NUCLEAR JAUNDICE IN NEONATAL (UMBILICAL) SEPSIS WITH JAUNDICE*

BY

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It is a well-known fact that after familial jaundice in the new-born there not rarely remain certain cerebral symptoms which are related to a particular localization of the icteric staining in the brain substance, especially in the basal ganglia.

The first description of icterus gravis neonatorum was given by Orth, and the familial character was stressed by Schmorl. In recent years a number of articles on this subject have appeared. In America it was discussed extensively by Zimmermann and Yannet, and recently by Astrachan, in England by Hawksley and Lightwood, in France by Péhu, Brochier and Wang and in Holland by C. de Lange. The relationship of icterus gravis neonatorum to hydrops foetalis and congenital anaemia has been studied recently by Diamond, Blackfan and Baty and by Parsons, Hawksley and Gittins.

On the cause of the peculiarly localized icteric staining in the brain as well as on the etiology of icterus gravis neonatorum there exist different opinions which have been summarized recently in the articles of Zimmermann and Yannet, of Hawksley and Lightwood, and of Péhu, Brochier and Wang. Next to the question of the etiology of icterus gravis neonatorum and of nuclear jaundice occurring with it, two other questions related to this subject have occupied the attention of both older and more recent investigators. One is the treatment of icterus gravis neonatorum which has been and still is a widely-discussed problem. The other question which is to be specially discussed in the present article is whether nuclear jaundice in the new-born is a peculiarity of icterus gravis neonatorum.

As regards the last-mentioned question there are no cases with autopsy records which can help to solve the problem. There only exists the clinical description of a case of neonatal septic jaundice with extrapyramidal disturbances in motility, given by C. de Lange in which it is suggested that in this form of neonatal jaundice icteric staining of the basal ganglia may also occur. However, no autopsy was possible in this case.

Case Records

Recently it has been possible to observe two infants in whom there occurred neonatal umbilical sepsis with jaundice and typical extrapyramidal disturbances in motility pointing to the existence of a nuclear jaundice. Both infants died after some months; in both an autopsy was performed and the presence of a previous nuclear jaundice could be demonstrated.

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ARCHIVES OF DISEASE IN CHILDHOOD

Case 1. E. C., a male infant, was born spontaneously after a normal pregnancy at full time with a birth-weight of 2,700 gm.

Family History. The parents were healthy and the patient was the sixth child. The first three children were born at full time and are healthy. Then twins were born of which one child is alive and healthy, the other having died at the age of three days. The exact cause of death of this infant is unknown, but it may have been icteric soon after birth.

Clinical History. The patient was taken into the Propaedeutic Clinic when four days old. He had been ill one day. He was sleepy, did not suck, did not cry, had loose stools, black and yellow in colour, was whimpering all the time. According to the parents he became jaundiced shortly after birth. On examination in the hospital when four days old, the infant gave the impression of being seriously ill, the skin and mucous membranes were strongly jaundiced; the infant cried normally. There was conjunctivitis of both eyes, the temperature was 38°C. There existed an umbilical infection with a red coloured swelling at the insertion of the umbilical cord which had not completely separated. The abdominal wall around the umbilicus was swollen and muco-purulent fluid was discharged from it. The liver was slightly enlarged, the spleen was not felt. The urine contained urobilin and bilirubin, together with a trace of albumin. In the sediment were many leucocytes and erythrocytes.

![Fig. 1.-Case 1.](image)

The infant did not take food and tube feeding was necessary. On the fifth day of life distinct symptoms of rigidity were already noted in arms, legs and neck. The umbilical infection slowly subsided over some weeks, but it took about six weeks before the jaundice had disappeared and with it also the enlargement of the liver disappeared. During the time when the jaundice was still severe, the stools for several days were acholic. The fundus oculi was examined several times and found to be normal, but the impression obtained during the further course of the disease was that the infant could not see. The neurological symptoms remained nearly unchanged for several months and had a distinct extrapyramidal character. The head was pushed into the pillow with tendency to opisthotonus. There was strong hypertonia especially of the arms with clasp-knife phenomenon, a general lack of motility, monotonous crying, 'mumbling' of the lips and peculiarly irregular respiration. The hypertonia was especially pronounced at the wrists. In the legs it was distinctly less than in the arms. At the temporo-mandibular joints there was also distinct hypertonia. The arm reflexes were present and equal on both sides. The abdominal reflexes were present; the knee reflexes present and equal. The Achilles reflex was only present at
right side. The pupils reacted to light. The corneal reflexes were present. The child reacted to pain-stimulation over the whole body. A film was made of the movements of the infant which showed clearly the typical disturbances of an extrapyramidal disease. The accompanying figure 1 is taken from this film. The temperature, with the exception of the first two days after admission remained normal during the whole further course of the illness.

The general condition in the beginning improved slightly and then remained about the same for a long time. The stools were soon normal. Tube feeding was omitted after about one week. Some days after admission the infant on three occasions received an intramuscular injection of 10 c.c. of the father's blood. It took more than two months before bilirubin had disappeared from the urine. The sediment of the urine soon became normal. At the age of three months the infant died from bronchopneumonia.

LABORATORY FINDINGS. In the presence of a severe jaundice special attention was paid to the blood picture. During the first weeks there was a strong leucocytosis. The results of the blood investigation at different times are given in table 1. An important fact was that nucleated cells were never found in the blood, even during the first week of the observation.

TABLE 1.

<table>
<thead>
<tr>
<th>AGE</th>
<th>RED CELLS PER C.M.M.</th>
<th>HAMOGLOBIN (SAHL) PER CENT.</th>
<th>WHITE CELLS PER C.M.M.</th>
<th>ERYTHROBLASTS</th>
<th>BLOOD PLATELETS</th>
<th>ICTERIC INDEX</th>
<th>V.D. BERGH</th>
<th>RETICULOCYTES PER CENT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 days</td>
<td>—</td>
<td>—</td>
<td>28,300</td>
<td>0</td>
<td>normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>13 , ,</td>
<td>4,720,000</td>
<td>113</td>
<td>36,100</td>
<td>0</td>
<td>normal</td>
<td>90 dir. +</td>
<td>indir. +</td>
<td>—</td>
</tr>
<tr>
<td>23 , ,</td>
<td>3,360,000</td>
<td>68</td>
<td>28,900</td>
<td>0</td>
<td>normal</td>
<td>50</td>
<td>—</td>
<td>14½</td>
</tr>
<tr>
<td>1 month</td>
<td>—</td>
<td>66</td>
<td>14,100</td>
<td>—</td>
<td>—</td>
<td>40</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1 ½</td>
<td>—</td>
<td>68</td>
<td>—</td>
<td>—</td>
<td>normal</td>
<td>40</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>4,200,000</td>
<td>71</td>
<td>16,100</td>
<td>0</td>
<td>normal</td>
<td>5</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Further, the increase in the mean diameter of the erythrocytes, found by the Price-Jones method in cases of icterus gravis neonatorum during the first week of the illness¹, was absent in this case and during the further course a greater diminution in mean diameter occurred than in the normal child, probably due to severe haemolysis*. The decrease of the haemoglobin content as compared with normal figures was only small; there was no question of a hyperchromic anaemia. A decrease of thrombocytes as often found in icterus gravis neonatorum was absent during the whole course of the disease and there was, further, no haemorrhagic tendency. The number of reticulocytes, nearly always increased in icterus gravis neonatorum during the first weeks, was normal here. As regards the van den Bergh reaction it was directly and indirectly positive, as is generally the case in icterus gravis neonatorum. The Wassermann and Sachs-Georgi-tests in the blood of the infant and of the parents were negative.

The possible effect of the septic jaundice on the liver was investigated during life by performing some liver function tests. The protein spectrum of the blood plasma was studied twice, at the age of two-and-a-half months

* Compare the same findings in icterus gravis.
and directly before death. The results are given in table 2, which also contains the results obtained in some control infants of about the same age and in the second patient. It is noteworthy that a definite increase was noticed even at this age in the globulin content, which resembles the fairly constant increase of globulin in parenchymatous liver affections. The Takata-Ara test and the sedimentation rate of the erythrocytes, the results of which show a definite parallelism to the globulin content, were also increased in this infant. As regards the increased sedimentation rate the relation to the increased globulin content may be deduced from the fact, that it was about the same in the defibrinated blood as in the non-defibrinated blood. The blood-cholesterol was normal. The fasting blood sugar at the age of ten weeks was 0.081 per cent.; the galactose-test (investigation of urine) and the fructose-test (blood-sugar curve) at the time gave normal figures.

TABLE 2.

PROTEIN-SPECTRUM.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Total Protein per cent.</th>
<th>Fibrinogen per cent.</th>
<th>Globulin per cent.</th>
<th>Albumin per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pat. E.C., 2½ months</td>
<td>61.2</td>
<td>—</td>
<td>18.9</td>
<td>42.3</td>
</tr>
<tr>
<td>... nearly 3 months</td>
<td>67.8</td>
<td>4.1</td>
<td>23.2</td>
<td>40.5</td>
</tr>
<tr>
<td>Healthy baby ...</td>
<td>...</td>
<td>...</td>
<td>—</td>
<td>4</td>
</tr>
<tr>
<td>... ...</td>
<td>59.8</td>
<td>—</td>
<td>16.1</td>
<td>43.7</td>
</tr>
<tr>
<td>... ...</td>
<td>61.2</td>
<td>—</td>
<td>14.1</td>
<td>47.1</td>
</tr>
<tr>
<td>... ...</td>
<td>50.3</td>
<td>—</td>
<td>10.2</td>
<td>40.1</td>
</tr>
<tr>
<td>Pat. M.H., 13 days ...</td>
<td>57.9</td>
<td>—</td>
<td>18.3</td>
<td>37.2</td>
</tr>
</tbody>
</table>

Pat. E.C., 12 weeks. Takata-Ara test—positive. Sedimentation rate 12, in defibrinated blood also 12 (micro-method; normal value 6-8 mm.)

Laevulose test normal.


POST-MORTEM EXAMINATION at the Pathological-Anatomical Institute (Prof. H. T. Deelman), twenty-four hours after death. Pathological details of the internal organs noted were:—Lobular pneumonia, haematoma of cardiac valves, left-sided hydronephrosis. As concerns the liver and spleen the following was communicated:

The liver was somewhat enlarged (170 gm.), had a firm consistency and sharp edges. The umbilical vein for the greater part was obliterated, as also the ductus venosus. The capsule was humid, glossy, dark brown, with no haemorrhages. The cut surface was smooth, moist, with liver markings visible. The microscopical investigation of frozen sections showed that there was a slight central fatty change. The portal spaces contained some young connective tissue cells. No myeloid tissue was seen. In some of the bile ducts there were bile thrombi; in some of the liver cells, as well as in some of the portal spaces, there was a fine-granular pigment which did not give a positive iron reaction. Glycogen staining did not show any abnormalities.
NUCLEAR JAUNDICE

The spleen was slightly enlarged, weight 20 gm. The capsule was smooth, glossy, spotted and blue-red. The cut surface was regular, moist, dark red with small grey follicles and no trabeculae. Microscopical investigation showed normal follicles; the trabeculae showed no abnormalities. Brown pigment was present in the pulp cells. From the investigation of preparations stained to demonstrate iron, it appeared that there was a fair degree of siderosis.

MORbid Anatomy of Brain (Anatomical Laboratory of the Neurological Clinic). Macroscopical investigation: the cerebrum was pale, not yellow, very soft, symmetrical and externally showed no abnormalities. After section it appeared that cerebrospinal fluid was present in normal amount; it was uncoloured. There was no hydrocephalus. On section no icteric staining of the basal ganglia was seen, but on inspection with a magnifying glass it appeared that striation of the globus pallidus was absent at both sides.

Microscopical investigation: the cerebrum was investigated by serial sections after Kulschitzky-van Gieson and preparations of different parts of the cerebral cortex and of the basal ganglia were stained after Nissl, and with haematoxylin-eosin. To some portions of the basal ganglia staining with Sudan III and Penfield and Holzer’s method were further applied. The study of the serial sections showed that there was much demyelination of the globus pallidus (fig. 2) and of the corpus subthalamicum (fig. 3) on
both sides. The demyelinization was greatest at the internal segment of
the globus pallidus and appeared to increase in the occipital direction. The
putamen only showed slight demyelinization, whereas the nucleus caudatus
proved to have normal fibre proportions. From the cell preparations it
appeared that in the regions of demyelinization there was a severe loss of
ganglion cells, followed by a moderate gliosis. It was striking that generally
the demyelinization was more intense than the loss of cells; this was especially
evident on inspection of the corpora subthalamica, which still showed several
well-formed ganglion cells, whereas the myelin sheaths had almost com-
pletely disappeared. No signs of inflammation, haemorrhages, nor
accumulations of pigment or fat were seen. The cell preparations of different
parts of the cortex did not show definite changes. The substantia nigra was
normal. The investigation of the fibre preparations in serial sections showed
that the corpus callosum, especially its frontal part was abnormally thin,
and it was hardly possible to discover the fornices. The explanation of the
latter fact was made more difficult by the incomplete myelinization of these
parts of the brain in the young infant. Comparison with the brain of an
infant of about the same age indicated, however, that here was a definite
hypoplasia of the corpus callosum and of the fornices.

Case 2. M. H., a female infant, born spontaneously after a normal
pregnancy, at full time, had a birth-weight about 4,000 gm. There was no
asphyxia and no icterus at birth.

Family history. Mother was healthy; father suffered from bronchial
asthma. Two other children were normal. There had been no miscarriages.

Clinical history of the patient. The patient was taken into the
Propaedeutic Clinic when three days old. Twelve hours after birth the
father had noticed that the infant was slightly icteric. On the following
day the jaundice had increased and subsequently deepened. On the second
day of life the infant refused to suck. On examination in the hospital the
baby was deeply icteric, of an orange-yellow colour, and somewhat drowsy.
Distinct rigidity was noted in both arms. The temperature was 37.5° C.
The heart and lungs were normal. The liver was slightly enlarged, the
spleen not palpable. The umbilicus was thickened, red and infiltrated;
above the umbilicus there was infiltration of the abdominal wall. The stools
were normal. The urine was deep dark brown. Thus also in this case there
existed a distinct umbilical infection. The urine contained bilirubin,
together with a trace of albumin, and some leucocytes and erythrocytes in
the sediment. The child was given fluid subcutaneously and frequent small
feeds.

On the second day after admission the infant was very ill; the rigidity
had extended. The stools were undigested and slightly pale. The
umbilicus was much infiltrated, the liver more enlarged, the spleen not palpable. The
fontanelle was not depressed. There were some haemorrhagic spots on the
face.

On the third day after admission the jaundice was extremely severe.
The neurological picture showed a varying hypertonia, especially of the arms.
This hypertonia was strongest in the joints of wrists and fingers; the hands
were constantly clenched (fig. 4). The neck and back were stiff and there
was a tendency to opisthotonus. The patellar reflex was present on both
sides. The Achilles reflex was absent. The reflex of Babinski was present
on both sides which is normal at this age. No abdominal reflexes and no
arm reflexes could be obtained. The pupils reacted normally. Fairly
strong dermographia was present. Pain-stimulation produced a reaction
over the whole body.

It took a long time (about six weeks) before the jaundice disappeared;
the umbilical infection also slowly cleared up. The neurological symptoms
remained constant. The fundus oculi in this patient also showed no abnormalities; this infant also probably could not see. At the age of four months the infant died from bronchopneumonia. The liver had remained palpable two finger breadths below the costal margin; the spleen was also slightly enlarged.

**Fig. 4.—Case 2.**

**Laboratory findings.** The stools contained bile pigments and the urine contained bile pigments and a trace of albumin for several weeks. The results of the blood examinations at different times in this case are given in Table 3. From this it appears that also in this case there was no

<table>
<thead>
<tr>
<th>Age</th>
<th>Red cells per c.mm.</th>
<th>Haemoglobin (sahli) per cent.</th>
<th>White cells per c.mm.</th>
<th>Erythroblasts</th>
<th>Blood-platelets</th>
<th>Icteric index</th>
<th>v.d. Bergh</th>
<th>Reticulocytes per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 days</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0</td>
<td>normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>3,840,000</td>
<td>86</td>
<td>16,200</td>
<td>0</td>
<td>normal</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>13</td>
<td>3,350,000</td>
<td>65</td>
<td>24,000</td>
<td>2</td>
<td>normal</td>
<td>100</td>
<td>dir. +</td>
<td>—</td>
</tr>
<tr>
<td>25</td>
<td>—</td>
<td>57</td>
<td>17,000</td>
<td>0</td>
<td>normal</td>
<td>60 dir. +</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>6 weeks</td>
<td>2,540,000</td>
<td>59</td>
<td>16,200</td>
<td>2</td>
<td>slight increase</td>
<td>normal</td>
<td>—</td>
<td>4</td>
</tr>
<tr>
<td>*8</td>
<td>2,990,000</td>
<td>67</td>
<td>17,600</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>24</td>
</tr>
<tr>
<td>3 months</td>
<td>3,670,000</td>
<td>80</td>
<td>8,400</td>
<td>0</td>
<td>normal</td>
<td>—</td>
<td>—</td>
<td>6</td>
</tr>
</tbody>
</table>

*Had been given 300 mgm. of reduced iron for 1 week.*
question of an erythroblastæmia. The blood platelets were not increased; the number of reticulocytes was not abnormally high. The mean diameter of the erythrocytes on the day of admission was slightly decreased as compared with normal figures; an increase as recorded in icterus gravis neonatorum was thus absent. The van den Bergh reaction was directly and indirectly positive. The Wassermann and Sachs-Georgi tests in the blood of the infant and in that of the parents were negative. The protein spectrum at the age of fourteen days also here showed a slight increase of the globulin content. The Takata-Ara test was negative, as also was the result of the galactose test. A blood culture at the age of twenty-two days had a negative result. The morphological blood study of the parents gave normal results, the fragility of the red blood corpuscles was also normal in both parents. In view of the rare occurrence of cystic changes in the bones in icterus gravis neonatorum (Braid') an x-ray study of the bones was made in this second patient, but no changes were found.

A POST-MORTEM EXAMINATION was made twenty-four hours after death, at the Pathological Institute. The pathological diagnosis of broncho-pneumonia was made. As concerns the liver and spleen the following was communicated:—

The liver was slightly enlarged (250 gm.), had a normal shape and elastic consistency; the colour was brown-violet. The capsule did not show abnormalities. The cut surface had a dark yellow-brown colour with normal design. The vessels and bile ducts did not show abnormalities. The microscopical examination of sections stained with Sudan III demonstrated a fatty change consisting of large and small droplets and principally of peripheral localization. In the sections stained with haematoxylin-eosin there was a fairly large amount of bile pigment between the cells. Spread all through the sections there was also much blood pigment (iron staining). Nowhere could be seen myeloid tissue, nor signs of fibrosis.

The spleen also was slightly enlarged (weight 18 gm.). The capsule was smooth, glossy, moist and transparent. On the cut surface the follicles were visible in the normal way. The microscopical investigation demonstrated that the spleen contained much blood; blood pigment also could easily be shown here.

MORBID ANATOMY OF THE BRAIN (Anatomical Laboratory of the Neurological Clinic).

Macroscopical investigation. The brain in this case also did not show abnormalities on external inspection. After cutting the brain and inspection with magnifying glass it appeared however that there existed a slight icteric staining of the globus pallidus and of the corpus subthalamicum on both sides. Also here it appeared that the striation of the globus pallidus was absent on both sides. There was no hydrocephaus and the cerebrospinal fluid was uncoloured.

Microscopical investigation. The cerebrum was investigated in serial sections stained after Weigert Pal–van Gieson. Nissl and haematoxylin-eosin preparations were also prepared from several pieces of the cerebral cortex and of the basal ganglia. Finally some pieces of the basal ganglia were stained by Sudan III and by the method of Penfield and Holzer. The pictures obtained showed a striking resemblance with those of case 1. Also here there existed a marked demyelination of the globus pallidus (fig. 5) (which was most striking in the medial segment), and of the corpus subthalamicum (fig. 6) on both sides, whereas the putamen and nucleus
Fig. 5.—Demyelinization of the globus pallidus (×) in case 1. (Weigert-Pal-staining.)

Fig. 6.—Demyelinization of the corpus subthalamicum (×) in case 2. (Weigert-Pal-staining.)
caudatus remained free. Here also there existed in the demyelinated regions a marked loss of ganglion cells (with moderate gliosis), which was however far less than the loss of fibres. Signs of inflammation as well as haemorrhages and fatty changes were absent.

The similarity with case 1 was also evident as regarded the structure of the corpus callosum and fornices which here also showed a slight but undeniable hypoplasia.

**Comment**

I. In both infants there existed an analogous morbid picture with nearly the same course of the disease. The most important characteristics of this morbid picture may be summarized as follows:

(a) Development of an extrapyramidal neurological disturbance in connexion with a severe jaundice which arose shortly after birth.
(b) Absence of cases of icterus gravis neonatorum, of hydrops foetalis or of anaemia gravis of the new born, in both families.
(c) Definite umbilical infection.
(d) In both cases erythroblastema and at the autopsy also erythroblasticosis which occur in the early stage of nearly every case of icterus gravis neonatorum were absent. The number of thrombocytes was not decreased, the number of reticulocytes was not increased, and increase of the mean diameter of erythrocytes, recorded in the early stage of icterus gravis, was absent in both cases*. These and other points of difference between the clinical and laboratory findings in the two patients with icterus gravis neonatorum are given in table 4.

| TABLE 4. To show the similarity to and differences from icterus gravis neonatorum of the cases here described. |
|-------------------------------------------------|-----------------|
| Icterus present at birth or arising shortly after birth | E.C. | M.H. |
| Rapid increase of intensity of the icterus | + | + |
| Other cases in family, or of hydrops foetalis or of congenital anaemia | ... | ... |
| Drowsiness during the period of severe icterus | + | + |
| Pale stools | ... | ... |
| Bilirubinuria | ... | ... |
| Bilirubinaemia | ... | ... |
| Van den Bergh test in serum, mostly directly or indirectly | + | + |
| Liver enlarged | ... | ... |
| Spleen at least temporarily much enlarged | ... | ... |
| Anaemia (often hyperchromic) | ... | ... |
| Purpura | ... | ... |
| Erythroblastema during first days of life | ... | ... |
| Megalocytosis with increase of mean diameter, especially during the first week of life | ... | ... |
| Decrease in mean diameter in later stage | ... | ... |
| Thrombocytes decreased | ... | ... |
| Reticulocytes increased | ... | ... |
| Toxic blood picture | ... | ... |
| Symptoms of nuclear jaundice | ... | ... |

* Of course this increase was observed in cases of icterus gravis neonatorum in which there was erythroblastema. Whether it would be present in those rare cases of icterus gravis neonatorum without erythroblastema or not has never yet been studied.
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(e) In some cases recovery from icterus gravis neonatorum may be accompanied by cirrhotic changes in the liver. During life both of the present infants showed some signs of a parenchymatous liver affection (increase of the globulin content of the serum in both cases, with positive Takata-Ara test and increased sedimentation rate in the defibrinated blood in case 1), which corresponded in case 1 with a slight hepatic fibrosis found at the autopsy.

(f) Demyelinization and loss of ganglion cells in the globus pallidus and in the corpus subthalamicum on both sides (only in one of the two cases a slight icteric staining of the basal ganglia macroscopically was still visible at the autopsy; this causes no surprise as both infants remained alive for a long time after the jaundice had disappeared.)

II. As regards the cause of nuclear jaundice in icterus gravis neonatorum different opinions have been given in the course of years. A survey of these theories may be found, e.g., in the recent article of Zimmermann and Yannet. The present cases give further information on the histo-pathological side of this problem as the preparations only show the residual effect (demyelinization and loss of cells) and the bile pigment originally present has completely or almost completely disappeared. It can only be said that these cases prove that nuclear jaundice is not definitely related to icterus gravis neonatorum, but may also occur in septic jaundice of the new born.

III. From the literature (e.g. from the data of Schmorl who only found six cases of nuclear jaundice in 120 icteric new-born infants, making no distinction between familial and septic forms) it must be concluded that nuclear jaundice is very frequent in icterus gravis neonatorum, but on the contrary is exceptional in neonatal sepsis with jaundice. To explain this fact the symptoms of hypoplasia of the corpus callosum and fornices seen in both these cases, may be noted. These must be explained as a disturbance in development. It is a well-known fact that in brains which show disturbances in development the function of the barrier between blood and cerebrospinal fluid is insufficient. Perhaps this may explain why in these cases a nuclear jaundice developed. A similar state of affairs is seen in the frequent occurrence of encephalitis in infants with a congenitally malformed brain.

Summary

The clinical and pathological description of two cases of septic jaundice of the new-born (umbilical infection) combined with nuclear jaundice, giving rise to an extrapyramidal neurological syndrome, is recorded.
REFERENCES
10a. Hawksley, J. C., *Personal communication*.