wave was often small and inverted in the left chest leads, and left bundle-branch block developed in four cases. Radiography showed from slight to gross cardiomegaly. The myocardium at necropsy showed the presence of small patches of fibrosis in the left ventricle with, in one case, a recent small area of necrosis in the base of the papillary muscle, with overlying mural thrombus. There was no evidence of coronary arterial disease.

More recently W. Evans[7] has described 20 patients who had been assembled because of bizarre symptoms and signs and an abnormal electrocardiogram, and before a history of alcoholism had been obtained. The clinical features were similar to those described by Brigden, except that chest pain occurred in six, though it was not typical of that associated with coronary arterial disease in its site, character, or response to either exercise or rest. In 17 of the 20 patients the electrocardiogram showed changes confined to the T wave. Evans divides these into three groups—the "dimple" T wave, the "cloven" T wave, and the "spinous" T wave—and considers they are characteristic of alcoholic cardiomyopathy. Other abnormalities of the electrocardiogram included auricular fibrillation, extrasystoles, paroxysmal tachycardia, transient bundle-branch block, and depression of the S–T segment. Abstinence from alcohol in some cases was associated with a change of the electrocardiogram towards a normal pattern.

In Brigden's series, the results of treating patients in established heart failure with digitalis and diuretics was moderately good at first, and there was little, if any, difference in the response of patients who received large doses of thiamine and those who had none. Repeated attacks of myocardial failure showed a progressively diminishing response to therapy. The duration of symptoms was from two and a half to five years, and five out of the 13 patients died.

The myocardium, like the liver, appears to be vulnerable to a high intake of alcohol over a long period of time, and this beverage should be considered as a possible aetiological factor in a patient who presents with cardiomegaly and heart failure or an electrocardiogram with abnormal T waves and in whom there is no obvious cause for these abnormalities. In early cases total abstinence may possibly halt or reverse the disease.

[1] Mackenzie, J., *Diseases of the Heart*, 1908, London.
[2] Sansom, A. E., *Diseases of the Heart and Thoracic Aorta*, 1892, London.
[3] Steell, G., *Textbook on Diseases of the Heart*, 1906, Manchester.
[4] Benchimol, A. B., and Schlesinger P., *Amer. Heart J.*, 1953, **46**, 245.
[5] Brigden, W., *Lancet*, 1957, **2**, 1179 and 1243.
[6] Weiss, S., and Wilkins, R. W., *Ann. intern. Med.*, 1937, **11**, 104.
[7] Evans, W., *Brit. Heart J.*, 1959, **21**, 445.

PARALYSIS IN MOROCCO

Reliable information is now available about the recent distressing outbreak of poisoning in Morocco, which afflicted about 10,000 of its inhabitants late last summer. According to an account of the epidemic by H. V. Smith and J. M. K. Spalding[1] the toxic agent was *ortho*-cresyl phosphate, a substance which is used in aeroplane engine oils to prevent the deleterious effects of great heat, such as the formation of deposits on valve stems and sparking-plugs. Apparently unwanted stocks of oil containing the *o*-cresyl phosphate found their way, through the agency of mistaken or unscrupulous merchants, into oil which was sold as cooking fat. The consumers of such fat soon developed paralysis in the legs, and later the hands were often affected. The condition was not fatal, and the symptoms were sometimes mild. Recovery was slow, and it is feared that in some cases the injuries may be permanent.

Besides its inclusion in lubricants *o*-cresyl phosphate is used for various other purposes, including the manufacture of plastics. Outbreaks of poisoning have been frequent and well authenticated, early ones occurring in many parts of the U.S.A. in 1930. On that occasion the paralysis appeared in thousands of consumers of certain brands of Jamaica ginger extract, which were adulterated with tri-cresyl phosphate.[2] The ginger extract was used as a source of alcohol, either neat or diluted with soft drinks, or as a cure for dyspepsia. From the evil effect of one well-known beverage called "Ginger Jake" the name "Jake" paralysis was applied. It is remarkable that after a lapse of 30 years "Jake" should have turned up in such a different disguise to claim a fresh batch of victims. Three cases of accidental poisoning in industry were reported in Great Britain in 1944.[3]

Research into the mode of action of *o*-cresyl phosphate has indicated that it causes injury to the myelin sheath, but the specificity of this lesion is doubted.[4] Some animals, such as the calf and mature hen, are vulnerable, but others, such as the rabbit and young chicken, are very resistant. The commercial substance, generally described as tri-*ortho*-cresyl phosphate, is never pure, and the impurities may be even more toxic than the pure substance. It has been suggested that the toxicity is due to interference with the action of the enzyme pseudocholinesterase. Tests on a wide range of substances, however, have shown that neurotoxicity and enzyme inhibition do not always run parallel.[5] Another theory is that tri-*o*-cresyl phosphate may antagonize the action of vitamin E. Thus the paralysis seen after dosing lambs with the poison is superficially similar to "stiff-lamb disease," a manifestation of vitamin-E deficiency seen in the field.[6] Dosing lambs with vitamin E, however, will not cure them, or even completely protect them, from the injurious effects of tri-*o*-cresyl phosphate. Though the exact mechanism of the injury to the nerves remains uncertain, it is clear that many derivatives of cresol are poisonous, and that they may obtain access to the body, either orally or through the skin, in very different vehicles. People who use them commercially have a great responsibility that their products do not endanger the public.

[1] Smith, H. V., and Spalding, J. M. K., *Lancet*, 1959, **2**, 1019.
[2] Burley, B. T., *J. Amer. med. Ass.*, 1932, **98**, 298.
[3] Hunter, D., Perry, K. M. A., and Evans, R. B., *Brit. J. industr. Med.*, 1944, **1**, 227.
[4] Cavanagh, J. B., *Lancet*, 1959, **2**, 1188.
[5] Susser, M., and Stein, Z., ibid., 1959, **2**, 1089.
[6] Draper, H. H., James, M. F., and Johnson, B. C., *J. Nutrit.*, 1952, **47**, 583.

PEANUTS AND HAEMOPHILIA

Severely affected haemophilic patients often note that episodes of spontaneous bleeding come in cycles. A severe haemarthrosis may be accompanied, or rapidly followed, by spontaneous bruising or haematuria. Several joints may be affected at any one time. In intervening periods the patient may be very well and even withstand minor trauma which would cause bleeding at a less favourable time. In the laboratory no known haemostatic test is altered in the good or bad phases.

Thus a claim for clinical effectiveness of any substance in haemophilic patients is difficult to substantiate. The patient may take the material in a "good" phase or at the end of a "bad" phase and claim much relief, while if he had taken the material at another time he might have formed a less optimistic view. Moreover, patients with chronic incapacitating diseases tend to feel relief from new treatment, but the relief is not always so apparent to the objective eye of their medical advisers.

These difficulties should not prevent the careful investigation of a substance thought to be effective in the treatment of haemophilia. Such a claim has been made by H. B. Boudreaux and V. L. Frampton[1] for the use of peanut derivatives taken by mouth. One of the authors is himself a haemophiliac, and he has found that the ingestion of peanuts or peanut flour has aborted attacks of haemarthrosis and when taken continuously has prevented their occurrence. The material has been tried on three other volunteers, with similar results. Eating peanuts does not affect laboratory results on the patient's blood, and the effective substance is not in the fatty part of the peanut but in the residual meal obtained after extraction with hexane.

Ingestion of the material does not correct the haemophilic clotting defect, but if it reduces the incidence of spontaneous bleeding it would do much to alleviate the lives of severely affected patients. It is to be expected that many haemophilic patients will try this simple treatment, and they would be well advised to do so with the co-operation of their medical advisers and of the Haemophilia Society. In this way an objective record of episodes of bleeding can be kept, accurate descriptions of the type and amount of peanut product used can be available, and the records of all the patients' experiences can be pooled and assessed.

An article on the Royal Commission's Report appears in this week's *Supplement*.

[1] Boudreaux, H. B., and Frampton, V. L., *Nature (Lond.)*, 1960, **185**, 469.