Diseases of the Newborn Period*

BY

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The neonatal period, though occupying so short a part of the normal life span, is a fascinating one and I am sure one which deserves to be treated with respect. I hope that I will be able to show that all the enthusiasm of the paediatrician and research worker for this epoch of life is justified.

As soon as the baby is born and its umbilical cord is tied and cut, it no longer subsists as a biological parasite; it becomes at that instant a separate individual both physically and legally. This change from the complete dependence on the maternal organism in an aqueous environment to a relatively independent status in air has been rather neatly portrayed by Oliver Wendell Holmes in the following verse:

> "So the stout foetus, kicking and alive,
> Leaps from the fundus for his final dive.
> Tired of the prison where his legs were curled,
> He pants, like Rasselas, for a wider world.
> No more to him their wonted joys afford,
> The fringed placenta and the knotted cord."

Never in the later life of man do such climatic changes occur in so short a time. The first few seconds must suffice for the first breath, adequate expansion of lungs and the adjustment of the circulation to pulmonary respiration. Other adjustments, such as the maintenance of body temperature, the establishment of digestion and the regulation of metabolism and water balance, are completed in a few days.

Apart from these academic and philosophical considerations, there is a very definite and practical aspect to this period. This is the increasing relative importance of the neonatal period as a time of potential mortality.

More than half of the neonatal deaths occur during the first 48 hours of life, and it is often only a matter of chance whether the child is born dead or dies shortly after birth.

"Perinatal mortality" is a term which refers to the number of stillbirths and neonatal deaths (per 1,000 births) occurring during the first week of life.

In England and Wales, whereas the death rate between four weeks and one year has been reduced by 68 per cent. since 1928, the perinatal death rate has been reduced by only 41 per cent.

If the number of deaths in infancy is going to be further reduced, it is obvious to which group attention and effort will have to be directed.

Crosse and Mackintosh (1954), in their analysis of the perinatal deaths in the Birmingham area for the years 1945 and 1952, have divided the causes into the following groups:

(1) Complications of pregnancy, which include toxaemia, positive W.R., blood group incompatibilities, separation of placenta.

(2) Congenital malformations.

(3) Complications of labour.

(4) Postnatal complications, e.g., infections, haemorrhages.

(5) Prematurity.

(6) Unknown causes.

I propose to refer to a few examples of these groups with which I have had to deal recently and to say something about these conditions.

Congenital Malformations

Oesophageal atresia with tracheo-oesophageal fistula (Fig. 1). The presenting symptoms include difficulty in feeding, cynosis and excessive frothing at the mouth due to inability to swallow saliva. The gas-filled stomach demonstrates the communication between the trachea and the distal portion of the oesophagus.

Congenital diaphragmatic hernia. Fig. 2 shows displacement of the heart by the viscera present in the left hemithorax. These babies may present with cardiac, respiratory or abdominal symptoms. Indiscriminate administration

* Address to Clinical Club on 29th September, 1960.

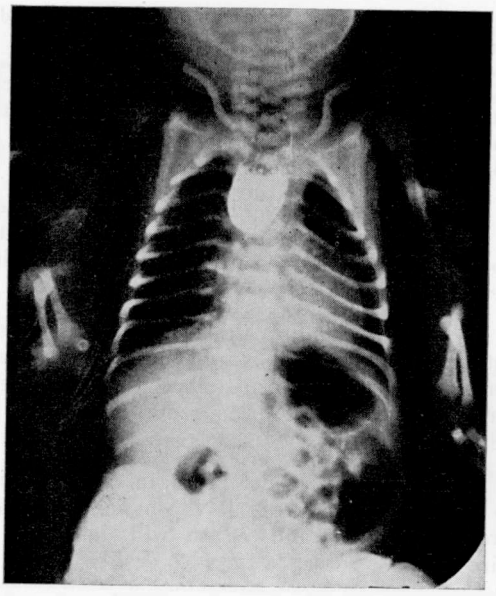


Fig. 1—Oesophageal atesia.

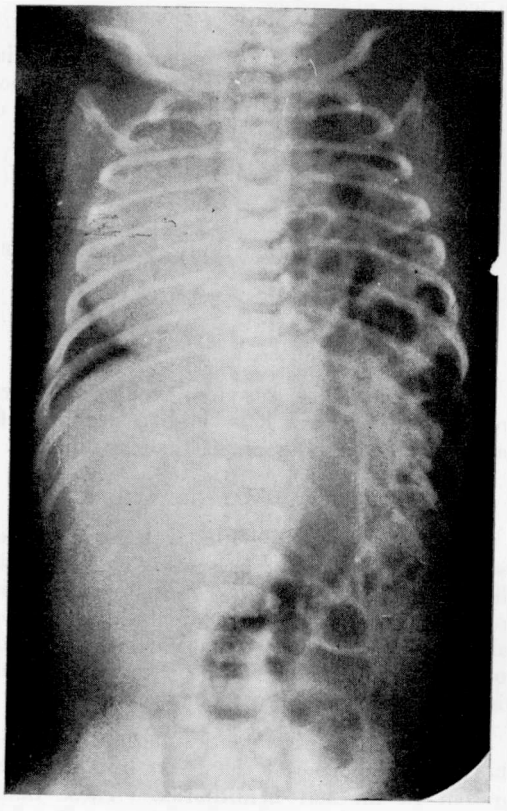


Fig. 2—Congenital diaphragmatic hernia. Note displacement of the heart to the right.

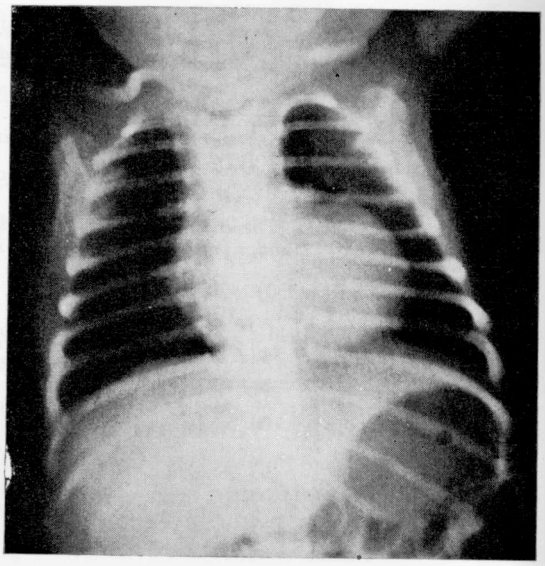


Fig. 3—Cyanotic congenital heart disease.

of oxygen to these infants may cause distension of the abnormally placed gut with further cardiac and respiratory distress.

An example of respiratory distress due to congenital cyanotic heart disease (Fig. 3). Note boot-shaped heart and oligaemic lung fields.

COMPLICATIONS OF LABOUR

An example of depressed fracture of skull following forceps delivery was shown.

Conditions Arising After Birth

Pneumothorax. — Asymptomatic pneumothorax, either unilateral or bilateral, is estimated to occur in as much as 1 per cent. of all newborn infants.

Since pneumothorax is seen frequently among infants who have been subjected to resuscitative measures, it seems likely that the most common cause is over-inflation and resulting alveolar rupture. If the ruptured alveoli are on the pleural surface, pneumothorax without pneumomediastinum occurs. If they are not, pulmonary interstitial emphysema results. If the volume of escaped air is great enough, it is believed to follow the vascular sheaths to the mediastinum, causing mediastinal emphysema. In turn, the mediastinal air may break into the pleural space to cause pneumothorax, or into the subcutaneous tissues of the neck and chest to cause subcutaneous emphysema.

Ball valve types of bronchial or bronchiolar obstruction resulting from aspiration may also cause alveolar overinflation, which, if mild, produces local emphysema; but if severe, results in alveolar rupture and pulmonary interstitial emphysema, pneumomediastinum or pneumothorax.

Pneumothorax may also result from direct trauma as puncture from a broken rib or from rupture of lung abscess and pulmonary cysts. It occurs rarely as a result of alveolar rupture in lobar emphysema (Fig. 4).

Hyaline Membrane Disease

This is a condition characterised by respiratory difficulty occurring soon after birth.

Incidence.—From autopsy studies of neonatal deaths, Miller and Jennison (1960) found hyaline membrane disease in at least 15 per cent. of all live born premature babies weighing between 1,000 and 2,000 g. The incidence decreased as the babies' weight increased and was practically non-existent in infants over 8,000 g.

According to Potter, hyaline membrane is responsible for almost all deaths of premature babies born in the Chicago lying-in hospital if they were normal at the time of birth.

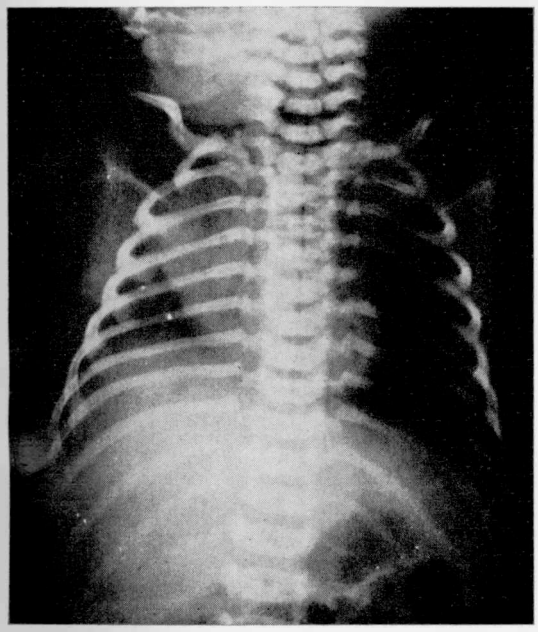


Fig. 4—Left-sided tension pneumothorax.

Claireaux (1953), in his histological examination of the lungs in 376 cases of neonatal deaths, found hyaline membrane in 108 (29 per cent.), of which four-fifths were in premature infants; and in no less than 21 per cent. of the 276 cases hyaline membrane was not the only abnormality discovered.

It also occurs in babies of diabetic mothers. In larger babies it occurs mainly in those born by caesarean section. The condition is particularly common after caesarean section, and some workers have found it to cause 45 per cent. of the neonatal deaths following this form of delivery (Bound *et al.*, 1960).

Etiology of Hyaline Membrane Disease.—It is now widely accepted that hyaline membrane can be produced as the result of—

(a) effusion from the pulmonary circulation;
(b) conversion of fibrinogen in the eflusion fluid to fibrin, possibly enhanced by the thromboplastic activity of aspirated amniotic fluid;
(c) the syneresis of the fibrin to form a membrane.

Left-sided heart failure, aspiration of the regurgitated amniotic fluid present in the stomach at birth and the use of oxygen have all been proposed as factors contributing to the pathogenesis of the membrane.

Pathology.—The lungs appear deep purplish-red and non-crepitant. On microscopy the main features include extensive atelectasis, engorgement of the intra-alveolar capillaries and a number of the alveolar ducts, and alveolar respiratory bronchioles are lined by acidophilic homogenous or granular membranes.

Clinically it presents as respiratory distress. There is often difficulty in initiating respirations if carefully looked for, or increasing respiratory rate during the first hour of life. By observing the respiratory rate during the first hour of life it may be possible to anticipate the condition. In some cases evidence of emphysema may be marked.

Pathogenesis.—The formation of the hyaline membrane is most likely due to pulmonary oedema, caused by the reaction of the immature respiratory epithelium to various postnatal factors.

There can be very little doubt that delayed onset of respiration is a most important factor in its etiology. This may result from depression of the respiratory centre by anoxia from foetal distress or asphyxia at delivery or by the effect of anaesthesia. This latter is a big factor,

especially in caesarean sections. Indeed, if regional anaesthesia is used the Apgar score for infants born by caesarean section is very little worse than those born by vaginum. An additional factor may be the increased extracellular fluid volume which is present in premature infants, the babies of diabetic mothers and infants born by caesarean section, especially when this takes place before the onset of the labour pains.

There has been evidence for a shift of fluid into tissue spaces in hyaline membrane disease, and this is reversed as the child improves. One suggestion is the exudation of plasma and possibly blood from bronchopulmonary anastamoses due to pulmonary hypertension in the presence of left ventricular failure leading to unbalanced flow from the pulmonary artery into these anastamoses. Certainly in infants with prolonged asphyxia there exists a high pressure in the pulmonary artery, together with a falling systemic pressure.

It has been suggested that early ligation of the cord in the presence of delayed onset of breathing might be a significant factor in the etiology.

Radiography in Hyaline Membrane.—Three different stages have been described:

(1) First there appears a fine miliary mottling throughout the lung fields.

(2) This is followed in the progressive lesion by a coarser and more coalescent type of opacity. At this stage the bronchial tree is often clearly demarcated.

(3) Finally, the shadows become confluent as a result of lobar or lobular consolidation and collapse.

Jaundice in the Newborn

In hyperbilirubinaemia the level of serum bilirubin is above 18 mg. per cent. Its incidence among full-term infants without blood group incompatibility is about 5 per cent., but among premature infants without blood group incompatibility it varies from 10 to 40 per cent. in different series.

It is now generally accepted that the one definite factor in the production of kernicterus is a high level of circulating indirect reacting (unconjugated) bilirubin. The critical level seems to be 20 mg. per cent. and the risk of brain damage increases as the level is exceeded.

Bilirubin Metabolism

When red cells break down they liberate globin and haem. The haem consists of pyrrol groups and iron, and on the further breakdown of the pyrrol groups the pigment bilirubin is produced. This indirect reacting pigment is fat soluble and the plasma albumin acts as a carrier.

Removal of bilirubin from the body entails transformation from the fat soluble substance to a water soluble one. This is achieved by conjugation with a highly water-soluble sugar acid, glucuronic acid. The process of coupling probably does not involve glucuronic acid directly, but a donor substance, uridine diphosphate glucuronic acid, from which the glucuronyl residue is passed on by a transferring enzyme. This process takes place in the intercellular canaliculi of the liver. Bilirubin can be excreted only after transformation to the water-soluble glucuronide.

This glucuronyl transferase (enzyme) system which aids the conjugation of bilirubin and glucuronic acid to form the water-soluble direct reacting pigment or bilirubin glucuronide is deficient at birth. As the removal of bilirubin before birth is probably carried out by the placenta rather than by the liver, the development of this enzyme in the late stages of gestation is understandable. Even in infants who do not become jaundiced, the liver capacity to excrete bilirubin is much smaller than that of the adult. For that reason even a minor increase in bilirubin production will produce a startling rise in plasma bile pigment. Obviously excessive red cell destruction occurring in cases of haemolytic states causes a rapid rise in the level of indirect reacting bilirubin; and in view of the incompletely developed glucuronyl transferase system, the excretion is delayed and severe and sustained jaundice develops.

As a rule the less mature an infant, the less developed is the transferase system and the more likely is hyperbilirubinaemia to develop. Also it is possible that the brain of the premature baby is more susceptible to bilirubin; possibly the blood-brain barrier is poorly developed and hence premature infants are particularly prone to develop kernicterus and also at relatively lower bilirubin levels.

Other factors predisposing to hyperbilirubinaemia and kernicterus: vitamin K analogues. Only the diphosphate derivaties Synkavit and

Kappadione have been incriminated. It is possible that vitamin K is toxic only in vitamin E deficient states, and the newborn's serum is said to have a fifth as much vitamin E as the mother's serum. Gantrisin medication has been attended by an increase in the incidence of kernicterus in premature infants, and this occurred at relatively low bilirubin levels. This may be due to a direct effect on the blood-brain barrier, but it may be that the drug displaces bilirubin from plasma albumin, on which both are transported.

Methaemalbumin, which occurs in association with haemoglobinaemia, is another possible factor.

Prolonged neonatal cyanosis, bacteraemia and maternal diabetes predispose to hyperbilirubinaemia. Uterine anoxia may be responsible in some infants.

The glucuronyl transferase system also participates in the metabolism of hormones and steroids and in the excretion of many drugs, e.g., salicylates, morphine, chloramphenicol, sulphonamide and meprobomate, and hence the susceptibility of the newborn to these drugs, especially in prematures. Certain premature infants on the usual dosage of chloramphenicol have died, though the original infections cleared up.

Neonatal Infection

The diagnosis of infection in the newborn period is not an easy one, as the manifestations are not as definite as in the older child. One of the important facts to remember is that the normal rectal temperature of the newborn is around 97° F., and a temperature of 99 is roughly equivalent to 101 in an adult. Often, of course, the temperature is subnormal in the face of overwhelming infection.

Spence (1941) stated: ". . . A newborn infant who becomes abnormally drowsy and refuses its feeds and is not suffering from cerebral haemorrhage should be suspected of an 'acute neonatal infection.'" Moncrieff (1953) makes the same observation: "Any disturbance in the newborn baby after the first few days of life should be regarded as due to infection until proved otherwise."

Infections are acquired before, during and after birth. Infections of special interest are those caused by the staphylococcus, *B. coli*, viruses, especially coxsackie, the herpes virus

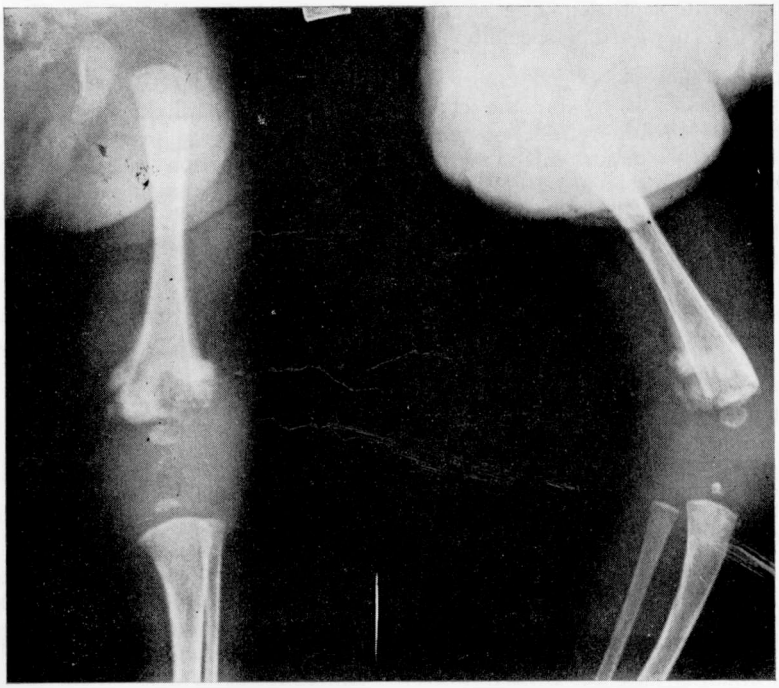
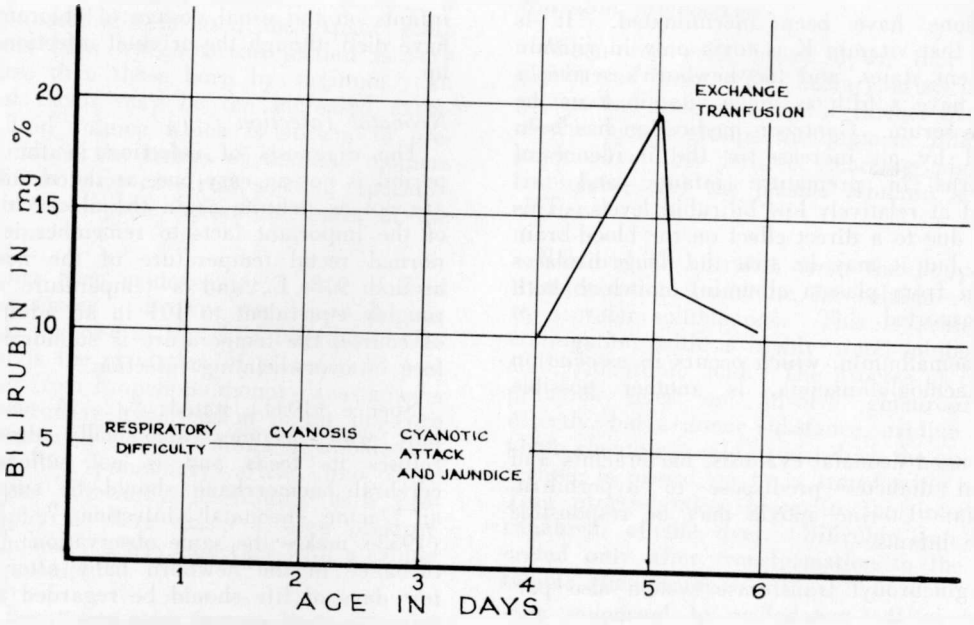


Fig. 5—Acute staphylococcal osteomyelitis of the lower end of the femur.



PATTERN OF HYPERBILIRUBINAEMIA IN A PREMATURE BABY.

and the virus causing cytomegalic inclusion disease and certain protozoa, e.g., toxoplasmosis.

Infections enter via the respiratory and conjunctival mucosa, skin and alimentary tract, and spread of infection with septicaemia is a constant danger in the newborn, especially in prematures.

Staphylococcus pyogenes is by far the commonest organism found in minor infections and is prominent also in the major infections of the newborn period (Corner *et al.*, 1960).

It is generally agreed that most infants in maternity units become colonised by staphylococci soon after birth and are then a potent source of cross-infection. The sites of colonisation are the umbilicus, nose, groin and perineum. Infants who become heavily colonised by the second day of life subsequently suffer from clinical infection more often than other infancts.

The umbilicus, which is an open wound, is especially liable to bacterial colonisation. Normally the umbilical cord mummifies and sloughs off cleanly at the junction of the cord membrane and skin on the sixth to tenth day. The blood vessels close functionally at birth, but do not obliterate with fibrous tissue until about the end of the third week. The thrombi which seal them during this period form dangerous potential channels for infection, and the umbilical stump requires special cleanliness for a week or more after the cord has sloughed off.

Manifestations of infections often occur after discharge from hospital and may cause an outbreak in the family. Breast abscesses may occur in the mother in this way.

Even if staphylococcal colonisation is inevitable in a large proportion of newborn infants, the introduction of these organisms into the infant's environment should be gradual in order that the initially weak defences of the infant should not be overwhelmed by large numbers of organisms.

Preventative measures include attention to skin and cord and limitation of number of other infants and adults who enter the baby's environment.

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