THE ROCKEFELLER FOUNDATION

BESIDES discussing some major innovations in the Foundation's programme in 1962, the President's Review of the Rockefeller Foundation, 1962*, notes some features of the current and operating programmes. In medical education substantial grants were made in 1962 to the medical schools of the University of Minas Gerais in Brazil and of the University of Cuyo in Argentina to assist in the establishment of a pre-medical curriculum and strengthen research and teaching. The University of Khartoum was assisted in reorganizing its Department of Physiology and the King George's Medical School, University of Lucknow, the development of its Department of Pharmacology, while the Medical Training Centre of the Ministry of Health and Labour of Tanganyika received a grant towards a new training programme for rural physicians. Help was also given to the Departments of Preventive Medicine and Pædiatrics, Makerere University College, in developing a field research and training centre in preventive medicine at Kasangati, to the Institute of Child Health of the University of Ibadan, and to the All-India Institute of Medical Science, New Delhi, in developing a teaching and research unit in rural medicine.

In the humanities and social sciences a current grant is helping the International Press Institute, Zurich, to promote more effective use of the daily newspaper press in the countries of south and south-east Asia, and the Educational Broadcasting Corporation, New York, was assisted in the initial operation of an educational television channel. Among research projects supported in the field of land economics, one at the University of Arizona, Tucson, relates the availability of water to social and economic growth in an arid environment, and programmes in agricultural economics are being supported at the Catholic University of Chili, Santiago. In agricultural sciences, on June 30, 1962, 236 students from 28 countries held Foundation scholarships or fellowships for M.Sc. or Ph.D. courses at 40 different universities in the United States and Europe. Continued support was given to an orientation programme for foreign students entering graduate schools of agriculture in the United States; the Texas Agricultural and Mechanical College System received a grant for studies with a mechanical device for measuring the nutritive value of forage crops during the digestive process in ruminants; and the University of Arizona a grant for investigation of the economic use of scarce water supplies, while establishment of an animal nutrition research centre at Nova Odessa, São Paulo, Brazil, was also assisted.

For virus work in 1963 and its operating programme in the general development of professional education the Foundation appropriated some 1·5 million dollars, and the Review outlines the work which led to the discovery of the new virus, oropouche, and the investigation of arboviruses. For co-operative projects in agricultural sciences in five countries, the Foundation has appropriated more than 2·6 million dollars in 1963 in addition to 515,000 dollars for the International Rice Research Institute. These projects include the Mexican Agricultural Programme, now in its twentieth year, and similar projects in Colombia, at first concentrated on corn, wheat, potatoes and beans, but now yielding results from livestock research of great value in improving beef and dairy cattle, poultry, sheep and swine, Chile (concentrated on wheat and forage legumes and grasses), and India, where hybrid maize varieties adapted to all the major agricultural regions have been developed.

During 1962, 723 persons from 58 countries held Foundation fellowships and scholarships, of which 265 were new awards; of the total, 298 were in agricultural sciences and 231 in medical and natural sciences; 3·2 million dollars were appropriated for these activities.

* The Rockefeller Foundation. President's Review, 1962. Pp. v+87. (New York: The Rockefeller Foundation, 1962.) See also p. 97 of this issue of *Nature*.

CONGENITAL ABNORMALITIES

THE decreasing rate for infant mortality in Great Britain and other parts of the world is bringing greater interest to bear on congenital abnormalities, which, apart from the effects on the children, cause so much distress to their parents. The greater part of the August issue of *The Practitioner*[1] is taken up with a symposium on the subject.

As C. O. Carter points out, it was not until 1956 that new cytological techniques confirmed that human beings have a normal complement of 46 chromosomes. Non-disjunction may result in gametes being produced possessing 22 or 24 chromosomes. Other abnormalities arise through fragmentations, with parts of separate chromosomes coming together in irregular ways, the remaining bits becoming lost. About 2 per thousand babies are trisomic for the sex chromosomes, of the patterns *XXX*, *XXY*, and *XYY*. Some of these arrangements produce no obvious defect, but all *XXY* persons suffer from Klinefelter's syndrome, with a eunuchoid body build and azoospermic testes. In contrast to these, *XO* individuals exhibit Turner's syndrome, with dwarfism and abnormalities of the heart and kidneys. About 2 per thousand babies are either trisomic for autosomes such as *G*21, *E*18, and *D*15, or they may have a compound of chromosomes *D*15 and *G*21, from which other parts may be lost. All these are held to be suffering from Down's syndrome, exhibiting a great variety of derangements, such as deafness, polydactyly and mosaicism. As Carter suggests, these findings provide some limited scope for genetic counselling.

The most familiar case of abnormality associated with a chromosome derangement is that of the infant mongol. This is discussed by A. J. Keay. The affected children have 47 chromosomes, probably through the trisomy of *G*21. The clinical signs are easily recognized, and the intelligence quotients of the affected children range from about 25 to 68. These children are cheerful and responsive to affection; they all should be given some chance of responding to educational care. The risk of producing a mongoloid child depends on the age of the mother, amounting to about 1 in 1,000 for young women and rising to around 1 in 50 for those of more than 40 years.

The existence of inborn errors of metabolism inherited on a Mendelian basis was first noticed by Fölling in 1934. That was a case of phenylketonuria. The frequency of incidence is about 1 in 30,000, and the disease is now known to be due to a recessive gene which leads to an inability to metabolize phenylalanine properly, and the affected children show hypertonicity of the muscles and are on the verge of imbecility. They respond favourably to a diet low in phenylalanine if it is started sufficiently early. This and other inborn errors of metabolism are described by A. Goldberg. They include alkaptonuria, non-endemic familial cretinism with goitre, some forms

of diabetes, galactosæmia, glycogen deposition disease, and many other abnormalities concerned with the metabolism of adrenal steroids, purines, metals, lipids, hæmoglobin and the clotting of blood, porphyrins, bile pigments and renal tubular transport. In most cases the abnormalities are the result of enzyme irregularities dependent on recessive genes. As Goldberg remarks, it would seem that no metabolic pathway is exempt from the occasional, and sometimes not so occasional, genetically expressed deviation.

In their paper on congenital abnormalities of the limbs, J. I. P. James and D. W. Lamb show that these may take many forms: the absence of a hand, arm or fibula, for example, extra digits, syndactyly, 'club foot', etc., along with an extensive list of less-serious defects. Some of them appear to be the result of chromosome derangements, others are known to be produced by agents of external origin; while congenital dislocation of the hip is now thought to be brought about by maternal hormones, especially relaxin. Clubbed feet and related defects can be improved by gentle manipulation and strapping at an early age; a number of other abnormalities call for surgical treatment; but great care should be taken not to remove stumps of limbs which can be made use of in prosthetic replacement, with which, if in a simple form, the child should be allowed to grow familiar as soon as possible.

A. D. M. Jackson deals with congenital abnormalities brought about by agents of external origin, of which the most general are infections. Leaving aside infections gaining entry at the act of birth, like gonococcal ophthalmia, and those passed on from mother to fœtus at a late stage in pregnancy, like chickenpox and Coxsackie *B* virus disease, Jackson draws on the investigation initiated by the Ministry of Health and General Register Office, in 1950, and a still larger one in Sweden. These investigations show that the most serious abnormalities are due to infections of rubella during the first three months of pregnancy. The effects are seen in higher rates than normal for abortions and stillbirths, low birth weight, cataract, heart defects, and deafness. The risk that a child will be born with some affliction is about 30 per cent, with deafness as the commonest; deafness appears to be the only serious handicap if the mother becomes infected at later stages in pregnancy. To avoid these defects the mother should be immunized against rubella before marriage; even passive immunization within a few days of exposure may be of some help.

The British investigation also covered the risk of abnormalities produced by other infections, such as measles, poliomyelitis and influenza, but no clear association between infection and abnormality could be established.

Among the congenital defects produced by external agents of an artificial kind, the tragedy of the thalidomide episode has directed attention to those resulting from drug treatment. J. M. Robson deals with these. Thalidomide itself is a mild sedative; even in large doses it produces scarcely any toxic effect on man and animals. Why it should exert such a drastic influence on the fœtus is a question which still remains obscure. There are other drugs, like sodium salicylate and nicotine, in wide clinical use which have not yet been shown to be teratogenic in man although in high doses they have serious effects on the fœtuses of experimental animals. A number of other drugs seem to act in much the same way. The action on man of 5-hydroxytryptamine still awaits elucidation; it is naturally present in the body, but in large doses it produces many malformations in animals, probably because of its interference with placental function. Robson recommends that in introducing new drugs for clinical use great caution should be exercised over those which are teratogenic in experimental animals, particularly if there is a wide discrepancy between the dose which has a harmful effect on the fœtus and that which is toxic to the mother.

The remaining paper in the symposium, by J. W. Millen, is on the effects of radiation. He refers to the large amount of work which has been done on experimental animals: many congenital abnormalities have been produced, affecting every organ system, and depending on the time, intensity and nature of the radiations, together with the stage in pregnancy. Experiences with therapeutic irradiation have shown that similar defects can be produced in man. The effect appears to be directly on the fœtus, not mediated by the mother. Surveys of the results of the atomic bombs exploded in Japan have reported many cases of microcephaly, which is the only defect that can be linked directly with the intensity of exposure; but other effects may have been masked by fœtal deaths. So far there is no convincing evidence that mutations can be produced by irradiation in man; and the risk of harmful mutations being caused by the background radiation of present-day living would seem not to be serious.

R. WEATHERALL

[1] *The Practitioner*, **191**, No. 1142 (August, 1963).

WORLD DIRECTORY OF VETERINARY SCHOOLS

A *World Directory of Veterinary Schools** has recently been published by the World Health Organization, Geneva, under the auspices of the Food and Agriculture Organization of the United Nations and the World Health Organization. There has, in the past, been no available source of information about veterinary schools as a whole, and the *Directory* will be of great use to all those concerned with veterinary science.

During the past decade and a half there have been great changes and extensions in veterinary schools. The end of the Second World War led to considerable changes in certain European countries; in some instances the changes were merely the result of opportunity after hostilities had ended and there was return to normal life, a matter merely of delay. Altered frontiers and other political matters resulted in changes. The achievement of self-government in certain former British territories and in those of other European powers has been an important cause of development. Whereas there were 6 schools prior to 1947 in India there are now 16. Pakistan has 2.

The details for each country are set out according to a standard plan under the same sets of headings, beginning with tables showing the population of the country, the numbers of livestock and details of veterinary activity. In the case of each country a table is given of the veterinary schools, date of foundation, numbers of teaching staff, total enrolment and tuition fees. Information is given for each country concerning administration, conditions of admission, curriculum and examinations.

Scrutiny of the *Directory* shows extraordinary disparity in the numbers of graduates, the numbers of veterinary schools and the numbers of livestock in a country. It is of interest to compare essential figures given for livestock populations and the numbers of veterinarians. The figures for the United Kingdom concern only the numbers resident in the country, and about 1,800 of the graduates are resident overseas. A defect in the quotations of essential figures given in the first table for each country is that there has been some or even considerable delay in

* *World Directory of Veterinary Schools*, 1963. (Published under the auspices of the Food and Agriculture Organization of the United Nations and the World Health Organization.) Pp. 216. 16 Sw. francs; 26*s*. 8*d*.; 5..25 dollars.