BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 4 1948

"TOWARDS A LOWER PAEDIATRIC MORTALITY"*

BY

WILFRID GAISFORD, M.D., F.R.C.P.

Professor of Child Health, University of Manchester

Although much progress has been made in paediatrics in the past thirty years a great deal yet remains to be done. Repeated reference has been made to the divergence of the curves showing the fall in infant and neonatal mortality rates respectively. There is no doubt about the improvement in the infant mortality rate—a drop from 105 per 1,000 in 1910 to 45.5 per 1,000 in 1944 is certainly significant. Yet for neonates (i.e., in the first month of life) the lag is pronounced—from 38 in 1910 only to 24.5 in 1944. This is partly to be explained by the number of congenital abnormalities which cannot at present be prevented, but also by a big loss of premature infants which could be reduced by stricter attention to antenatal diet and by better immediate post-natal care.

In childhood generally improvement has been steady. Increased interest in paediatrics and especially in prophylactic paediatrics, better nursing care, more health education, smaller families, priorities in food and milk, and the Government issue of free vitamins have all helped. In addition certain specific factors have also helped—for example, the chemotherapeutic drugs and antibiotics, intensive immunization campaigns, and a natural decrease in virulence in certain organisms, notably the scarlet fever streptococcus. Extensions of the immunization programmes may still further improve matters in the future.

Methods of lowering the mortality rate during infancy and childhood may be considered from three aspects—antenatal, neonatal, and post-natal.

Antenatal Paediatrics

The term antenatal paediatrics was introduced by Sir Leonard Parsons in his Blair Bell Lecture to the Royal College of Obstetricians and Gynaecologists in 1945. This lecture provided an immense stimulus to paediatricians throughout the country.

The significance of virus infections in early pregnancy and their relationship to congenital malformations seem now definitely confirmed. The work on the rhesus factor is another example of modern research. From the region supplied by the North-Western Blood Transfusion Service there are approximately 150 Rh-negative pregnant women (with anomalous agglutinins in the serum) every year, and it is hoped to devote a ward specially to the immediate post-natal care of the infants born of these women. The problem may, however, be tackled antenatally—assuming a routine testing to be, as it should, universal. Every female should be tested early in life and careful note taken of those found to be Rh-negative—lest a blood transfusion

should ever be necessary and sensitization result from the use of Rh-positive blood, with consequent danger of producing an affected infant from pregnancy in later life. Diamond has shown that such infants are the most severely affected.

Two possible methods of attack have been suggested, both in the experimental stage at present: (1) chemical prevention of the antigen-antibody reaction; and (2) immunological inhibition of antibody formation. T.A.B. injections have been employed for the latter—without success so far; neutralization of maternal antibody has been attempted by Kariher and Miller (1947) using ethylene disulphonate, giving weekly injections during the last half of pregnancy, with suggestively satisfactory results in their first few cases.

There is no doubt that research on these prophylactic lines offers more hope than the present methods of treating the infants after birth, even with replacement transfusions; for nothing can be more disheartening than hours of work spent in transfusing a yellow baby only to find subsequently that a kernicterus already present but unsuspected at birth results ultimately in a mentally defective child. Nevertheless improvement in the prognosis generally has undoubtedly occurred following adequate treatment. The mortality was formerly something over 50%; since the introduction of Rh-negative blood transfusion it has dropped to something like 30%, and with improvements in the technique of replacement transfusions immediately after birth it may be expected to show a further fall.

The Neonatal Period

Prematurity is still one of the major causes of neonatal death, and, although the cause of prematurity is still undiscovered in something like 50% of cases, it is known that diet is a matter of outstanding importance in preventing it. Antonov (1947) found that 50% of the births in Leningrad during the siege in 1941 were premature, and that the mothers produced less breast milk and that it lasted for a shorter time. He also noted that mastitis neonatorum—the swelling of the breasts in the newborn that is so common and usually betokens a plentiful milk supply—occurred in only 2% of the infants.

The Australian discovery, reported by Gregg in 1941, of the relationship of German measles in early pregnancy to congenital abnormalities has opened up a large field of inquiry into a hitherto completely obscure subject. The possibility that other infections than rubella—e.g., mumps, influenza, and herpes—may be aetiological is probable, and other deformities than malformation of the heart and eyes may subsequently prove to be related to such infections. If

*Abridged from a lecture given to the Halifax Division of the British Medical Association on March 24, 1948.

allowance be made for the incubation period and for the time taken by the virus to penetrate the placental barrier the actual maternal infection may be placed earlier than the fifth week.

The logical sequel to this knowledge is, of course, that every precaution should be taken to prevent such infections in pregnancy, either by ensuring that they have already taken place earlier in life—e.g., by deliberate exposure in childhood, due care being taken that the child's general condition is satisfactory—or by the rigorous avoidance of exposure during the first three months of pregnancy, or by the administration of gamma globulin if exposure has occurred at this time. Unfortunately the efficacy of gamma globulin in preventing rubella is by no means certain.

The Post-natal Period

It has been generally accepted that newborn infants and infants under three months of age are poor antibody producers and that there is no great point, therefore, in attempts at early active immunization. Recent work by Sako *et al.* (1945) has cast doubts on the truth of the accepted findings, and early immunization may prove to be effective to some extent at any rate. For example, Waddell and L'Engle (1946) immunized 129 infants with pertussis vaccine at one week, one month, and two months after birth, and 70% showed an adequate response. Controls showed no carry-over from the mother.

The site of antibody formation is still a matter of dispute, but if, as Harris and his co-workers (1945) hold, one of the chief sites is the lymphocyte then there is no reason why newborn infants should not produce antibodies, as they normally have 66% of their total white cells in the form of lymphocytes after the first week of life, and gamma globulin is one of the constituents of the lymphocyte. Nevertheless, such immunity takes time to develop. For example, whooping-cough immunity certainly requires two months. Whooping-cough is not common in the first few months of life, yet when it does occur it is fatal in a large percentage of cases (686 infants under a year old died from whooping-cough in 1944 in England and Wales). Diphtheria is also a fatal illness in infants, but it is much rarer.

The idea of immunizing the mother during the later months of pregnancy so that the immunity may be carried over to the infant to last him until such time as active immunization may be capable of carrying on the immunity is well worth considering. It has already been done on a small scale in America by Cohen and Scadron (1943), and was found to be harmless to the mother and child and to result in a reasonable titre in the infant's blood in the first months of life. Similarly, immunization of Schick-positive pregnant women might be a worth-while procedure. Schick-negative women produce Schick-negative infants, who would not need immunizing immediately.

Cohen (1947) has drawn attention to the altered immunity in adult populations as a result of mass inoculations: 85% of adults were immune to diphtheria in 1920—only 50% are now, owing to the loss of artificially acquired immunity from the lessened chances of exposure. This affects the newborn also, who in 50% of cases may thus get no carry-over from the mother. Similarly, a high proportion of adults are not immune to whooping-cough and therefore their babies are susceptible.

Close collaboration between obstetricians and paediatricians is the first requisite in reducing neonatal mortality. We all realize that not every infant can be born at full term, and one of the most important problems is how to deal with premature infants.

Nursing

The most important factor in saving the lives of these infants is nursing. A good gamp in a humble cottage is better than a poor nurse in the most up-to-date "prematatorium." As is well known, most premature infants who die do so in the first 48 hours, and very often death occurs shortly after a feed. There is a tendency to atelectasis, the swallowing reflex is poorly developed, and feeds are easily regurgitated and inhaled. Clement Smith, of Boston, gives no fluids at all to premature infants for two to four days after birth. By that time they have got over the shock of birth, their lungs are expanding, and their swallowing reflex is less immature. I have tried this technique for the past six months and the results have been most satisfactory. It is little short of amazing to find that a 2½-lb. (1.13-kg.) baby will go for between 70 and 80 hours without fluids of any sort and yet do very well. Weight loss is not excessive; feeding, when it is started, is a less precarious procedure, and subsequent progress is most satisfactory. Oedema is lost more quickly. The infants are kept warm, given oxygen, and left completely alone except for changing until they indicate by their cry that they are hungry; this crying also expands their lungs. Jaffe (1948) has reported on the progress of infants so treated in the premature station at St. Mary's Hospital.

The question of the advisability of giving vitamin K in all cases, either to the mothers just before labour commences or to the infants at birth, is still debated. Some give it as a routine; others only in cases of difficult delivery where cerebral haemorrhage may be expected; while others reserve it solely for infants who have already bled (i.e., cases of melaena neonatorum). As it is perfectly harmless and it is difficult to judge in any given case whether there will be a hypoprothrombinaemia of pathological intensity or not, it should always be given. Another reason is the possibility of preventing a subdural haematoma from slowly accumulating—giving rise to convulsions later and involving, if diagnosed, surgical evacuation of the clot. Such haematomata are often found at necropsy, and have undoubtedly been the cause of death.

Kerpel-Fronius (1948) has suggested that vitamin P should be given as well; that there are two factors concerned with the diathesis—one the hypoprothrombinaemia and the other an increased capillary fragility—both resulting from vitamin deficiency in the mother's diet. The seasonal incidence has of course been known for a long time, which adds some weight to this theory.

Another frequent cause of death is *infection*. This too is often unrecognized, being rapid both in onset and in spread, and terminating fatally perhaps within 24 hours. Because of the frequency of *Bact. coli* and other Gram-negative organisms—some not generally pathogenic in later life—streptomycin may well come to be the drug of choice in treating such cases. Short intensive treatment is all that is needed, so there should be no question of drug-fastness as in the treatment of tuberculosis.

As the tendency is for more and more women to go into hospital to have their babies the question of nurseries in maternity wards is an interesting and still undecided problem. The advantages of having mother and infant together are obvious, yet comparatively few hospitals make such arrangements. I have made a point of asking mothers in the maternity wards I have visited whether they would like their babies in a cot within reachable distance all the time or whether they would prefer them in a nursery and just brought in for feeds. Their replies have been fairly consistent: the primiparae would like their infants with them; the multiparae prefer a nursery. This is just what is wanted really—the primipara to be taught how to feed and change

and wash her infant, and instructed in the various difficulties to be overcome in breast-feeding, and the multipara to have a well-earned rest. In other words, our new maternity hospitals might well provide special wards for primiparae, each bed having a cot attached, with only a small nursery for the occasional use of a fractious infant who would need to be put out for a night or two; and wards for multiparae as at present, associated with a regular nursery for all their infants.

There is a great need for accommodation for infants born of tuberculous mothers so that they may be removed from "open" contact. The provision of tuberculosis-free foster-homes is the ideal solution: there is less risk of cross-infection than in an institution for babies. Even when B.C.G. vaccination is undertaken on a large scale such accommodation will still be necessary, though for a shorter period of time.

The infant of a diabetic mother may have an urgent need of glucose immediately after birth, and preparations should be on hand to meet this need. Although newborn infants are comparatively insusceptible to hypoglycaemia (blood-sugar levels of 50 mg. per 100 ml. are common in normal infants) the hypertrophy of the islets brought about by the foetal hyperglycaemia may occasionally cause severe symptoms. The very sudden drop in blood sugar which these infants may undergo may easily result in death from hypoglycaemia, yet they may all be saved by prompt treatment. As the infants who manifest these changes are usually large—indeed, over large—the glucose can be given quite adequately by mouth, but if necessary gavage should be used, either intermittently or by continuous drip through a catheter passed into and left in the stomach; or in extreme urgency intravenous injection may be necessary. An essential prophylactic measure is the careful control of the mother's blood sugar during pregnancy.

After the neonatal period the reduction in mortality becomes more and more a preventive programme, the stress being on child health rather than on curative paediatrics; for, though research into curative methods—especially new chemotherapeutic agents and antibiotics—goes on, a distressingly large number of infant and child deaths are due to preventable conditions.

Preventable Diseases

As Davison (1934) has pointed out, of the 100 important diseases which may attack a child 37 are preventable, and these 37 cause more than half the deaths in childhood.

Active immunization has been responsible for a considerable reduction in the death rate in childhood, especially from diphtheria. Every child should have adequate immunization against diphtheria, smallpox, and whooping-cough, and, if he lives in the country, typhoid and tetanus as well. Furthermore, boosting doses should be given at intervals: the rise in antibody titre is both prompt and high after even minute doses—e.g., 0.1 ml. given intradermally. The fact that two or three antigens may be combined with advantage is helpful and reduces the total number of injections necessary: diphtheria and pertussis go well together; so do typhoid and tetanus. When gamma globulin becomes generally available we may have another potent agent against infection.

Deaths from tuberculosis in infancy are still far too numerous. They may be prevented by (a) prevention of exposure, as, for example, by the use of foster-homes for infants born into homes where there is "open" tuberculosis; (b) by setting up "preventoria" where children suffering from primary infection may be watched till the first three months after their primary infection, which are so vital prognostically, have been successfully passed;

(c) by B.C.G. or Wells's vole-bacillus vaccination; or (d) by not allowing milk that can possibly contain tubercle bacilli to be given to any infant or young child—a point of practical importance which could and should be tackled immediately.

The percentage of cases of tuberculous meningitis which is bovine in origin doubtless varies geographically, but it is by no means negligible—and all could and should be prevented. The Animals' Bill is a big step forward. The Minister of Agriculture reported (*B.M.J.*, 1948, 1, 371) that even to-day nearly seven-eighths of the cattle population in Great Britain were not attested and that it would take from ten to fifteen years to clear the country of bovine tuberculosis. Till then compulsory adequate pasteurization would help enormously with our problem.

Rickets was a disease which indirectly caused many deaths every year. The fact that a case of florid rickets is now hard to find is a triumph of preventive paediatrics largely due to public-health work and education. The full value of this improvement will not be appreciated till the next generation of infants is born—of women without rachitic pelves.

Advances in Surgery

The amazing advances in cardiac and thoracic surgery provide a contrast: here curative treatment has indeed advanced by leaps and bounds. The names of Blalock and Ladd and Gross have added lustre to the list of brilliant pioneer surgeons. No recovery from oesophageal atresia or tracheo-oesophageal fistula had ever occurred before 1939; now there are several such reported. Swenson (1948) has recorded 57 survivals out of 113 operations. The mortality in congenital diaphragmatic hernia has dropped by 60% in the last fifteen years, and the prognosis in certain types of congenital heart disease and in bronchiectasis has been materially improved. As Ladd (1948) says, the treatment of congenital anomalies may be expected to advance even more rapidly during the next few decades.

Appendicitis—or, rather, peritonitis resulting from delayed diagnosis of acute appendicitis—is still responsible for a formidable number of deaths every year. It occurs at all ages, and unfortunately with the most equivocal signs and symptoms in the youngest infants, when the diagnosis indeed is often not considered. The differential diagnosis of the acute abdomen is a matter calling for clinical acumen of the highest degree, but I am quite sure that in any case of doubt the correct thing is to play for safety by doing a laparotomy.

And what can one say about deaths from road accidents? Though hardly a paediatric problem, it certainly has repercussions that sadden paediatricians as much as everyone else. In 1945, 1,540 school-children were killed in accidents in England and Wales—651 of them on the road. It is a depressing thought, and one that should come home to doctors who are allowed adequate petrol to keep their cars on the road, that one of the advantages of the abolition of the basic petrol ration has been a lowering of the death rate among children from motor accidents.

Conclusion

Research is constantly proceeding all over the world: in the wards of hospitals, in laboratories, and in the field workers of all sorts are engaged on curative and prophylactic problems alike, and many of their puzzles will be solved in due course—doubtless to be replaced by others again in their turn to be solved. As soon as we get an effective bactericidal agent, up crops the resistant strain; as soon as we immunize infants we get a susceptible adult population; as soon as we find the cause of a group of diseases and their specific treatment a new organism