4. The clinico-pathological features of endometrioma are described, and stress is laid on the multiple character of the lesions resulting from endometriosis.

5. Surgical treatment is discussed, and radical measures are advocated for all but the earliest cases.

6. Statistics are quoted from a personal series of 137 cases operated on during the last five years, and individual cases referred to where necessary.

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JAUNDICE IN CHILDHOOD*

BY

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Although, strictly speaking, the term "jaundice" implies staining of the skin, mucous membranes, or conjunctivae, such general staining by bile-pigments is always associated with an excess of bilirubin in the blood; and as such excess is the most constant finding, and precedes the staining of the tissues, it is convenient to regard excess of bilirubin in the blood as the measure of the condition under discussion. Before dealing with the various conditions, which in children are characterized by jaundice, it is useful briefly to review the mechanism of its production.

The modern view, well supported by experimental and clinical evidence, suggests that bilirubin is formed from haemoglobin by the cells of the reticulo-endothelial system, chiefly by those of the spleen, liver and bone-marrow. The bilirubin so formed is further changed by the polygonal cells of the liver and excreted through the bile-channels into the alimentary tract. The two forms of bilirubin are not physico-chemically identical, and can be distinguished by the test devised by Hijmans van den Bergh.¹ The bilirubin produced by the action of the endothelial cells gives an "indirect reaction" to the test, while that formed by the action of the polygonal cells gives a "direct" reaction. When the latter accumulates in the circulating blood, it is excreted as bile by the kidneys, but the former variety is rarely so excreted, the urine containing only an excess of urobilin. According to this conception, jaundice may be produced by (1) obstruction at any point in the biliary channels, the bile stagnant in the ducts being re-absorbed into the blood stream (van den Bergh's reaction "direct"); (2) disease of the polygonal cells, in which bilirubin, unchanged by and not excreted by these cells, passes into the general circulation (van den Bergh's reaction "indirect"); (3) disease of the liver, which may in one part involve the polygonal cells, and in another cause obstruction of the bile-channels (van den Bergh's reaction "biphasic"); and (4) excessive haemolysis, with the production of more bilirubin than the polygonal cells can change and excrete, the excess passing into the general circulation (van den Bergh's reaction "indirect").

Certain types of jaundice which will be discussed in this paper are undoubtedly due to toxins, and these types illustrate very well the important principle, perhaps even now not sufficiently realized in our attempts to understand and combat disease, that seldom if ever are morbid processes

due to one factor only: practically always it is necessary to consider what may be termed the "seed" and the "soil," and often, in addition, factors which we may liken to "fertilizers" in the parallel suggested. The liver is markedly prone to suffer from the presence of certain toxins in the circulating blood, but there is an equally marked tendency for some individuals to suffer more than others. As an example of this idiosyncrasy may be mentioned the well-known tendency of certain people to become jaundiced after comparatively small doses of atophan or novarsenobillon. But, in addition to this personal idiosyncrasy, the same individual may show a greater effect at one time than at another. During pregnancy, for example, the function of the liver appears to be more easily upset. Age, too, exerts an influence: other conditions being equal, the child's liver is more prone to suffer than that of the adult, though the effect may be counterbalanced by the greater tendency to repair in the former. Poisons which exert their toxic effects on the liver usually show a maximal effect in the infant.

The study of jaundice in childhood is therefore of considerable value, and deductions drawn therefrom may often with advantage be applied to corresponding conditions occurring in adults.

It follows from what was said in the opening paragraphs of this paper that jaundice is a symptom or sign found in a variety of conditions, and is in no sense to be regarded as a disease in itself. Some of the conditions which will be discussed are clinically quite distinct and comparatively easy of diagnosis: others, though fairly obvious in typical cases, show a tendency to merge into related conditions, of totally different prognosis: as an example of the latter class may be instanced the cases of acute or sub-acute necrosis of the liver which appear to have commenced as so-called "catarrhal jaundice."

JAUNDICE OF THE NEWLY BORN

Jaundice is such a common sign during the early days of life that it is convenient to discuss these cases as a group.

Icterus Neonatorum (Physiological Jaundice)

Obvious jaundice occurs in a considerable percentage of infants during the early days of extrauterine life. In a still larger percentage it is masked by the pink coloration of the skin, and in these it can be rendered apparent by carefully emptying the capillaries of blood. Probably all infants at birth show an excess of bilirubin in the blood: this was so in every case of a large series I personally investigated, the results being in agreement with those obtained by Bang² and Ylppo.³ The average concentration of bilirubin was 1:75,000, the normal in the adult being 1:400,000 to 1:1,000,000. Obvious jaundice does not appear before the second day, when it can usually be seen on the face, chest and back. It then makes its appearance on the upper parts of the limbs and on the abdomen. The sclerotics are the next to show the coloration, which appears last on the hands and feet. Mild cases may only show staining of the face and chest. The colour deepens for a few days and then gradually fades, fading taking place in the reverse order to the appearance, except that the sclerotics and the nails of the fingers and toes may retain the colour for a considerable time. The condition is more likely to be marked in premature babies. Except for a little drowsiness when the jaundice is deep, the health of the infant appears to be entirely unaffected, and the condition should be regarded as physiological. When an opportunity is obtained for post-mortem examination, as when death follows a birth-injury, it is of interest to note that staining of the tissues involves cartilage, cerebro-spinal

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fluid, and the nuclei of the brain, parts not stained in other forms of jaundice.

Many suggestions have been made in order to explain the origin of the jaundice—cooling of the skin after birth, compression of bile-ducts by dilated liver veins, re-absorption of bile from the alimentary tract, post-natal infection, and obstruction of the bile-ducts by mucus. Obstruction has not been demonstrated; indeed, all the evidence is in favour of a considerable flow of bile into the alimentary tract; and no striking evidence has been adduced in favour of infection. Observers were naturally impressed by the advent of jaundice after birth and sought post-natal causes to account for it.

In an attempt to investigate this problem some seven years ago, I was impressed by the high value of the bilirubin in the umbilical vein at birth. While the work was being conducted, an opportunity occurred to examine a case of paroxysmal haemoglobinuria; an attack was induced by immersing one of the patient's legs in cold water; although haemoglobin did not appear in the urine till six hours later, the plasma gave a well-marked indirect reaction to van den Bergh's test within half an hour. It appeared that quite a short time was sufficient for the production of an excess of bilirubin in the blood, and it was therefore possible that in the case of the newborn infant the jaundice was due to changes occurring during parturition.

Through the kindness of a number of obstetric surgeons, I was able to obtain specimens of blood from infants delivered by Caesarean section under spinal and under general anaesthesia. These all showed quantities of bilirubin in the blood of the same order as was found in infants delivered *per vias naturales*. In a series of cases of induced abortion, bilirubin was present in small amounts between the fourth and fifth months of gestation, and in increasing amounts up to term. After birth, there is a sharp rise in the value up to the third or fourth day, and then a gradual decline, till at the fourth to the sixth week the normal value is attained. It would appear that the post-natal rise differs in degree only from that occurring ante-natally. Before birth, the foetus has two possible methods of excretion—through its liver and its own alimentary tract, and through the placenta into the circulation of the mother. At birth, the second method is withdrawn, and the liver of the infant must take upon itself the entire work of excretion. It is possible that the liver may be some time after birth before assuming its full function; the presence of bile-salts in the pericardial and other body-fluids supports such a supposition, and similar delays are found in the case of the kidney and of the alimentary tract. Such a supposition might explain the degree of the post-natal rise.

There is another consideration which bears on this problem. During intrauterine life, haemosiderin is deposited in certain organs of the foetus, and a study of the age of the foetus in relation to the extent of the deposit suggests a parallel to the bilirubinaemia. Immediately after birth there is a considerable degree of haemolysis, and this may also account for the increase in bile-pigment in the blood after birth. Such an explanation would regard the condition as being allied to a haemolytic anaemia. In work carried out in association with M. Maizels,⁴ it was found that in pernicious anaemia and other haemolytic anaemias there was a large difference in acidity between the red cells and plasma, the degree of this being correlated with the degree of haemolysis. In all these cases, the difference was due to increased acidity of the cells, that of the plasma being about normal. In a few observations I have had the opportunity of making on blood from the umbilical vein of newborn infants, the reaction of *both* plasma and cells

has been more acid than normal, the *difference* being about equal to the normal difference found in the adult. Further observations tend to show that an increase in the alkalinity of the plasma has comparatively small immediate effect on the reaction inside the red cells. Under conditions where the plasma becomes more alkaline, a condition of the red cells would be established, comparable to that found in haemolytic anaemias—i.e., there would be a large difference in acidity between the red cells and plasma. In the placenta, where the plasma of the foetus becomes oxygenated by the mother's blood, such conditions would be to some extent realized; and after birth, when pulmonary respiration is established, to a much more marked extent.

The observations on which these remarks are based are few, and estimations other than on blood from the umbilical vein are exceedingly difficult, but if further work confirms them, a definite theory can be advanced for the explanation of icterus neonatorum, an explanation certainly independent of bacterial invasion of the alimentary tract, which is the basis of a theory still held by a number of authorities.

Icterus Gravis Neonatorum

I have discussed at some length the benign icterus neonatorum because of its similarity to another condition, which if untreated is almost invariably fatal. This is a condition tending to recur in successive members of the same family, though often the first-born escapes. Of 130 cases collected by Sir H. Rolleston⁵ in 1920, 77 per cent. proved fatal, and in an account which I published in 1929,⁶ 83 per cent. of 90 untreated cases occurring in 17 families had been fatal. The condition appears to be commoner than the published figures suggest. From the returns of the Registrar-General for England and Wales, it appears that during the seven-year period from 1921-1928, at least 1,800 infants died of jaundice during the first four weeks of life, without obvious cause, such as sepsis; syphilis, or obliteration of the bile-ducts, and in arriving at this figure all deaths from such conditions as umbilical sepsis have been deducted from the figures for jaundiced infants—although only a proportion of these develop jaundice: the figure, therefore, probably errs in being too low. Personal communications from doctors, and the histories in more recent cases which I have seen, suggest that many lives are still lost from a condition which is in many cases probably open to successful treatment.

The jaundice usually appears within twenty-four hours, and may be noted a few hours after birth, or even in a few instances at birth. The colour then rapidly deepens. At birth, apart from possible jaundice, the infants appear strong and healthy, but with the increasing jaundice become drowsy, take the breast poorly, and lose weight. The liver and spleen are not usually enlarged; indeed, it is suggested that cases with considerable enlargement of these organs probably belong to a different group, for there can be little doubt that the group is a composite one. The temperature usually tends to be sub-normal, but occasional cases show a considerable rise; here, again, in several instances there has been evidence of maternal toxæmia during the pregnancy—a condition strikingly absent in the majority of cases—and the cases probably belong to a separate group; from the point of view of treatment it seems important to recognize this differentiation. The stools are normal in colour and the urine is dark, containing an excess of urobilin and at times bile. Haemorrhages may occur near the end, particularly in the subcutaneous tissues over the forehead, where they give rise to a bruised appearance, not to be confused

with the spider-naevi which are common in all jaundiced babies. The infants become increasingly anaemic. Towards the end there are often attacks during which the infant's face shows a peculiar shade of greyness mixed with the icteric tint. In these attacks respiration is very shallow and the pulse is barely perceptible. Often there are convulsions, and the child usually dies in coma within three weeks of birth. In all cases the Wassermann reaction is negative, and at necropsy there is nothing to suggest a syphilitic basis: indeed, the post-mortem appearances are very like those of the simple icterus neonatorum.

Excluding such cases as those of Nason,⁷ Tylecote,⁸ Rolleston,⁹ Smith,¹⁰ and Ritchie,¹¹ and a number of cases within my own experience in which there was evidence of maternal toxæmia, the resemblance to physiological jaundice is sufficiently striking to suggest a common basis. Assuming a delay in assumption of hepatic function in the simple variety, a lesser competency on the part of the liver or an increased haemolysis in icterus gravis might result in a fatal toxæmia. Working along these lines, in young rabbits it was found that injection of haemolytic products invariably retarded growth, though proportionate amounts in older animals appeared to have little effect: in the pregnant animal the procedure resulted in the death of the foetuses *in utero*, and in two such cases in which the pregnancy was early there was the formation of a mole. It is of interest that in the animals which survived, the teeth became green, and remained so until the part of the tooth affected was worn away; green teeth have been reported in icterus gravis by Thurstfield and Langmead.¹²

If toxæmia be due to haemolytic products, treatment should be directed to decreasing haemolysis. Experimental work suggested that serum might have this effect, and for this reason human serum has been given intramuscularly in these cases in amounts of about 15 c.cm. daily for three or four days. In 22 out of 23 cases I have personally treated, the recovery has been perfect, and the remaining case was practically *in extremis* when seen. In marked examples of simple icterus neonatorum, serum seems to have led to more rapid subsidence of the condition. In other cases in which the liver and spleen were enlarged, or in which the infant was pyrexial, the results have not been so good: the jaundice has subsided, but the infant in some cases has died of complications, such as cerebral haemorrhage or haemorrhage into the suprarenals. In these cases I have for some time associated the injection of serum with the inunction of mercurial ointment, which in many cases gives good results, though not so strikingly satisfactory as in the main group, in which, if recovery occurs, it appears to be complete. One such case is of sufficient interest to record.

The child was born at full term. Jaundice appeared within twenty-four hours and progressively deepened. When seen on the fourth day, the lower edge of the liver extended to the umbilicus: it was fairly hard, but not as hard as that usually found in obstruction of the bile-ducts. The spleen could be felt one inch below the costal margin. The head was retracted, and the fontanelle was rather full. Meconium had been passed, and the stools contained bile. The child was comatose. Lumbar puncture showed bile-stained fluid containing blood. The Wassermann reaction was negative. The child was treated with injections of serum and with daily inunctions of mercurial ointment. She appeared to make a good recovery and liver and spleen became impalpable: now, two years later, she shows a well marked cerebral diplegia.

It is of interest that Spiller¹³ has reported four cases of cerebral diplegia in association with icterus gravis. I have twice encountered it in association with congenital obliteration of the bile-ducts, of which the case recorded may have been another example. Head retraction does not necessarily mean haemorrhage: one of the most

marked cases I have seen in association with jaundice was one of obliteration of the ducts, and at necropsy there was no evidence of haemorrhage, but intense bile-staining of the cerebral nuclei, especially the lenticular nuclei.

Congenital Obliteration of the Bile-ducts

In this condition, jaundice is usually manifest on the second day and is progressive, though the degree is variable. Meconium is usually passed, and this is followed by pale stools. Occasionally the stools are white from the beginning: on the other hand, the passage of meconium may be followed by pale stools which contain a fair amount of bile pigment. The urine is dark and contains bile. The liver is large, even after death, thus contrasting with the enlarged liver of obstructive jaundice at a later age; but the clinical observation which impresses one most is the extreme hardness of the organ. The spleen is also enlarged in the majority of cases. The condition runs a variable course, and the infant is often surprisingly fit till late in the disease, when wasting may be marked. There is, however, a great tendency to haemorrhages from the mucous membranes and subcutaneously. Often, too, there are periods of pyrexia, sometimes accompanied by convulsions, though these usually only occur terminally. According to Weber,¹⁴ the cerebro-spinal fluid does not contain bile, but in cases of my own, in which death has occurred early, the fluid has been stained, and in one case referred to above the cerebral nuclei were very deeply stained. At necropsy there is usually complete obstruction to the flow of bile, the obstruction in the majority of cases being extra-hepatic; the lower part of the common bile-duct may be represented by a fibrous strand. The lumina of the ducts above the obstruction are not dilated, thus contrasting with the condition usually found in adults as the result of obstruction. The hard, enlarged liver shows evidence of biliary cirrhosis, and is often dark green in colour. The glands in the portal fissure may be enlarged. Syphilis has been suggested as a cause, but there is no evidence for this either in the Wassermann reaction on parents and infants, or in section of the organs after death.

Two main theories have been advanced to account for the condition. First, that supported by Thomson,¹⁵ Beneke¹⁶ and Milne¹⁷ suggests a developmental narrowing of the ducts, giving rise to partial obstruction, predisposing to a catarrhal condition which completes the obstruction. The stagnant bile is presumed to be toxic, and this, it is suggested, gives rise to the cirrhosis. In support of the theory it may be mentioned that the condition has on rare occasions been associated with other congenital abnormalities, as for example hypertrophic stenosis of the pylorus (Barker and Mackey),¹⁸ and in two cases recorded by Poynton and Wyllie¹⁹ in association with congenital heart lesions—one of these also showing deformity of the feet and the other occurring in a mongol.

The experiments of Rous and Larimore²⁰ are of interest in the discussion. By obstructing the large bile-ducts they produced a stellate fibrosis around them; obstruction in the intra-lobular canaliculi led to a diffuse intra-lobular cirrhosis; while obstruction in the small bile-ducts produced a pure unilobular cirrhosis. From the experimental point of view it would appear that the lesions, if primary in the ducts, would have to be multiple, though perhaps it is unfair to compare the foetal liver with that of experimental animals. The other suggestion, supported by Rolleston,²¹ is that toxins passing from the mother through the placenta reach the foetal liver through its double circulation and are excreted into the bile-ducts: in their passage through the liver they give rise to a mixed cirrhosis, and after excretion give rise to inflammation of the

ducts, and ultimate obstruction. There is much in the latter theory which fits in with the clinical facts: the lesion is undoubtedly progressive in the majority of instances, and occasionally a patient dies before obstruction is complete, but cirrhosis is found to be advanced. On the other hand, one would perhaps expect the mother to show some evidence of the toxæmia, and this is surprisingly absent; other conditions, however, which markedly affect the foetal liver—for example syphilis—may have very little obvious effect on the mother.

Treatment, in the main, has been inefficacious. A few cases would appear to lend themselves to surgery, especially when the gall-bladder is dilated, but it must be admitted that good results from such treatment form surgical curiosities. During the last four years, I have been treating these and allied conditions by mercurial inunction. In some, serum has been given in the earlier stages with the object of reducing hæmolysis and so lessening the production of bile. The results are, I think, the most promising hitherto obtained. The mercury must be pushed, suspending treatment for a time if signs of mercurial poisoning such as buccal ulceration appear, but continuing again after an interval.

One case so treated appeared to improve for a time, and was discharged for the mother to continue treatment at home. The child was later re-admitted into hospital and died. The liver had decreased in size, and necropsy confirmed that the organ was much smaller than that usually found in this condition. The common bile-duct was completely impervious. The interesting feature, however, was that above the obstruction, the bile-duct was greatly dilated and contained a large quantity of bile. The case is suggestive of partial recovery.

From experience of the use of mercury in other conditions of the liver, I have formed the impression that it is more likely to be beneficial when the smaller bile-ducts are mainly involved, and the results of treatment so far support the theory of a descending change rather than the reverse. Other cases of biliary cirrhosis show on the whole fairly satisfactory results from the same form of treatment, though it must be stated that the older the patient the less satisfactory have the results been.

Syphilis

Congenital syphilis may rarely produce a peri-cholangitis with enlargement of the liver and spleen. The liver is firm, but not so hard as that found in the previous condition; it is usually tender. Jaundice is not rare in this condition, though it is usually absent; it is probably due to inflammation of the small bile-ducts, though occasionally it may owe its origin to enlarged lymph glands. When jaundice is present at all, the infants are usually icteric when born, but it may commence weeks later, and then may be recurrent and associated with multiple hæmorrhages: such cases are possibly due to secondary infection. Other evidence of syphilis is usually present, and the infants are debilitated, wasted and anaemic, with a tendency to vomiting and diarrhoea. The treatment of the condition is well known and needs no amplification here, save to stress that, unless it is persisted in, relapses are common. In gauging the effects of treatment it should be remembered that the results of the Wassermann test on the infant may be fallacious.

Toxic Jaundice

Jaundice in the young infant may be associated with sepsis of the umbilicus or with alimentary infection (cf. Winckel's disease and Buhl's disease). Such infants are extremely ill, and the extremities are usually cyanosed. There is a very marked tendency to hæmorrhages. In the less marked cases, the temperature is generally raised, but

in the worst forms, may be sub-normal. The condition usually rapidly progresses to coma and death, though the end may sometimes be delayed for weeks by vigorous treatment.

EPIDEMIC INFECTIVE JAUNDICE (CATARRHAL JAUNDICE)

Of cases of jaundice occurring at a later age, the commonest are examples of so-called catarrhal jaundice. The name is bad, implying as it does the original conception of an obstructive jaundice, secondary to plugging of the ducts with mucus—an explanation which has been offered in so many different types of jaundice and almost without exception proved to be incorrect. On rare occasions the condition has occurred in pandemic form, but is usually met in epidemics or sporadically. The causal virus is unknown. Apart from possible relapses during the course of the complaint, it appears to confer a lasting immunity. It is essentially a disease of childhood, but may be encountered in adults. The age incidence is of interest in that adults may have increased general resistance, or may have had the condition previously without manifesting the main symptoms. Cases illustrating the latter occur during epidemics; Wallgren²² stresses their incidence, and I have personally encountered the case of a child with typical catarrhal jaundice in whose sister the only abnormality found was a temporary enlargement of the liver; this was only discovered during the course of a routine examination which I was at that time conducting.

It is well known, of course, that a child may be brought to the doctor for malaise alone, the jaundice being so slight that it is not noticed by an untrained eye. It appears more than likely that some patients acquiring the disease may have only the slightest symptoms. A consideration of increased resistance with age is also of interest. During epidemics, I have encountered two families in which in one instance three children out of seven, and, in the other, two out of five acquired the disease; the five who became jaundiced gave a very strong history of cyclical vomiting, such a history being entirely absent in the remaining members of the families. It is well recognized that cyclical vomiting is pre-eminently a condition of childhood, and whatever its exact etiology may ultimately prove to be, it is generally admitted that the liver plays a part in the manifestation. It is, of course, not suggested that catarrhal jaundice only occurs in the subjects of cyclical vomiting, but the example given does suggest that the "soil" is of importance. In the same connexion, the effects of toxins on the liver at various ages have already been referred to. The maximal incidence appears to be between the ages of five and ten. The majority of the cases occur in the autumn.

At the onset there is usually slight fever, but in cases not seen early this is generally missed. The first symptom as a rule is malaise, associated with anorexia: nausea and vomiting are not uncommon. Jaundice then makes its appearance, first noticed in the sclerotics; the liver becomes enlarged and tender, the enlargement often being associated with pain in the epigastrium and over the right lobe of the organ; the urine is dark with bile, and this may be the first manifestation noticed by the parents; the stools are pale, both from diminution or absence of bile, and from excess of fat associated with the same deficiency; the spleen is enlarged in a fair proportion of cases. Van den Bergh's test usually gives a positive direct reaction in the earliest stages, and thereafter is biphasic. The rapid and tender enlargement of the liver is presumably due to vascular engorgement, and usually precedes the diminution of the flow of bile; the degree of enlargement bears no direct relationship to the depth of the jaundice. The picture suggests a hepatitis, and this is confirmed by sections of the liver

taken from living patients by Nordmann²³ and Eppinger, and also by sections obtained from patients who have died from other causes (Eppinger²⁴).

The course of the disease in the vast majority of cases is uneventful, though the duration of symptoms is variable; the liver in many cases may be enlarged for weeks after all jaundice has disappeared; it is no longer tender, but remains as evidence of a hepatitis which has not entirely subsided. When the jaundice does not rapidly subside, it must always give rise to a doubt as to whether the case may not be one of subacute necrosis of the liver; and occasionally cases suddenly take on grave characters and pursue the course of acute necrosis. How far these were originally true examples of the condition under discussion is difficult to prove, but it is suggestive that during the epidemic in Gotenburg between 1924 and 1926, there were more cases of this grave type than in other years, and that the increase of such cases was confined to the epidemic area. Such statistics are fortunately easy to obtain, the condition being a notifiable one in Sweden. In epidemics, cases may be seen in which the jaundice recurs; how far such cases are due to the original virus, and how far to superadded infection in a patient whose liver has not fully recovered from an inflammatory attack, is again difficult to say. If seen for the first time in the second attack, such cases may readily be diagnosed as biliary cirrhosis, for prodromal symptoms are usually absent. One of Wallgren's cases,²² occurring during the Gotenburg epidemic, I quote rather fully, as it demonstrates many of the points under discussion, though unfortunately he does not prove a source of infection by contact in this case:

A boy, aged 14, was taken ill in April, 1926, with some fever, vomiting, and abdominal pain. Jaundice developed and the condition was diagnosed as catarrhal jaundice. The icterus subsided and in May he is stated to have been perfectly well. Later, he suffered from attacks lasting about two days, during which he "felt ill," complained of pain in the abdomen, and became icteric. The urine contained bile. At the end of August, he was admitted to hospital. The liver was not palpable and appeared small. The spleen was greatly enlarged. There was no ascites. The temperature was normal; the pulse rate about 80. The urine contained bile. The red cells showed slightly increased resistance to hypotonic salines. The haemoglobin was 80 per cent., colour index 1.2. The Wassermann reaction was negative. After investigation, he was sent home under the care of his doctor. On October 11th, he had a sore throat with raised temperature, and vomited blood. He was again admitted to hospital, where he had repeated haematemesis, and passed dark blood per rectum. The haemoglobin fell to 40 per cent. and the patient died. At necropsy, the veins at the cardiac end of the stomach were grossly varicose and presumably formed the site of the bleeding; the spleen was enlarged, the surface being irregular; the liver weighed only 89 gms, and had a nodular surface, each nodule being about the size of a hazel nut. On section, the nodules showed a yellow-brown surface with spots of a greyish colour. The bile-ducts showed no obvious abnormality. Histologically, there was much fibrous tissue, with many cells showing an obvious attempt at regeneration; there was, however, an entire absence of lobular arrangement.

Marchand,²⁵ and Pratt and Stengel,²⁶ have recorded similar cases, occurring almost entirely in children. With Mallory, they regard the condition as a "toxic cirrhosis"—an attempt at regeneration after an acute process.

The condition is obviously infectious. During epidemics, cases arise, in which after the most careful search no direct contact can be established; and this is an argument in favour of the existence of carriers. It would appear that cases must be regarded as infectious both during the prodromal period and for some time after the jaundice has subsided. It is certain that infection may take place during a short interview; there is no evidence in favour of infection through the alimentary tract. In some cases, a

running ear appears to have been responsible for spreading the infection. The incubation period is difficult to establish. During epidemics the majority of cases appear to develop the condition between 21 and 28 days after contact. A few appear to occur after one or two weeks, but in these it is difficult to exclude a previous contact. In Wallgren's cases, occurring among patients who were in hospital at the time of actual infection, the average time was about 21 days.

From the point of view of treatment there is little to add to that commonly advocated, but I would condemn the use of atophan suggested by Grunenberg and Ullmann,²⁷ as being contraindicated in a condition which appears to be essentially an acute hepatitis. In those cases where a graver condition is suspected I think that intravenous glucose, together with small doses of insulin, may be of considerable value, as also may be the administration of calcium, given intravenously in the form of a 10 per cent. solution of the gluconate.

OTHER CONDITIONS WITH WHICH JAUNDICE IS ASSOCIATED

It is not possible in this paper to discuss fully the association of jaundice with *Mumps*. Usually, it follows the enlargement of the salivary glands, but may occur apart from this. Possibly the occurrence of diarrhoea, and the greater degree of abdominal pain, not so obviously associated with the enlargement of the liver, may help in the differentiation from the previous condition. *Cholangitis*, *Cirrhosis*, and *Haemolytic Jaundice* are conditions which might profitably have been discussed, and I hope that we may hear something of them from subsequent speakers.

There are many other conditions which may be associated with jaundice in childhood, examples being infective conditions such as pneumonia and typhoid fever, syphilis in forms other than that discussed above, heart failure, and such rare conditions as Wilson's disease, and obstruction due to gall-stones; but I have confined myself in the main to a short survey of comparatively common conditions, where suggestions as to pathology and treatment may, I hope, form the basis of a discussion not entirely without profit to us.

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