Rubella during Pregnancy

Ten years ago Gregg (1941), an ophthalmologist, first drew attention to congenital malformations in the offspring of mothers who contracted German measles in pregnancy. He recorded a series of 78 cases, in 67 of which the woman had developed the disease early in pregnancy. All his cases had congenital cataracts and 44 of them also had a heart lesion. Two years later Swan (1943) and his co-workers carried out an investigation for the National Health Medical Research Council of Australia and published their results in a series of papers. This research was carried out during the years 1942 to 1946, the total number of cases recorded being 120. In 101 of these, congenital abnormalities were found. Out of this series there were 111 cases in which the diagnosis was established as rubella; in seven the disease was associated with other exanthemata, and in two the diagnosis was doubtful. The abnormalities reported in order of frequency were microcephaly, cardiac disease, deaf mutism or deafness, cataract, mental deficiency, strabismus, cryptorchidism, inguinal hernia, spina bifida occulta, high-arched palate, speech defects, epilepsy, cleft palate (soft) and pyloric stenosis. The series also included one case of each of the following:—buphthalmos, hypospadias, hydrocele, bifid sternum, spastic diplegia, bilateral optic atrophy, naevus, fusion of the upper ends of the radius and ulna, and talipes equinovarus. Swan (1948) also discussed the etiology of the disease in relation to stillbirth, abortion and miscarriage.

Evans (1947) examined some of these cases and reported on the dental defects found in these children. Many reports of cases from Australia, America, Great Britain and the continent of Europe have since appeared.

In Australia the 1940 epidemic of German measles differed greatly from the ordinary virus infection bearing that name (Gregg, 1941; Swan et al., 1943). Its severity was greatly enhanced, but there is a general agreement that the disease was German measles because many of the cases in the series published were diagnosed and confirmed by medical practitioners. The increased severity of the disease was not confined to Australia; writers in America and France have stressed this point. The severity of the illness in the mother did not appear to be of any significance, bearing no relation to the extent and severity of the lesions in the baby.

As more cases were investigated it became apparent that the earlier the disease was contracted in pregnancy the greater was the likelihood of congenital defects. It was concluded that the first trimester was the most 'critical period' with an upper limit at the end of the fourth month.

The pathological lesions found in the foetus are thought to be due to the virus of rubella penetrating the chorionic barrier, and affecting those parts of the embryo which are undergoing the most active cell proliferation at the time, whilst organs already formed are likely to escape. It is suggested also that when the placental tissue is formed the barrier between mother and embryo is less likely to be penetrated. This would account for the prevalence of eye, heart and ear lesions, these organs being formed in the first trimester.

Brown (1947) put forward the hypothesis that the abnormalities in the foetus were caused by virus damage to the adrenal cortex of the embryo. It was pointed out by other workers that the adrenal develops after the first three months and that, if it were damaged, a hypoplastic adrenal would be found, which is not the case.

All the work involved by the many researches has established beyond doubt that there is a relationship between the disease and the malformations it produces. In the original papers it appeared that almost all the cases of maternal rubella produced lesions in the baby. This was undoubtedly due to the fact that only 'positive' cases were investigated. Abnormal children were traced back to mothers who had had rubella.
during pregnancy, and no cases were published of mothers who had had the disease but were later delivered of perfectly healthy babies.

With the publication of recent papers it becomes evident that the ‘percentage of babies affected is not higher than 25 to 50, and that of these only 1 in 4 to 1 in 10 have lesions sufficiently severe to make them a burden to society’ (Lemmon, 1950). Even so, the implications are serious, although the true figures cannot be known until much time-consuming investigation and research has been done. In this country a Member of Parliament asked the Minister of Health (Lancet, 1950), what steps had been taken to publicize the dangers of German measles in early pregnancy, and the need to notify this illness in order to minimize deafness at birth in children. The reply was that the evidence of danger so far available was indefinite, and that an enquiry on a national basis was about to be made. The investigation is being carried out by the Ministry with the kind offices of the Medical Officers of Health of ten regions with populations of over 40,000, and with the records of the Registrar-General, but it is stated that it will be two to five years before a report can be published. Would not the work of all concerned be made easier if German measles was a notifiable disease? Apparently Manchester is the only city where notification is obligatory. Surely if the disease can cause such terrible injury to the unborn child, every town, city, country and state should make notification compulsory, then a world survey could be undertaken.

Swan (1949) discussed the possibility of immunization against the disease, and in a rider to his paper mentioned the work of some colleagues in Australia. Since then some excellent papers have been published.

Anderson (1950) discussed experimental work on the active immunization of human volunteers with rubella. He and his co-workers obtained the virus from the throat washings of patients suffering from the disease on the first day of the rash, and produced rubella in susceptible subjects. (The virus so obtained can retain its infectivity for two years if kept at a temperature of \(-70^\circ\) C.) They noted nine cases in which the disease did not develop, in all of which the subject had had rubella six to nine years previously, a finding which strongly indicates that one attack of rubella confers prolonged immunity. Two disadvantages were noted, both of which will be solved:—(a) that the virus can be obtained free from bacterial pathogens but may have other viruses; and (b) that it will be necessary to isolate all cases being immunized because they are infective to other susceptible subjects.

McLorinan (1950) discussed the work done by himself and his colleagues on temporary passive immunization by the use of the \(\gamma\) globulin fraction of the convalescent's serum. The blood was collected by many units from camps where an epidemic had developed. He stated that this method of immunization had been used in Victoria for 2½ years and that out of 520 cases who had been traced, seven only developed the disease although all were contacts. The dose suggested was 2 ml. intramuscularly, but after five failures the dose was raised to 4 ml. Of the seven cases who developed the disease, three had their pregnancies terminated, one miscarried and three went to term and produced normal babies. The investigation and survey is continuing but will take years to complete. He makes no claims for its potency but suggests that its efficacy could be tested in a closed camp in which an outbreak of rubella appears.

In New South Wales the Red Cross Blood Transfusion Unit, under the direction of R. T. Walsh, has prepared a rubella convalescent serum which can be given intravenously, the dose recommended being 30 ml. Sixty subjects who had been exposed to infection were treated. None developed the disease.

It is stressed by McLorinan and others that passive immunization should be given within eight days of contact with infection, that is before the eruption of the rubella rash.

The question of termination of a pregnancy in cases where the mother has developed the disease in the first trimester of the pregnancy has been discussed by many writers including Lemmon (1950), Mayes (1950) and Dods (1950). It is stressed that the only possible grounds for advising such a course would be the harm caused to the mental health of a mother who, knowing the present facts about rubella in pregnancy, would dread the thought that she would reach term and produce an abnormal baby. Lemmon (1950) states ‘the obstetrician should not advise termination of pregnancy but should get the opinion of a psychiatrist, and if he advises termination the opinion of a second obstetrician should be obtained. If all are in agreement the termination of the pregnancy may be performed.’ In conclusion he states ‘even in such circumstances the act is illegal, but it is doubtful if the Crown Law Department would prosecute the doctor responsible, or if a jury would convict a doctor even if he was prosecuted.’

Prof. Dods (1950) agrees with various authorities that no exact statement about the prognosis for the infant can be offered without a more accurate method of diagnosis of the disease, and carefully controlled wide-scale prospective studies of infants and mothers suffering from rubella in pregnancy. If termination of pregnancy becomes an
accepted thing, such studies cannot be true evaluations because the embryo is destroyed before an assessment of the damage, if any, can be made. In the light of the work of Anderson, McLorinan and Walsh it would appear wiser to concentrate the efforts of the profession on offering active immunization to all women of marriageable age, and passive immunization to all expectant mothers known to have been in contact with the disease. If the results of such treatment prove as successful as is hoped, the risk of producing an abnormal child will be banished from the mind of the mother and no question of interrupting a pregnancy will then arise.

Ivor Hughes, F.R.C.S., F.R.C.O.G.

BIBLIOGRAPHY

Evans, M. W. (1947), Ibid., 1, 780.
Kelly (1951), Med. J. Austr., 1, 132.
Lancet (1950), 1, 1056.

R. R. Wilcox, M.D.
A. R. D. Adams, M.D., F.R.C.P.
Horace Joules, M.D., F.R.C.P.
J. G. Scadding, M.D., F.R.C.P.
Peter H. Buxton, M.R.C.P.
Prof. F. Murgatroyd, M.D., F.R.C.P.
Arthur Jacobs, F.R.F.P.S.
F. R. Kilpatrick, M.S., F.R.C.S.
G. Brownlee, Ph.D., D.Sc.

'CHEMOTHERAPEUTIC AND ANTIBIOTIC DRUGS' SERIES

The Postgraduate Medical Journal's series of articles on the present status of the chemotherapeutic and antibiotic drugs started in August 1951. Continuing monthly, in this present number the series reaches its fifth article on the 'Chemotherapy of Non-Pulmonary Tuberculous Conditions' by Dr. Buxton. The remaining articles will appear successively in the January, February and March issues of the coming year.

Written by experts in the various fields, the series is planned to give the clinician the most up-to-date practical information on each subject. In so progressive a field it is more than ever important to keep up to date. The Editors are confident that this series will prove of the greatest interest and value.

Chemotherapy and the Venereal Diseases
The Chemotherapy of Tropical Infections of the Bowel
The Chemotherapy of Non-Tuberculous Diseases of the Chest
The Chemotherapy of Pulmonary Tuberculosis
Chemotherapy of Non-Pulmonary Tuberculous Conditions
Recent Advances in Malaria
The Chemotherapy of Tuberculous Infections of the Urinary Tract
The Chemotherapy of Non-Tuberculous Infections of the Urinary Tract
The Most Recent Antibiotic Agents