BANTI'S DISEASE

POSSIBLE RELATIONSHIP TO Rh FACTOR

BY

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Clinicians and research workers were quick to grasp the significance of the discovery of the Rh factors, and their combined labours have shed a flood of light on many hitherto perplexing problems. Not a little of the work was done in the Birmingham Children's Hospital, where Sir Leonard Parsons (1933) and his co-workers helped to establish the essential unity of icterus gravis, haemolytic anaemia of the newborn, and hydrops foetalis, and where the subject of kernicterus was investigated. Even before the role of Rh incompatibility in those conditions became known ever-increasing inquiries were being made into the possibility of haemolytic disease being at the root of other

known that in severe haemolytic disease of the newborn, in addition to jaundice, there may be an enlargement of liver and spleen, and that this enlargement may persist for some time after the jaundice has subsided. It is therefore natural that when we find young patients with enlargement of the liver and spleen of seemingly unknown aetiology we should ask ourselves whether Rh incompatibility may not have had something to do with it.

No doubt this question has occurred to many clinicians, but, surprisingly enough, only one paper could be found in which an endeavour was made to answer it. Drummond and Watkins (1946) record three families with hepatomegaly and splenomegaly. They make it clear that in only two of these families could the Rh factor have played a part, and for the sake of brevity the main details of these are summarized here in the form of family trees (Fig. 1). Drummond and Watkins state that in neither of their families did the mother have a transfusion, and one is struck straight away by the fact of the firstborn being affected in No. 1 family, while the disease, after skipping the next Rh-positive child, caused the same condition in the third one, and thereafter was probably responsible only for the death of the sixth child. Family No. 2 conforms more with our conception of how Rh incompatibility works—the first one or two, in this case two children, being responsible for sensitizing the mother and seemingly escaping, while those who follow bear the brunt of the disease. In both these families the mothers had no Rh antibodies when examined, but suffered severe reactions when transfused with 50 ml. of Rh-positive ABO compatible blood, and subsequently showed abundant Rh antibodies.

Details of Family T.

In the family about to be described the possibility of Rh incompatibility playing a part in the incidence of hepatomegaly and splenomegaly stands out even more clearly. The genetic make-up of the family for the various blood groups is set out in the accompanying table.

Table Showing the Various Blood Groups of Family T.

Name	Age	Group	Antisera				Rh Genotype	M	N	P
			C	D	E	c				
Father ..	52	A	+	+	—	+	CDe/cde	+	+	—
Mother ..	51	A	—	—	—	+	cde/cde	—	+	+
Arthur ..	28	A	—	—	—	+	cde/cde	+	+	+
John ..	26	O	+	+	—	+	CDe/cde	+	+	+
Frank ..	23	A	+	+	—	+	CDe/cde	+	+	+
Edward ..	19½	A	+	+	—	+	CDe/cde	+	+	+
Kathleen ..	17	A	+	+	—	+	CDe/cde	+	+	+

Here, then, an Rh-negative woman, who had never had a transfusion, married a heterozygous Rh-positive man and had five children. The parents, who have been examined, are normal clinically. The first child of the marriage, Arthur (28), who is Rh-negative, is perfectly normal. The next one, John (26), is Rh-positive, and he too is normal, which is quite understandable considering he must have been the first in a position to sensitize his mother against the D antigen. The next three children, all Rh-positive, revealed enlarged spleens and palpable livers, and their more detailed history is as follows.

Case 1

Frank, now aged 23, was sent to the Children's Hospital, Birmingham, in 1936 on account of abdominal discomfort. There his liver was found to be moderately enlarged, firm, and smooth, and his spleen very large. Liver-function tests were within normal limits, he was not anaemic, and his white blood count was normal—8,000 (71% polymorphs, 1% eosinophils, 1% basophils, 14% lymphocytes, 13% monocytes).

DRUMMOND & WATKINS TWO FAMILIES

FAMILY "T"

SQUARE DENOTES MALE, CIRCLE FEMALE (+) & (-) AFTER SYMBOL REPRESENTING SEX DENOTES Rh + & Rh- RESPECTIVELY. A HETEROZYGOUS INDIVIDUAL IS DESIGNATED AS (±)

FIG. 1.—Genealogical tree of Drummond and Watkins's two families and of Family T.

ills which befall mankind, and now they include studies of the genetic make-up of families of imbeciles and mental defectives, those with chorea-athetosis, Wilson's disease, and congenital obliteration of bile ducts, and of some individuals showing enlargement of liver and spleen.

No convincing proof has so far been found that either mental defect in the broad sense or Wilson's disease is caused by Rh incompatibility; but Skelton and Tovey (1945) reported congenital obliteration of the bile ducts in association with haemolytic disease. It is generally

A diagnosis of Banti's disease was made, and later in the same year he was readmitted for splenectomy. Dr. H. S. Baar very kindly looked out the original sections of the spleen, and his comment on them and on those of the other two affected sibs is that they are typical of Banti's disease.

FIG. 2.—Graph showing decreased fragility of red cells in Case 1.

This lad remained well for over a year after the splenectomy, and early in 1938 he was admitted to this hospital following his first haematemesis. A second haematemesis at the end of 1938 necessitated a blood transfusion. In all he was admitted on ten occasions because of haematemeses, the last one being in April, 1949. At no time, however, was his condition really desperate, and transfusion had to be carried out on only three other occasions. Liver-function tests which were repeated here showed no evidence of serious dysfunction.

Examination of his blood and urine did not point to any excessive haemolysis, and in fact there was a small but significant decrease in the fragility of the red cells (Fig. 2), a point also noted by Drummond and Watkins (1946) in their patients. His white cell and platelet counts were within normal limits, too. This patient's liver is now only just palpable and he himself is reasonably well and earning a living as a bakelite moulder.

Case 2

Edward, now 19½, was brought to this hospital in August, 1938, following his first haematemesis. His spleen was appreciably enlarged, while the liver exceeded the normal limit only slightly. Again Banti's disease was diagnosed. This boy's bleeding and clotting times and his white cell count were normal. In September, 1938, Mr. James Gore performed a splenectomy on him; recovery was uneventful. The pathologist's report states: "The spleen shows fibrosis extending through the organ, slight thickening of capsule, and dilated sinuses. Hyaline swelling present in endothelial layers of the vessels of the Malpighian bodies."

Fifteen months after splenectomy this patient had a further haematemesis, and by July, 1948, he had had eight haematemeses in all. He also showed remarkable recuperative powers, though at one time in 1945 his condition was critical. His liver-function tests were normal, too, and he showed no evidence of excessive blood destruction.

Case 3

I saw Kathleen, the fifth child, for the first time in October, 1947, when her brother Frank was an in-patient with haematemesis. It was then that I began to make tentative inquiries into the possibility that we were dealing here with a familial affection due to Rh incompatibility. Clinical examination of the girl revealed an enlarged spleen and a cleft palate but no anaemia. Till then she had never had any overt bleeding, and although somewhat delicate was able to work as a box-maker.

She was not seen again till June 27, 1948, when she was brought into hospital as an emergency case following haematemesis. Her blood count showed 8.4 g. % Hb, 3,220,000 red cells, 5,100 white cells, with 64% polymorphs. At first her condition did not give rise to anxiety, but on July 2 she rapidly became very ill following a severe melaena and haematemesis. There was a temporary rally after a transfusion of 3 pints (1.7 litres) of blood, but next day she collapsed again and became almost moribund. A further 3½ pints (2 litres) of blood was given, but profuse melaena continued and she died on July 4.

Post-mortem examination showed varices at the cardio-oesophageal junction, and on the greater curvature of the stomach about 1 in. (2.5 cm.) from the cardiac sphincter an acute ulcer which had eroded one of the dilated veins. The mucosa round the ulcer was injected, but, apart from this

and much altered blood in the small intestine, no other abnormality was found in the gut. The spleen, which weighed 13½ oz. (383 g.) and was about 6 in. (15 cm.) long, contained localized patches of fibrosis in the capsule, and was partly adherent to the diaphragm. Its pulp was beefy and showed an increase in fibrous tissue. The liver, which weighed 45 oz. (1,276 g.), had a finely granular surface. It showed great increase in fibrous tissue, grey strands of which were visible to the naked eye. Sections of the liver and spleen are shown

FIG. 3.—Section of liver in Case 3, showing cirrhosis.

FIG. 4.—Section of spleen in Case 3, showing fibrosis.

in Figs. 3 and 4. No other gross abnormalities were found, and in particular the basal ganglia of the brain showed no degenerative changes.

Discussion

The parents in our family never noticed any jaundice in their children either at birth or subsequently. This is in conformity with the findings in the cases of Drummond and Watkins (1946), and does not, of course, rule out the possibility that a considerable degree of neonatal anaemia may have been present in these patients. In this connexion it is worth recalling the statement by Vaughan (1946), who found no correlation between the incidence of kernicterus and the degree of blood destruction—in other words, the symptoms we associate with kernicterus may occur in children who have never been jaundiced. This too was

pointed out long ago by Sir Leonard Parsons and his associates.

All this raises the question whether Mollison *et al.* (1948) are right in maintaining that the evils which flow from Rh incompatibility can be put down to the effects of blood destruction or whether the Rh antibody is able to fasten on fixed somatic cells and wreak damage there. Support for the second view is given by Boorman and Dodd (1943), who have shown that the Rh factor is a general characteristic of many tissues, and consequently many if not all tissues are likely to be susceptible to injury by Rh antibodies. The Birmingham school (Baar, 1946) also produced evidence of what we may term primary hepatic damage by Rh antibodies.

Another point of interest is that the mother of our patients showed no Rh antibodies and failed to produce them after an injection of 0.05 ml. of Rh-positive blood obtained from one of her sons, but showed them after injection of 5 ml. of her husband's blood. Something similar was found by Drummond and Watkins (1946), and the assumption is that the antibodies which the mother had originally died out with the passage of time, only to reappear under suitable stimulation. On the other hand, Gerrard (personal communication, 1949) found blocking antibodies in a woman 18 years after she had given birth to a child with icterus gravis. The child concerned died of cirrhosis of the liver at the age of $3\frac{1}{2}$, and the case was reported by Braid and Ebbs (1937).

If, from the fate of my patients, I may be allowed to draw any conclusions about the outlook in similar cases, I may be tempted to say that splenectomy improves the prognosis, but cannot be sure that this is the case when I recall that Frank did not bleed until after his splenectomy, and that Kathleen's death was almost certainly the result of a fortuitous gastric erosion superimposed on a dilated vein. Whitby and Britton (1946), however, are of the opinion that splenectomy influences the prognosis favourably. It may be that in future instead of a simple splenectomy some form of porto-caval anastomosis will be undertaken in similar cases.

The three patients described, though they showed no leucopenia or progressive anaemia, would qualify for inclusion in the so-called Banti's syndrome. What Banti (1894, 1910) had in mind when he described the disease to which he gave his name is not absolutely plain, and subsequent commentaries have not helped to clarify the issue. It has been obvious for some time, however, that the name Banti's syndrome has been used as a cloak for a variety of diseases. It may be that further work will sort out one of the entities lumped together under the title of Banti's disease by confirming that fibrosis of the spleen and liver, with enlargement of these organs, and especially of the former, occurring in the young and young adults and accompanied by a tendency to haematemesis, is at times due to Rh incompatibility.

Summary

A family is reported in which three out of five sibs were affected with hepatomegaly and splenomegaly and a tendency to haematemesis.

Reasons are given why this may have been caused by Rh incompatibility.

It is suggested that the condition observed may eventually be segregated from the Banti syndrome.

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MIKULICZ'S SYNDROME

BY

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A considerable number of cases of combined lacrimal and salivary glandular enlargement have been reported since Mikulicz (1888) first described the syndrome which now bears his name. Nevertheless the condition is rare enough to prompt the recording of a recent case seen in the Western Infirmary, Glasgow. Since this hospital was opened in 1873 there apparently have been only two other in-patients in whom this diagnosis has been made, both in 1936. On fuller investigation, however, it seems that neither showed enlargement of the lacrimal glands, and their cases can hardly be considered to fall into this syndrome. One was a boy aged 7 with acute myeloid leukaemia and moderate enlargement of the salivary glands, and the other a man of 26 who had bilateral parotid enlargement but no other abnormality. It would seem, therefore, that this is the first case of Mikulicz's syndrome to be seen, at any rate as an in-patient, in the Western Infirmary in 75 years.

Case Report

The patient, a man aged 73, was admitted for the first time on Sept. 30, 1947, complaining of swellings in front of both ears, under the lower jaw, and above both eyes. These had appeared gradually over a period of 12 months, and for a month before admission vision had been much impaired by the presence of the large supraorbital swellings. Apart from these swellings there was no complaint, and the patient had given up his job as a forester only on account of difficulty in seeing. He could remember no previous illnesses. Both parents died when over 90, and all siblings had survived to similar ages.

Examination revealed a well-built healthy-looking man. The most striking abnormality was the symmetrical enlargement of all salivary and both lacrimal glands (Fig. 1). Chemosis of the conjunctivae of both upper lids was present, but neither xerophthalmia nor xerostomia was a feature. In addition there was generalized enlargement of all groups of

FIG. 1.—Appearance on Oct. 6, 1947—before treatment.