ICTERUS NEONATORUM: ITS INCIDENCE AND CAUSE

BY

LEONARD FINDLAY, M.D., F.R.C.P.*
(From the Radcliffe Infirmary, Oxford)

AND

GEORGE HIGGINS, B.Sc. and MARGARET W. STANIER, M.A., B.Sc.
(From the Department of Biochemistry, The Radcliffe Infirmary, Oxford)

Introduction

In spite of the frequency of icterus neonatorum and the work done to elucidate the problems connected with it, there still remains much divergence of opinion regarding its incidence and pathogenesis. Estimates of the incidence vary from 40 to 80 per cent. of the newborn. Since the detection of jaundice is influenced by many factors, such as the vascularity of the skin and the nature of the light in which the observation is made, and since there are several definitions of jaundice, such varying estimates are not surprising.

Icterus neonatorum has been ascribed to excessive haemolysis of the blood, to immaturity of the liver, to increased viscosity of the bile, and to the breakdown of the mother’s blood in the placenta. The hypothesis that the jaundice was hepatic in origin has been replaced by one that it is caused by excessive haemolysis. Since bilirubin is a product of the breakdown of haemoglobin, all jaundice may be said to be the result of haemolysis, but the evidence of excessive haemolysis as a cause of icterus neonatorum is inconclusive.

During the past year, in the course of biochemical and haematological investigations of haemolysis, there occurred an opportunity to study newborn babies, and an investigation of icterus neonatorum was undertaken, (1) to determine the incidence, (2) to try to detect any difference in the rate of haemolysis in jaundiced and non-jaundiced infants, and (3) to seek evidence of impairment or immaturity of liver function.

Material and Methods. The children investigated were born in the maternity department of the Radcliffe Infirmary, Oxford. Foetal blood was collected from the umbilical cord before pulsation had ceased (from the umbilical vein by venepuncture, and from the artery after cutting but before ligation). Children’s blood was obtained by venepuncture of a scalp vein or by incision of the skin of the heel. Blood was collected in tubes containing heparin, and pipettes used for taking blood were washed through with liquid heparin.

Haemoglobin was estimated by Haldane’s technique, using a standard colour tube calibrated at the National Physical Laboratory. Reticulocytes were counted by the wet film technique. Plasma proteins were estimated by micro-Kjeldahl technique (Howe, 1921). Plasma bilirubin was estimated by the Thannhauser and Andersen method (1921). Faecal bilirubin was estimated by a modification of Hunter’s method (1930). Takata-Ara reaction was performed by Ragins’ technique (1934). Faecal urobilin was detected by Schlesinger’s test (1903). Fragility of red cells was measured by Creed’s technique (1938).

Incidence of Icterus Neonatorum

The diagnosis of icterus neonatorum was made on the basis of a hyperbilirubinaemia in the cord blood or post-natal blood of an infant otherwise normal. This criterion was taken because the plasma bilirubin level is a more objective and accurate standard than the observation of jaundice, that is, the yellow coloration of the skin and mucous membranes, since the observation of this condition is much influenced by the degree of hyperaemia and the nature of the light in which the examination is made. As the coloration is due to infiltration of the tissues by bilirubin, any patient with an excess of bilirubin may be considered the subject of icterus neonatorum, whether or not the yellow coloration is present.

It is proposed to define ‘hyperbilirubinaemia’ as a plasma bilirubin level greater than 1 mg. per cent. This arbitrary level is chosen because it is unusual to find in a normal adult a plasma bilirubin level above this figure. No figures are available for the plasma bilirubin levels of a large series of young infants, but in all the patients studied in this...
investigation the plasma bilirubin concentration was below 1 mg. per cent. at the age of two weeks.

Seventy-three infants were observed once during the first ten days of life, and of these, thirty-four (46 per cent.) had plasma bilirubin levels between 1·2 and 20·0 mg. per cent. at the time of examination. In twenty-eight of the infants the levels were 2·0 mg. per cent. or above, and eighteen showed jaundice. The absence of a definite bilirubin level at which jaundice appears was probably due to the difficulties of observation mentioned above. However, all infants (eight in number) who had a plasma bilirubin level above 5 mg. per cent. showed icteric discoloration of the skin and mucous membranes. The observations in this series of infants are recorded in fig. 1.

Hyperbilirubinaemia in foetus. Not only do a large proportion of infants have hyperbilirubinaemia during the early days of life, but also many normal infants are born with a high plasma bilirubin and, though not jaundiced, are nevertheless by our criterion undoubted examples of icterus neonatorum. This point is important and should be considered in any discussion of the etiology of the condition.

The plasma bilirubin concentrations of the cord blood in 110 infants was measured (fig. 2); in 68 cases (62 per cent.) a hyperbilirubinaemia was observed. However, the plasma bilirubin of the cord blood never reached the high levels seen after birth. It will be seen that, as previous workers have observed, there is some relation between the foetal hyperbilirubinaemia and the post-natal rise of plasma bilirubin, but in contrast with the results of Ylippö (1913) and Hirsch (1913), our figures fail to reveal an absolute correlation. Of eighteen infants in whom the cord blood bilirubin was over 2 mg. per cent., four did not develop jaundice. Nevertheless, it seems that in general the higher the level of foetal bilirubin, the greater is the chance of the development of jaundice (table 1, p. 73).

Relation between plasma bilirubin level and maturity of foetus. No correlation exists between cord plasma bilirubin concentration and the maturity of the foetus (fig. 2). This constitutes evidence against Ylippö’s view that there is in the foetus no means of excretion of haemoglobin derivatives, for, if this were so, it would be expected that plasma bilirubin concentration would rise with the age of the foetus. Possibly haemoglobin derivatives are excreted before birth through the placenta.

Plasma bilirubin concentration during the neonatal period. In sixteen infants the level of bilirubin was determined in the cord blood and in the blood at intervals for the first twelve days after birth (fig. 3). There are three groups of cases. In group A (eight infants, 50 per cent.) the plasma bilirubin level rose noticeably, reaching a maximum of from 3 to 9·4 mg. per cent. on the third to ninth day and usually declining rapidly thereafter to a figure below 1 mg. per cent. by about the tenth day. Jaundice was seen only in this group. In group B (six infants, 37 per cent.) the foetal bilirubin level was below 1 mg. per cent., and during the first few days of life there was only a slight rise, never exceeding 2 mg. per cent. and returning to a normal level by the tenth day. Though none of these patients showed jaundice, nevertheless by our standard three must be considered cases of icterus neonatorum. In group C (two infants, 13 per cent.) the foetal blood showed hyperbilirubinaemia which diminished after birth, the normal levels being reached by the first and the eighth days.

**Fig. 1.—Plasma bilirubin in newborn infants during first two weeks of life.**
Icterus Neonatorum

Duration of Pregnancy in Weeks

- • CASES WITH JAUNDICE
- ○ CASES WITH NO JAUNDICE
- X DIED WITHIN 48 HOURS

Fig. 2.—Plasma bilirubin in foetus.

These graphs bear out the finding that there is no absolute correlation between the foetal level and the post-natal rise of the plasma bilirubin. The plasma bilirubin of cord blood in group A was on the whole higher than in group B, but only slightly and not invariably. Of the whole series, hyperbilirubinaemia was present at some stage during the first ten days in all except three cases, i.e. it was present in 81 per cent. of the cases.

Relation of jaundice to maturity of infant. Although our figures show no correlation between cord blood bilirubin levels and maturity of foetus, certain findings confirm the view that the premature infants are more likely to develop jaundice than
the mature ones. One hundred and ninety-six infants were examined daily and the results are recorded (table 2, p. 73). In our experience all infants born after a pregnancy of thirty-five weeks or less develop jaundice, as against 67 per cent. of those born after thirty-six or thirty-seven weeks, and 47 per cent. of full-term infants. These findings refer to jaundice; some degree of hyperbilirubinæmia is present in almost all infants but is more likely to be severe and thus to cause jaundice in the premature.

Nature of Icterus Neonatorum

In this section we propose to discuss in turn excessive haemolysis and hepatic immaturity as causes of icterus neonatorum, to report our own findings and to show their bearing on the current theories of the origin of neonatal jaundice.

Current theories of etiology of icterus neonatorum. Several factors have been suggested in the past as possible causes of icterus neonatorum. Those most frequently mentioned in the literature are excessive haemolysis or hepatic immaturity or both. Snelling (1933) suggests that the condition results from the rearrangement of the circulation at birth, together with a delay by the liver in assuming its post-natal functions. Davidson et al. (1941) and Fallon (1943) attribute it to excessive haemolysis due to release of the foetus at birth from anoxia, together with functional immaturity of the liver. Tocantins (1940) mentions only hepatic immaturity. McIntosh (1941) declares that virtually all newborn infants show a hyperbilirubinæmia in their first week of life whether or not they develop jaundice, and that the origin of the extra bilirubin is the red cells no longer needed. Lightwood (1943) considers the condition to be haemolytic in origin, but states that the depth and duration of the jaundice is determined more by the functional capacity of the liver than by the amount of blood destruction. According to Schick et al. (1942), the condition is due to the breakdown of the mother's blood in the placenta.

Excessive haemolysis. The fall in haemoglobin concentration and red-cell count which undoubtedly occurs during the early days of life has led to the assumption of an excessive haemolysis at this period of life, a condition seen in haemolytic anaemia. The fall in haemoglobin and number of red cells could, however, be explained by a deficient production rather than a removal, or by an increased amount of plasma, thus causing a dilution effect. Our results show that this fall does not run parallel with the development of jaundice.

Rate of fall of haemoglobin and red-cell concentrations. A recent study by one of us (Findlay, 1946) showed that the most rapid fall in haemoglobin level and cell count occurs not in the first week of life, when there is a tendency to jaundice, but in the second week, when the bilirubin level is returning or has returned to normal (table 3). Further, this fall continues to the third month, long after there is any tendency to jaundice. The rate of fall of haemoglobin has also been studied in the jaundiced and non-jaundiced infants, and no difference could be detected in the two groups (fig. 4).
Absence of concomitants of excessive haemolysis. There was also in the newborn an absence of the usual blood findings in increased haemolysis, i.e., the presence of large numbers of immature cells (reticulocytes and nucleated red cells) in the circulating blood. Except for the first few hours after birth, nucleated red cells are absent from the blood of the newborn, and the reticulocyte count is not above 1 per cent. This contrasts with foetal blood from the umbilical cord, which contains fairly numerous nucleated red cells and always has a reticulocyte count above 1 per cent.

These facts suggest that a slow-down of haemopoiesis rather than increased red-cell destruction is the cause of the lowering of the haemoglobin concentration in the newborn. Considering the diminution of haemopoietic tissue which occurs in the change-over from foetal to post-natal life, it is not surprising that blood formation should slow down until extramedullary haemopoiesis is well established. It has been shown (Gilmour, 1944) that when there is a definite haemolysis, as in erythroblastosis foetalis, the extramedullary haemopoietic tissue is abnormally widespread and hyperplastic; we, however, have noticed an aplasia in the normal child.

Presence of a haemolysin. Many workers have searched for abnormal susceptibility to haemolysis of the red blood corpuscles in the newborn, or for the presence of some haemolytic agent, but the findings are conflicting. The presence of a haemolysin in the mother's serum which can affect the cord blood has been reported (Mitchell, 1928), but this could not be confirmed by other workers (Goldbloom and Gottlieb, 1929).

Fragility of red cell. The published results of the fragility of the foetal red cell in hypotonic saline are also contradictory. Some authors claim that the fragility is increased in the foetal and newborn child (Cathala and Daunay, 1908; Wollstein, 1928; Goldbloom and Gottlieb, 1929); on the other hand, Mitchell (1928), observed no difference in the red-cell fragility in early and adult life.

In a study of this question, one of us (Findlay, 1945) found a slightly increased fragility in the red cells in foetal blood and a decreased fragility during neonatal life. As far as our observations are concerned, there is no reason to assume an increased tendency to haemolysis during the period when icterus neonatorum occurs.

The effect on the foetus of the oxygen deficiency in the uterus has often been considered analogous to that of the low oxygen tension on people at high altitudes or in chambers under reduced pressures; polycythaemia present at birth has been compared with that found in residents at high altitudes. The results of experiments (Goldbloom and Gottlieb, 1930) in which guinea-pigs were placed in chambers in reduced atmospheric pressure and then removed, were very similar to the findings in people living at high altitudes and then descending to sea-level (Barcroft, 1925). However, these conditions are not analogous to life in utero, ending at birth. Although an increase in the icteric index was noticed in some animals, in several cases the increase occurred before the release from the reduced pressure, and in all cases it steadily declined on returning to normal atmospheric pressure. The raised icteric index could be explained on the basis of liver inefficiency, resulting from anoxaemia. In polycythaemia vera, in which higher red-cell counts are found than in residents at high altitudes, a raised plasma bilirubin level is most unusual except in the presence of a developing anaemia (Minot and Buckman, 1923).

Polycythaemia of reduced pressures cannot be compared with that of the newborn, or used as evidence of the haemolytic origin of icterus neonatorum. The evidence from red-cell fragility is dubious, and the evidence from red-cell counts is capable of alternative explanation. We therefore reject the theory of excessive haemolysis as the cause of icterus neonatorum.

Hepatic immaturity. If, as the foregoing evidence suggests, red-cell destruction and bilirubin formation take place in the newborn at a rate no greater, and perhaps lower, than in adults, it seems probable that the hyperbilirubinaemia is due to the failure of the
liver of the newborn child to excrete the pigment at the normal adult rate. Such a failure would not be surprising. Many tissues of the body do not reach their full powers until some time after birth. So, too, it may be expected that the premature child will be more likely to show a severe degree of hyperbilirubinaemia than the full-term child, just as the premature infant shows great variations in body temperature because of the incomplete development of the nervous system. If the curves of plasma bilirubin levels for the first ten days of life are grouped according to the duration of pregnancy, the relationship of post-natal rise to maturity can clearly be seen (fig. 5). In general, the longer the pregnancy, the less the rise.

It is only after birth that the liver starts to take on many of its functions. During foetal life, most of the portal blood is by-passed to the placenta, the liver being mainly a haemopoietic organ. Meconium contains bile pigment, so a small amount of pigment must be excreted by the liver; but probably a large proportion of the bilirubin formed in the foetus is transferred through the placenta to the mother's circulation.

Certain writers (e.g., Ylppö, 1913) have denied that foetal bilirubin is normally excreted via the placenta, on the ground that the mother's plasma bilirubin level is not raised during pregnancy. However, the daily amount of foetal bilirubin would be only a small fraction of the amount produced by the mother herself and could not cause a noticeable change in the maternal blood. Furthermore, there is positive evidence that the placenta acts as an excretory organ for foetal bilirubin. In seven newborn children the bilirubin level in the umbilical artery was higher than in the umbilical vein, the average difference being 20 per cent. (Cserna and Liebmann, 1923). We have confirmed this observation (table 4). We did not obtain the consistent results reported by the previous workers: the average bilirubin level, however, was 14 per cent higher in the arterial blood than in the venous blood.

There is reason, to think, then, that at birth the route of bilirubin excretion changes suddenly from the placenta to the child's own liver; and if the child's liver were functionally immature at birth a temporary accumulation of bilirubin in the blood could readily be explained.
Despite the practical difficulties, some attempts have been made to measure the efficiency of hepatic function in newborn infants. The results, however, have not been decisive. Heynemann (1915) tried to evaluate hepatic function in 109 male infants, using as a test the urinary excretion of laevulose after a standard dose. He concluded that there was evidence of impaired function of the liver in newborn babies, more marked in jaundiced than in non-jaundiced infants. Recent criticisms of this test, and also of the bromosulphophthalein test used by Herlitz (1926), however, render these results of doubtful value. Linzenmeier and Lillenthal (1922) used the post-prandial leucocyte reaction as a test, and, although they found the leucopenia after a breast feed more marked in the jaundiced than in the non-jaundiced child, other workers (Hainiss and Heller, 1923; Simon and Wellewa, 1924; Joseph and Guskar, 1924) were unable to confirm this. Ross et al. (1937) have reported an increased bilirubin and urobilin excretion in non-jaundiced infants as compared with jaundiced infants, and Waugh et al. (1940) have shown that the rise in plasma bilirubin in icterus neonatorum is confined to an increase in the indirect reacting type of bilirubin only.

We have investigated the state of hepatic function by a study of the plasma proteins and Takata-Ara reactions during the first ten days of life and of the excretion of faecal bilirubin during the first five days of life.

**Plasma proteins.** The total plasma proteins and albumin fraction were estimated in order to see if the changes in the protein fractions which are commonly seen in liver disease (Higgins et al., 1944), i.e., a lowered albumin and a raised globulin fraction, are observed in infants. Typical examples of our results are recorded in table 5 (p. 74). It will be seen that the results do not show any consistent changes in the albumin levels; in some cases it rose, and in others it fell. The two patients M1 and M2 were twins, and, although the jaundice in both was severe, in the less jaundiced child the plasma albumin level fell, while in the more jaundiced child it rose. Nor was any difference between the jaundiced and non-jaundiced infants observed.

The Takata-Ara reaction has been the subject of much discussion since its introduction (Takata and Ara, 1925) and opinions of its value vary considerably. Despite its limitations, the test has been used because it could be performed upon the small amounts of plasma obtainable from the newborn infants and because it is an indication of disturbed protein metabolism, since a positive test is associated with a lowered albumin and a raised globulin fraction. In so far as these are features of liver disease, this test can be regarded as an index of hepatic impairment (Higgins and O'Brien, 1947). Our results are summarized in table 6 and are not conclusive. Of the infants born after a pregnancy of forty weeks, 75 per cent. of those not developing jaundice showed a positive reaction, while of those who did develop jaundice only 66 per cent. had a positive reaction. It would appear, therefore, that there was no significant difference between the two groups. The number of tests made on infants born after a pregnancy of shorter duration was too small for any reliable opinion to be formed.

Of the twenty infants on whom we were able to do Takata-Ara reactions on both foetal and infant blood, the results were identical in twelve. In four the cord blood was positive, and in the other four the infant’s blood was positive. In eight instances the mother’s blood was examined during the first two days of the puerperium, and all gave a negative reaction. The changes in the plasma bilirubin and Takata-Ara reactions during the first ten days of life are recorded (fig. 6). It will be seen that there is no correlation between the changes in the plasma proteins, as measured by the Takata-Ara reaction, and the degree of bilirubinaemia.

It is evident that the changes in the plasma proteins do not reflect the ability of the liver to excrete bilirubin.

**Faecal bilirubin.** It is only natural in the study of icterus neonatorum that attention should be directed to the amount of bilirubinoid pigments excreted in the faeces, since this, in the absence of an extrahepatic obstruction, should be the best measure of the amount of bilirubin passing through the liver cells. In haemolytic anaemia the amounts excreted are increased, whilst in obstructive jaundice the amounts are often much reduced. Hess (1912), using a duodenal catheter, observed the rate and
amount of bile entering the gut in the infant from a few hours after birth to the age of twelve days, and reported very little bile excreted during the first twelve hours and varying amounts during the succeeding twenty-four hours, being profuse when jaundice was marked and scanty or absent when there was no jaundice. His conclusion that there was a defective correlation between excretion and secretion is doubtful in the light of modern knowledge. He records, however, the interesting observation that when jaundice manifests itself it precedes the excretion of bile into the duodenum. Ylppö (1913), in his comprehensive treatise on icterus neonatorum, reported that he found no difference in the total amount of bile pigment excreted in jaundiced and non-jaundiced infants and that the amount bore no relationship to the intensity of the jaundice. A scrutiny of his protocols, however, shows that the average amount of bile excreted in the faeces during the first five days of life does bear a relationship to the presence and degree of jaundice, being lower in the jaundiced cases (table 7). Although some of his arguments cannot be now accepted, Ylppö was one of the first to suggest that the underlying cause of icterus neonatorum was hepatic immaturity. Ross et al. (1937) found that the amounts of faecal bilirubin and urobilin excreted by the non-jaundiced infant were greater than the amounts excreted by the jaundiced infants.

We have made observations on the faecal bilirubin excretion during the first few days of life of jaundiced and non-jaundiced children. Like the previous workers, we did not get a sharp distinction between the amounts excreted by the two groups, great variations in output being present from day to day. This was probably due to the irregularity of the faecal output. Previous workers have expressed their findings in mg. per day or mg. per cent. of faecal weight. It seems to us, however, that the amount of bilirubin formed will depend upon the total blood volume of the infant, and will thus be related to the weight of the infant. It is not to be expected that a child weighing 5 lb. would excrete the same amount of bile pigment as a child weighing 10 lb. Our results, therefore, are expressed in arbitrary units per kg. body weight (table 8). It will be seen that, even when expressed in this way, the results do not reveal a sharp distinction between the jaundiced and non-jaundiced infant, and show great daily variations. The average daily figures, and the average total for the first five days, however, show the tendency to earlier and greater excretion in the non-jaundiced infants with the lowest and slowest excretion in the severely jaundiced ones.

The excretion of faecal urobilin was also studied, but the amounts of faeces obtained preclude accurate quantitative studies. Qualitative tests showed that little urobilin was excreted in the first few days, but it was not possible to detect any difference between the groups.

Discussion

Jaundice (other than the group of obstructive types, to which icterus neonatorum certainly does not belong) may be caused by at least two factors, either singly or in combination; namely, (1) excessive haemolysis in which the amount of bilirubin formed by the breakdown of haemoglobin is too great for the normal liver to excrete, and (2) hepatic insufficiency where for some reason the liver is unable to excrete the amounts of bilirubin normally formed.

Since icterus neonatorum appears during the first week of life, the excessive haemolysis, if it be the cause, must also occur in the first week. The haematological studies, however, show that not only is the rate of decrease of the red corpuscles and haemoglobin greater in the second week when the jaundice is decreasing than it is in the first week when the jaundice is increasing, but also that there is no difference in the rates of fall in the jaundiced and non-jaundiced children. It would appear, therefore, that excessive haemolysis is not the cause of icterus neonatorum.

The question of liver insufficiency is not so easily solved; the presence of some degree of hyperbilirubinaemia in so many infants may suggest a hepatic defect, but it does not explain the occurrence of jaundice in only a proportion of those children. Tests of hepatic function, such as laevulos and sucrose tests, hippuric acid tests, and dye retention tests, cannot be applied to the newborn, and indirect tests, such as plasma protein studies, do not aid the solution. Interest, therefore, becomes centred upon studies of faecal bilirubinoid pigments. The data presented in this study support the conclusions of the other workers that, while there are considerable daily variations in the amounts of bilirubin excreted, there is a diminished excretion of bilirubin by the jaundiced infant as compared with the non-jaundiced infant in the first few days of life. It would appear then that the liver of the newborn varies considerably in its ability to excrete bile, and that in some infants it takes longer to reach an adequate efficiency than in others. This is in keeping with the facts known of other organs of the newborn. The main factor underlying the appearance of icterus neonatorum seems to be a variable liver function which quickly reaches sufficiency.

Conclusions

1. The incidence of icterus neonatorum, as judged by hyperbilirubinaemia of the cord blood or post-natal blood, is 81 per cent. There is a greater chance of a severe and prolonged hyperbilirubinaemia in a premature than in a mature infant.
2. On the basis of haematological findings, the view that the condition results from excessive haemolysis in early post-natal life is rejected.

3. Evidence derived from studies of the plasma proteins and Takata-Ara reactions is not conclusive.

4. Faecal bilirubin studies support the view that icterus neonatorum is due to hepatic immaturity.

We thank Prof. Chassar Moir for access to patients, Dr. R. G. Macfarlane and Mr. J. R. P. O'Brien for help and advice, and the nursing staff of the Radcliffe Infirmary Maternity Department for co-operation.

REFERENCES


TABLE 5
PLASMA BILIRUBIN AND PLASMA PROTEIN LEVELS IN JAUNDICED AND NON-JAUNDICED INFANTS. (M1 AND M2 ARE TWINS.) PLASMA BILIRUBIN IN MG. PER CENT. PLASMA PROTEINS IN GRAMS PER CENT.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 day</td>
<td></td>
<td></td>
<td>1.0</td>
<td>5.7</td>
<td>3.7</td>
<td>2.0</td>
<td>6.4</td>
<td>4.2</td>
<td>0.8</td>
<td>4.6</td>
<td>2.7</td>
<td>0.8</td>
<td>4.5</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 or 4 days</td>
<td></td>
<td></td>
<td>6.0</td>
<td>6.0</td>
<td>4.0</td>
<td>2.0</td>
<td>6.8</td>
<td>3.5</td>
<td>1.7</td>
<td>4.1</td>
<td>2.0</td>
<td>2.0</td>
<td>4.7</td>
<td>3.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 or 8 days</td>
<td></td>
<td></td>
<td>1.2</td>
<td>5.6</td>
<td>3.5</td>
<td>1.0</td>
<td>6.4</td>
<td>4.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Non-jaundiced Infants

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 day</td>
<td>0.6</td>
<td>6.0</td>
<td>4.2</td>
<td>1.0</td>
<td>5.6</td>
<td>3.4</td>
<td>1.8</td>
<td>5.9</td>
<td>4.0</td>
<td>3.4</td>
<td>1.0</td>
<td>6.1</td>
<td>3.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 or 4 days</td>
<td>1.0</td>
<td>5.9</td>
<td>4.3</td>
<td>1.2</td>
<td>5.5</td>
<td>3.7</td>
<td>1.6</td>
<td>5.6</td>
<td>3.8</td>
<td>3.8</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 or 8 days</td>
<td>0.6</td>
<td>6.2</td>
<td>4.1</td>
<td>1.0</td>
<td>6.1</td>
<td>4.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE 6
TAKATA-ARA REACTIONS IN JAUNDICED AND NON-JAUNDICED INFANTS

<table>
<thead>
<tr>
<th>Duration of pregnancy</th>
<th>Total No. of patients</th>
<th>No. of patients with positive Takata-Ara reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-37 weeks</td>
<td>9</td>
<td>4 (66%)</td>
</tr>
<tr>
<td>38-39 weeks</td>
<td>4</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>40 weeks</td>
<td>27</td>
<td>10 (66%)</td>
</tr>
<tr>
<td>40+ weeks</td>
<td>6</td>
<td>1 (100%)</td>
</tr>
</tbody>
</table>

TABLE 7
BILE CONTENT OF FAECES DURING FIRST FIVE DAYS OF LIFE (IN MG.) (FROM YLPPÔ)

<table>
<thead>
<tr>
<th>No jaundice</th>
<th>Moderate jaundice</th>
<th>Marked jaundice</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.16 (case 1)</td>
<td>37.79 (case 3)</td>
<td>8.28 (case 2)</td>
</tr>
<tr>
<td>43.89 (case 5)</td>
<td>21.13 (case 4)</td>
<td>21.7 (case 8)</td>
</tr>
<tr>
<td>32.77 (case 7)</td>
<td>29.95 (case 6)</td>
<td>28.84 (case 10)</td>
</tr>
<tr>
<td>-33.85 (case 9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average 34.9</td>
<td>31.0</td>
<td>19.6</td>
</tr>
</tbody>
</table>

TABLE 8
AVERAGE FAECAL BILIRUBIN EXCRETION (IN ARBITRARY UNITS PER KG. OF BODY WEIGHT)

<table>
<thead>
<tr>
<th>Days of life</th>
<th>No. of patients</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total in first five days of life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-jaundiced</td>
<td>7</td>
<td>9</td>
<td>45</td>
<td>63</td>
<td>19</td>
<td>7</td>
<td>143</td>
</tr>
<tr>
<td>Moderately jaundiced</td>
<td>7</td>
<td>3</td>
<td>24</td>
<td>35</td>
<td>20</td>
<td>34</td>
<td>116</td>
</tr>
<tr>
<td>Severely jaundiced</td>
<td>2</td>
<td>0</td>
<td>7.5</td>
<td>11.5</td>
<td>61</td>
<td>12</td>
<td>92</td>
</tr>
</tbody>
</table>