

attempt to use the whole population. If, in addition, there are people willing to participate, then one has a 'living laboratory'. With a female population of 20,000 over 20 years of age yielding four or five epidermoid cancers of the cervix uteri annually, it is possible to screen by the cervical smear technique in a few years the 17,000 women between 20 and 70 years of age, and note the effect on the annual incidence of cervical carcinomas. Once the facilities for taking and examining the smears are provided it is necessary to persuade the women to come. The cancer educationalists' propaganda, using the mass media and lectures to women's organizations, forms a useful background. Only by working through their general practitioners is it possible, however, to persuade the bulk of the women to attend for the taking of the smears. In order to get the general practitioners' cooperation, it is necessary to give evidence of the value of the screening.

#### Some Aspects of Medical Genetics in Island Populations

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The study of island populations is of considerable potential interest for the investigation of genetic problems. There may be an increase in consanguineous marriages but popular guesses as to the extent to which breeding groups on an island are closed are often wrong, and this can be checked against parish register material. Furthermore, as was found in Japan, inbreeding may not necessarily be deleterious. The pattern of congenital malformations may be different from that of the mainland and a register of these should be kept, as among other things this is a useful stimulator not only of further research but also of better social care. Again, because of genetic drift, whereby chance exercises a considerable influence on gene frequencies, blood group distributions may be unusual and unfavourable mutations persist in isolated communities. These factors will be discussed in relation to the Isle of Man.

#### Genetics Survey of the Manx

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In recent years physical anthropologists and human biologists have carried out numerous surveys of the genetical characteristics of populations. In such a context this paper is a preliminary report on a study

of genetic variability in the Manx population. Included in the survey were those individuals having three or four grandparents born on the Isle of Man. Results are given for the following unifactorial traits: most of the blood group antigenic systems, including ABO, Rhesus, Kell, Duffy, Lu<sup>a</sup>, and Kp<sup>a</sup>, the red blood cell isoenzyme acid phosphatase, and the plasma proteins haptoglobin and transferrin. Non-serological inherited factors such as phenylthiocarbamide testing are also reported upon.

For some of the serological factors comparisons were made between blood donor and non-blood donor samples. Moreover the incidence of the genetic features was compared with those found in contiguous areas of Britain, particularly south west Scotland and Cumberland.

Mention is made of previous anthropological studies of the Island's population and their main findings. All previous work was of an anthropometric rather than serological nature. One aim of the present work is to discover whether genetic factors complement the variability in the Manx population found in the previous studies.

A very brief account of the main periods occurring in the Island's history is given because of its possible use in helping to interpret the results of the present survey.

#### Erythroblastosis Foetalis

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Erythroblastosis foetalis (haemolytic disease of the newborn) is an important, if decreasing cause, of perinatal death. Results obtained during the perinatal mortality survey (1958) (Claireaux, 1963) showed that it was responsible for 4.0% of all perinatal deaths and the incidence was 1.4 per 1,000 live and stillbirths. The final results of a similar study, British births (1970), are not yet available but preliminary evaluation of postmortem material shows that it is still a factor in perinatal death but the incidence is probably lower than in 1958.

Erythroblastosis foetalis was a term coined in 1933 to include the three main types of the disease: (a) hydrops foetalis; (b) icterus gravis neonatorum; (c) congenital haemolytic anaemia. This last is not to be confused with congenital spherocytosis. Hydrops foetalis was the most severe form of the disease and usually

resulted in a stillbirth or in the delivery of a moribund infant. Icterus gravis was, if untreated, also likely to have a fatal termination and the infant succumbed as a result of brain damage (kernicterus). The remaining cases, much less severe and seldom fatal, were clinically regarded as examples of haemolytic anaemia. The clinical features of the disease and the pathological changes in fatal cases were known some considerable time before the discovery of the Rhesus blood groups (1940). It was only then that it became clear the condition resulted from iso-immunization of the mother by a blood group she did not possess.

#### Reference

Claireaux, A. E. (1963). In *Modern Trends in Obstetrics*, ed. R. J. Kellar, p. 191. Butterworths, London.

#### The Role of RH Antibodies in Causing Haemolytic Disease of the Newborn and in Preventing It

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#### HAEMOLYTIC DISEASE OF THE NEWBORN

The relation between the amount of anti-Rh on the red cells of an Rh-positive infant and the severity of the haemolytic process is not very close; one reason may be the varying ability of different examples of anti-Rh to bring about red cell destruction.

In haemolytic disease of the newborn, the concentration of anti-Rh in the plasma of the Rh-positive infant is always very much lower than that in the mother's plasma, emphasizing that the relatively slow transfer of IgG across the placenta plays a crucial role in mitigating the severity of the damage. Because of this slow transfer, it is quite safe to give injections of the order of 200 µg anti-Rh to Rh-negative women who are pregnant with an Rh-positive foetus. Incidentally, even if such a dose is accidentally injected into a newborn Rh-positive infant, it causes only very mild haemolytic disease.

#### PRIMARY RH IMMUNIZATION

A single injection of Rh-positive red cells induces primary immunization in about 65% of Rh-negative subjects. With a relatively large dose (200 ml cells), anti-Rh is as a rule readily detectable three to six

months after the injection. After a single small dose of cells, anti-Rh can usually not be detected serologically, but its presence is indicated by the diminished survival of a second dose of Rh-positive red cells, followed by the appearance of readily detectable antibody.

There is evidence that the minimum effective dose for primary Rh immunization is less than 0.1 ml of red cells; if so, more than 20% of Rh-negative women receive an adequate primary stimulus during a pregnancy with an Rh-positive foetus.

#### SUPPRESSION OF PRIMARY RH IMMUNIZATION

Recent work suggests that with doses of red cells between 13 and 200 ml, 25  $\mu$ g of anti-Rh per ml of cells is effective in suppressing immunization (Dr W. Pollack, personal communication). For 1 ml of red cells, 15  $\mu$ g seems to be only partially effective and 75  $\mu$ g to be completely effective; intermediate doses have not been tested. Only about 2% of women have a 'TPH' of more than 1 ml of red cells.

There is no decisive evidence to show that either IgG or IgM anti-Rh, when given with Rh-positive red cells, augments the immune response.

Under conditions which have been shown to result in suppression of Rh immunization, only about 5% of the Rh antigen sites on the red cell are covered by antibody. This finding suggests the possibility that anti-Rh may exert its suppressing effect simply by causing the destruction of red cells, and so of antigen, rather than by 'masking' of antigen sites. On the other hand, ABO incompatibility, which also results in destruction of antigen, protects only partially against Rh immunization, supporting the idea that the role of 'passive' antibody is specific.

#### Liquor Examination in the Management of Rh Isoimmunization

W. WALKER (*Royal Victoria Infirmary Newcastle-upon-Tyne*)

Liquor examination, particularly for the presence of bile pigment, is widely used in the management of pregnancies complicated by Rh-isoimmunization. Neither the source nor route of entry of this pigment is known but high liquor levels are often associated with severe haemolytic disease of the newborn, nonetheless, application in management is essentially empirical. The purpose in forecasting severity is that

premature induction or intrauterine transfusion may be carried out to try and prevent intrauterine death.

Intrauterine death is relatively rare and both forms of treatment are relatively dangerous so that accuracy of prediction is essential and risks of amniocentesis must be minimal.

Various different methods of quantitating bilirubin in liquor amnii are employed. No method is significantly superior to the other and errors in prediction are rarely due to errors in detecting bilirubin, provided precautions are taken in the collection and preparation of the specimen.

A major source of error is in assessing gestation accurately, for the bilirubin value is closely related to this. It may also depend on variations in the value of other constituents of liquor, and some have been estimated in order to try and improve its predictive value.

The pattern of liquor bilirubin in normal pregnancy and those complicated by Rh isoimmunization will be considered, and mention will be made of other constituents. Particular reference will be made to cases in which wrong forecasts have been made.

#### Abnormalities of the Lower Spine and Spinal Cord in Manx Cats

B. E. TOMLINSON (*Newcastle-upon-Tyne*)

The 'tailless' Manx cat occurs in two forms, one with a very short tail and known on the Isle of Man as a stumpy, the other with no apparent tail (a rumpy). Tailless Manx cats are commonly described as having a characteristic rabbit or hopping gait, though many actually show severe physical disabilities, particularly incontinence of urine and faeces and hind-limb paralysis.

The lower spine and spinal cord of 13 Manx cats have been examined.

Three possessed short tails (stumpies), and all were said to be free from disability. Grossly the spinal cords and lumbosacral vertebrae were normal the only abnormality being the reduced number (four to six) of caudal vertebrae. Histologically the spinal cords were normal in two, but one showed severe hydromyelia of the sacro-coccygeal segments.

Nine of 10 rumpies showed other abnormalities in addition to absent or rudimentary caudal vertebrae. Five of these nine showed sacral dysgenesis, and all nine showed spinal cord abnormalities. In three the filum terminale and in five the lower sacral or coccygeal cord was attached to the dura beyond the sacrum and covered only by subcutaneous tissue and fur.

Traction on the rump fur pulled down the lower cord. Two animals had 'meningo-coele'-like cysts, four showed intradural fat masses (lipomas), one had a split lower cord (diastematomyelia), and two lumbosacral degenerative cord lesions with cavitation. Only one rumpy showed no apparent spinal cord lesion.

#### Leucocytic Infiltration of the Placenta: a Clinico-pathological Study

H. FOX AND F. A. LANGLEY (*Manchester*)

Leucocytic infiltration of the placenta or membranes was found in 24.4% of a series of 1,000 placentas. The only clinical factor significantly related to placental leucocytic infiltration was prolonged rupture of the membranes. Other clinical factors such as premature onset of labour, artificial rupture of the membranes, prolonged pregnancy, pre-eclamptic toxæmia, and prolonged labour showed an apparent relationship to placental leucocytic infiltration but this was due to the high proportion of cases in these groups in which prolonged membrane rupture occurred; if this factor was taken into account there was no significant relationship with these clinical factors. Placentas from hypoxic foetuses were more commonly infiltrated by leucocytes than were those in which there was no evidence of hypoxia. This was related to the high incidence of foetal hypoxia in cases in which there was prolonged membrane rupture, and analysis showed that, if this was taken into account, there was no significant association between the placental lesion and foetal hypoxia. Similar findings were found in 6.6% of cases in which leucocytic infiltration of the cord was present.

It is concluded that leucocytic infiltration of the placenta, membranes, or cord is indicative of bacterial infection and is not related to foetal hypoxia.

#### Quantitation of Tissue Components in the Bronchi in Chronic Bronchitis and Emphysema

G. R. MASSARELLA (*Royal Postgraduate Medical School, London*)

Bronchi from lungs obtained at necropsy from patients known to have had obstructive airways disease and from a control group of 16 patients were examined. The mean Reid index for the groups was 0.52 and 0.36 respectively. The area of the bronchial lumen, mucous glands, cartilage, and connective tissue (all tissue compo-



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