tion I would use the anterior vaginal wall approach and would cut through that band. A further operation was not done in this case because the woman had secondaries from a carcinoma of the larynx.

The other failure was in a case of moderate cystocele in which mobilization was again done through the Millin II approach. This woman has not yet had the cystocele repaired, but I feel confident that, when it is, the stress will be finally relieved. In this connexion Mulvany (1951) states: "The writer used to confine the suprapubic route to those cases of stress incontinence requiring also an abdominal operation and the vaginal one for those in need of repair, but these excellent results have prompted its employment also in the early to moderate prolapse, especially if there is a likelihood of future child-bearing, as in most cases it is the stress incontinence and not the prolapse which is the most prominent and troublesome feature." I cannot agree with this, and my results show that support from below is as important as mobilization.

Latterly, therefore, nearly all my cases have been done through an anterior vaginal wall incision, whether prolapse was present or not. The procedure when this approach is used consists of: (1) dissection of urethra and bladder-neck; (2) rupture of pudendal diaphragm by index finger or blunt scissors on either side of urethra; (3) pushing the bladder off the back of the symphysis pubis; (4) removal of redundant vaginal mucosa, if any; (5) re-uniting vaginal mucosa and para-urethral tissues. This operation now constitutes part of any prolapse operation when stress incontinence is present.

Many of my cases, but not all, had had several previous operations for prolapse and stress incontinence. One case had also had an Aldridge sling operation by another surgeon, but had not been improved. During operation on that case (suprapubic approach) no evidence could be found of the fascial sling inserted one year before. An immediate post-operative urinary infection tended to obscure the successful result, but one important point made by the patient (and since asked of other patients) was that she could now feel urine passing through the urethra. When the urinary infection was overcome the incontinence was completely relieved.

Conclusions

It would be wrong of me to make statistical deductions with so few cases. But my experience, gained in the study of many other procedures besides the present series, leads me to the following conclusions.

1. That cases of stress incontinence require careful radiographic and cystoscopic investigation, apart from clinical neurological examination, before operations are performed. There is nothing new in this, as has been repeatedly pointed out by Millin (1950) and Winsbury-White (1948). Measured cystography has shown that there is often a slight increase in descent of the bladder-neck after mobilization, although the stress is cured.

2. That Mulvany has introduced a new aetiological concept and an operation which has formed part of many sling procedures of the past.

3. That Mulvany's mobilization is not necessarily a sufficiency in itself. There must be adequate support to the bladder-neck from below. These two factors—mobilization and support from below—can be accomplished through an anterior vaginal approach. There should be no need for sling procedures if this is so.

4. That the mobilization can either be done from above in the absence of prolapse (as an accompaniment of an abdominal operation) or from below during plastic repair operations even when the urethral bulge is minimal.

5. That these cases require careful post-operative assessment of cure. Often the stress is replaced either by frequency because urinary infection is common, or

by urgency, particularly when the bladder is full—for example, in the morning. Urethral sensation of flow in some cases accompanies successful cure of stress.

REFERENCES

- Aldridge, A. H. (1942). *Amer. J. Obstet. Gynec.*, 44, 398.
 Millin, T. (1947). *Proc. roy. Soc. Med.*, 40, 364.
 — (1950). *Ibid.*, 43, 258.
 Mulvany, J. H. (1951). *J. Obstet. Gynaec. Brit. Emp.*, 58, 449.
 Studdiford, W. E. (1944). *Amer. J. Obstet. Gynec.*, 47, 764.
 Winsbury-White, H. P. (1948). *Textbook of Genito-urinary Surgery*, p. 688. Livingstone.

ICTERUS GRAVIS AND CIRRHOSIS OF THE LIVER

BY

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Braid and Ebbs (1937) reported the case of a child who had been deeply jaundiced in infancy, who subsequently developed coarse multilobular hepatic cirrhosis, and who died at the age of 3 years and 8 months, after a haematemesis. This child, the second and last in the family, became jaundiced on the third day of life. The jaundice persisted for two months, by which time the haemoglobin was 74% and the red blood corpuscles numbered 3,900,000 per c.mm., 5.8% being reticulocytes. At the age of 1 month the liver was firm and hard, and its lower edge reached the level of the umbilicus; the spleen was never felt during the neonatal period, but became palpable at 5 months. At the age of 3 years 8 months the child was readmitted to hospital with ascites; a few days later she had a haematemesis and died.

Drummond and Watkins (1946) have more recently given details of three families, in two of which Rh iso-immunization may have been the cause of hepatosplenomegaly in the children; but in these families the early history was not suggestive of Rh iso-immunization, for the affected children were never noticeably jaundiced or anaemic in infancy. Moreover, the maternal serum in each case contained no detectable Rh antibody; in one case this was only five years after the birth of the last child in the family—this child had died, deeply jaundiced, on the third day of life—and in the other case only two years after the last of three successive stillbirths. My own experience (Gerrard, 1951) suggests that, once iso-immunization has occurred, Rh antibodies persist for at least eight years, and often longer. However, both mothers in the two families mentioned above were eventually sensitized, for each had a rigor and each produced Rh antibodies when transfused with Rh incompatible blood. In Drummond and Watkins's third family the early history, as in Braid's case, was suggestive of Rh iso-immunization, for the affected child became jaundiced within a day or two of birth, and the jaundice persisted for three months; but in this instance Rh iso-immunization was excluded as a causative factor.

Nussey (1949) has also recorded a family in which Rh iso-immunization may have been the cause of hepatosplenomegaly in three siblings, but the early history of this family was not suggestive of Rh iso-immunization, for none of the three children with hepatosplenomegaly had ever been noticeably jaundiced or anaemic in infancy, and, though the children were Rh-positive and the mother Rh-negative, the maternal serum contained no Rh antibodies either in saline or in albumin. This was 17 years after her last pregnancy, by which time she might well have lost her antibodies.

An Earlier Review

I have recently reviewed (Gerrard, 1951) nearly all families from which cases of haemolytic disease of the newborn were admitted to the Children's Hospital, Birmingham, between the years 1927 and 1949 inclusive. The purpose of this review was to elicit the incidence and main sequelae of haemolytic disease of the newborn and to find out if hepatic cirrhosis might be one of these. I set out to trace 321 families; only 10 were finally unaccounted for, and four more had moved too far afield to be visited. The remaining 307 families were visited—often more than once—blood was taken for serological investigation, and a detailed family history compiled. In 81 haemolytic disease had almost certainly not been present. In retrospect it is not very surprising that in the early days quite a number of cases were misdiagnosed. In the other 226 families the family history and serological findings supported a diagnosis of haemolytic disease due to Rh iso-immunization in one or more of the siblings.

The mortality of icterus gravis before 1942 was high (46% of such patients admitted to this hospital between 1927 and 1942 died; during the next seven years only 23% of admissions died); the proportion of older children surviving was therefore small. In addition, before 1942 most infants with icterus gravis died at home; after 1942 there was an increasing tendency for them to be admitted hurriedly to hospital. Latterly the number of such admissions has fallen, for these cases are now nearly always treated in the maternity hospitals in which they are born. In my material 293 out of a total of 381 had survived the neonatal period; all these were re-examined.

Later Investigation

Blood was taken from all children aged 5 or more and from all cases of kernicterus, for in these jaundice tends to be greater and liver damage might therefore be expected to be more frequent. The serum albumin and globulin and the thymol turbidity were estimated in these cases and also in the first group of younger children who were reviewed; I did not, however, persist with this investigation in the younger children, for they all registered a hearty disapproval of this mode of approach and were clinically well. It was decided to estimate the serum albumin and globulin, because Higgins *et al.* (1944) have stated that "disturbances of the plasma proteins are an outstanding feature in subacute and chronic cases of hepatitis, and a persistent alteration of the albumin/globulin ratio indicates that the liver has suffered irreparable damage." The thymol turbidity was also estimated, as it is often raised in chronic hepatitis: according to MacLagan (1947) a thymol turbidity greater than 4 is pathological; in normal people it is rarely greater than 2. The combination of a careful clinical examination with these biochemical findings would, it was hoped, bring to light all cases with a persisting hepatic defect.

My findings in the 79 children submitted to both lines of investigation are recorded in Tables I and II. In Table I are recorded the results of the liver-function tests and other findings in the cases of kernicterus. The thymol turbidity was greater than 2 in Cases 13, 14, 20, and 21; in Cases 14 and 21 there was also a reversal of the albumin/globulin ratio; in one other case (No. 3) the normal albumin/globulin ratio was altered. In none of these cases was the spleen palpable, and in none was the liver either enlarged or unduly firm. In Table II are recorded the results of the liver-function tests and other findings in the cases of uncomplicated icterus gravis. When I examined these children I found the spleen palpable in Cases 51, 60, 67, 77, and 78; in all these cases it was firm, but in no instance was the liver either enlarged or hard. In Case 78, as also in Case 53, the normal albumin/globulin ratio was altered. The thymol turbidity was definitely pathological in Cases 30 and 56, but Case 56 had recently had an attack of infective hepatitis.

TABLE I.—The Serum Albumin and Globulin and the Thymol Turbidity in Cases of Kernicterus

Case No.	Age in Years	Albumin (g./100 ml.)	Globulin (g./100 ml.)	Thymol Turbidity (Units)	Duration of Jaundice	Comments
1	1	4.5	2.6	1.0	5 weeks	
2	1	4.4	2.6	2.0	12 "	
3	2	2.85	2.81	1.5	4 "	Teeth green
4	2	4.48	1.75	1.5	4 "	
5	2	4.79	2.30	1.5	4 "	
6	3	3.94	2.63	1.5	16 "	" yellow
7	3	3.76	2.25	1.0	16 "	
8	3	3.73	2.06	2.0	13 "	" "
9	3	5.2	2.1	1.5	4 "	
10	4	4.0	2.6	1.0	8 "	" green
11	4	4.2	2.7	2.0	4 "	" yellow
12	4	4.55	1.5	1.5	13 "	
13	5	3.10	2.46	2.5	13 "	" "
14	6	3.95	4.24	2.5	16 "	
15	7	4.5	2.7	1.5	7 "	
16	8	3.08	2.11	1.0	2 days	
17	9	4.81	2.65	2.0	3 weeks	" green
18	10	4.6	2.73	1.5	16 "	
19	10	4.54	1.65	1.0	6 "	" "
20	10	4.34	2.79	3.0	12 "	" "
21	12	3.38	4.12	2.5	1 week	" "
22	15	3.77	2.45	1.0	6 weeks	" "
23	16	4.51	2.05	1.0	3 "	
24	18	3.79	1.95	2.0	1 week	
25	20	4.62	2.2	2.0	1 "	
26	21	4.6	2.7	1.0	12 weeks	
27	22	5.04	2.67	1.5	2 "	

Cases 8, 20, and 22 had a transient obstructive jaundice in infancy. The colour of the teeth refers to the deciduous teeth only.

TABLE II.—The Serum Albumin and Globulin and the Thymol Turbidity in Late Cases of Icterus Gravis

Case No.	Age in Years	Albumin (g./100 ml.)	Globulin (g./100 ml.)	Thymol Turbidity (Units)	Duration of Jaundice	Comments
28	2	4.33	2.75	2.5	1 week	
29	3	4.03	2.88	2.5	2 weeks	
30	3	3.7	2.2	6.5	8 "	Teeth green
31	3	3.8	2.1	2.5	2 "	
32	3	4.7	2.3	1	1 week	
33	3	3.61	2.29	1.5	None	
34	4	4.21	2.03	2.5	"	
35	4	3.3	2.0	1	6 weeks	
36	4	4.23	1.45	1	1 week	
37	5	3.2	1.8	1	1 "	
38	5	3.9	2.4	2.0	10 weeks	
39	5	4.1	2.4	1.5	12 "	
40	5	4.2	2.4	2.5	3 "	
41	5	4.1	1.9	1.5	2 "	
42	5	4.6	2.1	1.5	4 "	
43	5	4.6	2.1	1.5	12 "	Teeth green
44	5	3.76	3.42	2.5	8 "	
45	6	4.91	2.74	2.5	4 "	
46	6	3.7	2.9	2.0	1½ "	
47	6	4.6	2.1	1.5	6 "	
48	6	3.9	1.6	1.5	None—only anaemia 3 weeks	
49	6	4.1	2.3	1.5	"	
50	6	3.9	2.4	2.0	3 "	Deaf
51	6	3.8	1.6	1.5	6 "	Spleen tipped
52	6	4.07	2.72	1	2 "	
53	6	3.6	4.02	1	14 "	
54	7	3.7	2.0	2.5	8 "	Teeth yellow
55	7	3.55	1.96	2.5	4 "	
56	7	3.8	2.3	4	3 "	Infective hepatitis 6 months previously
57	7	3.49	1.77	1.5	8 "	
58	7	4.19	3.17	0.5	11 "	Teeth green
59	7	4.56	2.63	1	14 "	" "
60	8	4.09	1.8	1	2 "	Spleen tipped
61	8	4.22	3.82	0.5	4 "	
62	8	5.0	2.7	1.5	3 "	
63	8	3.33	2.96	0.5	2 "	
64	8	4.12	2.46	1	2 "	
65	9	3.65	3.23	1.5	2 "	
66	9	3.59	1.89	1	2 "	
67	9	3.79	1.86	2	1 week	Spleen tipped
68	9	4.03	3.67	2	3 weeks	
69	10	4.39	3.34	1.0	10 days	
70	10	3.31	1.19	2.5	4 weeks	
71	10	4.66	1.66	1.5	10 "	
72	13	3.8	2.7	<1	3 "	
73	14	4.58	1.63	1	1 week	
74	14	5.2	1.41	1	6 weeks	
75	14	3.81	2.70	<1	12 "	
76	15	4.52	1.46	<1	2 "	
77	15	3.2	2.8	1	14 "	Teeth green; spleen tipped
78	15	3.2	3.5	<1	12 "	Spleen tipped
79	17	4.7	2.44	1	2 "	

Case 57 had a transient obstructive jaundice in infancy. The colour of the teeth refers to the deciduous teeth only.

The above findings suggest that Rh iso-immunization may result in some degree of hepatic insufficiency, for in 11 of the 79 cases (including the child who had recently had an attack of infective hepatitis) of which details are given there was clinical enlargement of the spleen, or a reversal of the albumin/globulin ratio, or an abnormal elevation of the thymol turbidity. The findings, however, do not suggest that Rh iso-immunization is commonly followed, in childhood, by hepatosplenomegaly.

It has been suggested that familial hepatic cirrhosis, although an uncommon condition, is related to Rh iso-immunization; I therefore took a full and careful family history in each of the 226 families reviewed, which included these and other cases; in no instance was there any evidence that siblings of children who had had haemolytic disease of the newborn had either developed or had died of cirrhosis of the liver, but I did not examine as a routine children who had not been jaundiced or anaemic in infancy.

Discussion

Nearly all infants with haemolytic disease of the newborn who live for more than a few hours show a variable degree of jaundice. This jaundice often deepens rapidly and may even become obstructive in character; the stools become colourless and the urine dark, and the liver and spleen are usually large and firm. If the infant dies at this stage the liver is found at necropsy to be large and green and its surface finely granular; on microscopy an early biliary cirrhosis is evident (Hawksley and Lightwood, 1934; Baar, 1946; Zollinger, 1946). Death, in our experience, has usually been associated with an intercurrent infection—for example, gastro-enteritis—but this was not so in two cases recorded by Lightwood and Bodian (1946) in which the infants developed ascites and died at 7 and 10 weeks of age; a third died at the age of 6 months, but with an associated otitis media and gastro-enteritis.

More commonly the infant survives the obstructive phase; the stools again become pigmented, the jaundice gradually fades, and the hepatic and splenic enlargements subside. At the Children's Hospital, Birmingham, we have not encountered any cases as severe as Lightwood and Bodian's Case 1, which developed ascites and required abdominal paracentesis on two occasions before making a spontaneous recovery; but we have had six cases which survived the obstructive jaundice and are now well. None required operative intervention. But if an obstruction occurs—for example, in the common bile duct—and is due to pigment stones, as in Lightwood and Bodian's Case 3, or to inspissated bile, as in Case "Hi" recorded by Skelton and Tovey (1945), this may be relieved surgically. Two cases of haemolytic disease of the newborn associated with obliteration of the common bile ducts have also been recorded (Pasachoff, 1935; Skelton and Tovey, 1945), but no comparable case has been seen at this hospital.

Biliary cirrhosis associated with haemolytic disease of the newborn is by no means rare (Zollinger, 1946; Craig, 1950), but the immediate prognosis, in our experience, seems to be good. In order to determine the more remote prognosis and also to determine whether any light can be shed on the aetiology of familial hepatic cirrhosis, this review of children who had had icterus gravis was undertaken.

A number of cases of familial hepatic cirrhosis have been reported (Parkes Weber, 1903; Bramwell, 1910; Gunn, 1926; Poynton and Wyllie, 1926; Langmead, 1934; Bateman, 1934; Debré, 1939). If the cases recorded by Drummond and Watkins (1946) and by Nussey (1949) are included, only 3 of the 29 cases were jaundiced in the neonatal period; this does not suggest that icterus gravis is a precursor of familial hepatic cirrhosis.

F. Braid (personal communication) has recently had under her care at this hospital two children, a girl and her brother, with hepatosplenomegaly. The mother is O Rh-positive, genotype R₁R₂ CDe/cDe; her serum contains no anomalous agglutinins or blocking antibodies. The father is O Rh-negative, genotype rr cde/cde. The first child in the family,

a boy, was born in 1947; he became jaundiced when he was 1 month old and the jaundice persisted for four and a half months. He remained in good health until he was 1 year old; he then developed ascites; he died of a coarse nodular cirrhosis at the age of 2½ years; his blood group was O Rh-positive, genotype R₂r cDe/cde. The second child in the family, born in 1948, had never been jaundiced or anaemic, his liver was palpable but not enlarged, there was no splenomegaly; his blood group was O Rh-positive, genotype R₁r CDe/cde. The third child in the family, aged 1 year, became jaundiced when he was 5 days old, the jaundice persisted for three months and was associated with the passage of pale stools; he had a large hard liver and spleen; his blood group was O Rh-positive, genotype R₁r CDe/cde. The indirect Coombs test, using the maternal serum and the erythrocytes of the youngest child, was negative. The family history in this case was suggestive of Rh iso-immunization, but the investigations revealed that Rh iso-immunization could not be the cause of the hepatosplenomegaly.

My own findings and a critical review of the literature do not suggest that Rh iso-immunization often, if ever, gives rise to hepatic cirrhosis later in life, and even when the child has been deeply jaundiced in infancy there is surprisingly little clinical evidence, in my material, of severe liver disease later in childhood. The only really suggestive case is that reported by Braid and Ebbs (1937), and, though the mother of this child was Rh-negative and her husband Rh-positive, her serum contained no detectable Rh antibodies, though this was 15 years after the birth of the affected child. It would appear, then, that hepatosplenomegaly as a late sequel of Rh iso-immunization is rare. If it is as unusual as my findings suggest, its occurrence in more than one member of a family would not be anticipated unless there was an underlying constitutional defect. Parkes Weber (1947) suggests that familial hepatic cirrhosis is analogous to other familial conditions associated with cirrhosis of the liver—for example, hepato-lenticular degeneration—and that it is, as he puts it, a congenital developmental defect. I do not think that my findings permit of a more detailed explanation. It would appear that familial hepatic cirrhosis, like hepato-lenticular degeneration, is not directly related to Rh iso-immunization, but it is possible that Rh iso-immunization may occasionally bring to light or accentuate an underlying latent hepatic defect.

Summary

Seventy-nine children who had had haemolytic disease of the newborn have been re-examined. In 11 instances evidence was obtained suggesting some degree of liver dysfunction, but no cases of frank hepatic cirrhosis were encountered, nor was any evidence collected which might support the thesis that familial hepatic cirrhosis is a sequel of Rh iso-immunization.

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REFERENCES

- Baar, H. S. (1946). *Brit. med. Bull.*, 4, 178.
 Bateman, D. (1934). *Proc. roy. Soc. Med.*, 27, 1327.
 Braid, F., and Ebbs, J. H. (1937). *Arch. Dis. Childh.*, 12, 389.
 Bramwell, B. (1910). *Clin. Stud.*, 8, 347.
 Craig, J. M. (1950). *Arch. Path.*, 49, 665.
 Debré, R. (1939). *Proc. roy. Soc. Med.*, 32, 1173.
 Drummond, R. J., and Watkins, A. G. (1946). *British Medical Journal*, 1, 984.
 Gerrard, J. W. (1951). Dissertation for D.M. thesis. Oxon.
 Gunn, F. D. (1926). *Arch. Path.*, 1, 527.
 Hawksley, J. C., and Lightwood, R. (1934). *Quart. J. Med.*, 27, 155.
 Higgins, C., O'Brien, J. R. P., Stewart, A., and Wits, L. J. (1944). *British Medical Journal*, 1, 211.
 Langmead, F. (1934). *Proc. roy. Soc. Med.*, 27, 939.
 Lightwood, R., and Bodian, M. (1946). *Arch. Dis. Childh.*, 21, 209.
 MacLagan, N. F. (1947). *British Medical Journal*, 2, 197.
 Nussey, A. M. (1949). *Ibid.*, 2, 414.
 Pasachoff, H. D. (1935). *Amer. J. Dis. Childh.*, 50, 1084.
 Poynton, F. J., and Wyllie, W. G. (1926). *Arch. Dis. Childh.*, 1, 1.
 Skelton, M. O., and Tovey, G. H. (1945). *British Medical Journal*, 2, 914.
 Weber, F. Parkes (1903). *Edinb. med. J.*, 14, 111.
 — (1947). *Rare Diseases and Some Debatable Subjects*, p. 112. London.
 Zollinger, H. V. (1946). *Helv. paediat. Acta*, 1, suppl. 2, p. 104.