

REMARKS ON THE VALUE OF
SPLENECTOMY IN THE TREATMENT OF
CERTAIN BLOOD DISORDERS.

T H E S I S

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by

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Until the present century the functions of the spleen were very imperfectly understood; indeed, even to the present day, a good deal of doubt exists as to the complete nature of those functions.

Amongst the Ancients, as recorded by Pliny, who perhaps derived his information from Herodotus, the spleen was removed in professional runners on the strange ground that the giraffe, the fleetest of known animals, was supposed to possess no spleen. Unfortunately no records remain of their subsequent efficiency.

In the Middle Ages, the spleen was the seat of all unpleasant characteristics, especially of envy and malice. Thus Shakespeare says in Julius Caesar,

"You shall digest the venom of your spleen
Though it do split you; for, from this day forth
I'll use you for my mirth, yea for my laughter
When you are waspish."

Malpighi in 1666 described the structure of the spleen, and his name is eponymically preserved in the Malpighian bodies of the spleen. He gave the first account of those lymphadenomatous formations which were fully described in 1832 by Hodgkin.

From this time until the beginning of the present century there was much conjecture but little increase of knowledge about the spleen. Thus in Kirke's Handbook of Physiology (1874)

it is stated that there are indications that the spleen is concerned in elaborating the albuminous materials of food and for a time storing them up; the small amount of fatty material in the plasma in its parenchyma leads to the inference that the gland has little to do in regard to the preparation of material for the respiratory process.

It is also suggested that there is a close analogy in function between the spleen and the lymphatic glands, both being engaged in the formation of germs of subsequent blood corpuscles. "There is reason to believe also that in the spleen many of the red blood corpuscles undergo disintegration. It is supposed also to act as a kind of vascular reservoir or diverticulum to the portal system, or more particularly to the vessels of the stomach. It must have peculiar and higher, though as yet ill-understood, offices."

By the year 1894, a total of 121 cases was recorded in which the spleen had been removed, mostly for cysts or rupture. These operations at least proved that the spleen was not an organ necessary for life.

In 1907 Schafer (Essentials of Histology) stated "the spleen is certainly concerned in the production of white blood cells and in the destruction of red cells." Since this time, an enormous amount of work has been done upon the functions

of the spleen in health and disease; by 1915 Kaznelson felt sufficiently secure of his pathology of Werlhof's disease which he called "thrombolytic purpura" to advise splenectomy as its treatment. The success of the operation in this case led to the extension of splenectomy as a form of treatment in many diverse conditions of splenomegaly. Splenectomy, indeed, became the favourite method of cutting the Gordian knot of pathology and treatment in all conditions which might reasonably be considered "diseases of the blood", both physicians and surgeons forgetting Trousseau's dictum - "Il n'y a pas de maladies; il n'y a que des malades."

Reaction followed this period, and now splenectomy is almost reserved for the treatment of three diseases - acholuric jaundice, splenic anaemia, including Banti's disease and purpura haemorrhagica. It is the object of this paper to discuss the pathology of these diseases, and to record an original case of acute purpura haemorrhagica, successfully treated by splenectomy.

The Structure of the Spleen.

The spleen is an organ of dark red colour whose weight varies normally with age and perhaps with other conditions such as the stage of digestion and of its repletion with blood corpuscles, but which may be stated generally as 5 - 7 ozs.. It is covered by a capsule consisting externally of a reflection of peritoneum; the inner layers of the capsule consist of fibrous and much elastic tissue, containing many unstriped muscle fibres. This capsule contracts rhythmically several times a minute.

The arteries pass in to the spleen at the hilum, and divide repeatedly; the smaller branches become surrounded by a mantle of lymphoid tissue which swells out in places to constitute the Malpighian bodies. These are ordinary nodes of lymphoid tissue which often present in their centre a group of large pale-staining cells with indefinite outline; their nature is not clearly known (Sampson Wright).

The pulp consists of a network of fibres derived from the capsule; a great number of red blood cells are found in the interstices. The venules have incomplete walls which readily permit the passage in and out of red blood cells.

The cells found in the pulp are of two types:-

(1) Elements of the blood; chiefly red cells and lymphocytes;

polymorphs are few.

(2) The special pulp cells; these are of three types:-

- (a) Large mononuclear cells, amoeboid and phagocytic.
- (b) Branched reticulum cells; these may be the same as the endothelial cells lining the venules.
- (c) Giant cells, numerous in young animals, and often containing ingested red blood cells.

The Physiology of the Spleen.

In the modern view, the spleen is not regarded as an isolated organ but as an integral part of the reticulo-endothelial system.

The reticulo-endothelial system is a specialised part of the connective tissue distinguished from other connective tissue elements, as well as from all forms of myeloid and lymphatic cells, by its capacity to store certain colloidal particles. Ranvier first described such cells in 1899, but after Ehrlich's introduction of various dyes, Goldmann showed that these cells could all be distinguished by an avidity for particles of pyrrhot blue and of certain other stains. Included in this category are many cells of the splenic pulp and of the splenic sinuses, and many cells of the follicles of the bone marrow and cords of lymphatic glands and other lymphatic tissues, of the liver capillaries, of capillaries in the formative bone-marrow and of the adrenal and pituitary glands.

From the point of this paper, the most important function of the reticulo-endothelial system is its capacity for taking up diffused Haemoglobin. Erythro-phagocytosis is seen mainly in the cells of the splenic pulp, but also in the Kupffer cells of the liver and in the lining of the vascular channels of the bone medulla.

The functions of the spleen are those of the reticulo-endothelial system, but it appears that much of this system is only potentially active while the spleen carries out its functions constantly. Von Haam, for instance, has shown (Proc. Soc. Exp. Biol. and Med. '31. 1206) that injections of adrenaline in a dog normally cause a great rise in the number of red cells in the circulation. After splenectomy, injections have no effect on the number of red cells for five or six months; but after this period are followed by a considerable rise in the red-cell count, though not to such a height as before splenectomy. Von Haam concludes that this recovery of response is due to other cells of the reticulo-endothelial system taking over the function of red cell storage which, as will be seen, is normally one of the important functions of the spleen.

The functions of the spleen are:-

1. Phagocytosis of Red Blood Cells.

This function is evidenced by the constant presence of

red cells engulfed in the spleen's reticulo-endothelial cells. The haemoglobin of these cells is converted in the spleen into bilirubin, part of which is conveyed to the liver by the blood for excretion in the bile, but part is stored in the spleen cells in combination with other substances as haemosiderin.

According to Sampson Wright, after splenectomy the storage of iron is interfered with, and increased excretion occurs by the kidneys. The Kuppfer cells proliferate and become increasingly infiltrated by iron; some iron may even be excreted by the hepatic cells into the bile.

There is some evidence (Botazzi, quoted by Piney, p. 263) that corpuscles in the splenic vein are less resistant to hypotonic saline than those in the artery. This would indicate that the spleen, at least in acholuric jaundice, has some injurious action even on those corpuscles it is unable to destroy.

2. The spleen regularly produces lymphocytes and monocytes, which indeed are produced solely in the lymphoid tissues of the body, even including that of the bone-marrow itself. Of those that reach the blood, most do so probably through the large lymph channels and the thoracic duct. They are of variable size and appearances; the smaller, which alone appears in normal blood in considerable numbers, is little

larger than a red cell and has a deeply staining nucleus and little cytoplasm. These cells have but little power of movement, and no oxydose granules or proteolytic ferment. They have no phagocytic power. As a group they have a function related to certain forms of immunity and they are characteristically sensitive to radium emanations.

In certain diseases of children, especially Von Jaksch's anaemia the spleen may resume its embryonic function of producing leucocytes and red cells. (Rolleston: Article on blood-diseases in Parsons and Banting's Diseases of Infancy and Children, p. 1083). But this is part of a compensatory process extending to embryonic blood forming tissue, for instance in the thymus and even in the kidneys. There is no evidence that the spleen normally forms red cells.

3. It acts as a reservoir for red blood cells, which may be extruded into the circulation in time of need by contractions of the spleen. Starling estimates that as many as one-fourth of the red cells are normally kept in reserve in the spleen. They are called into circulation particularly by conditions causing oxygen lack in the tissues e.g. big haemorrhages or CO poisoning. They are mobilised apparently in response to increased adrenalin secretion.

4. The spleen has a role of clinical importance in relation to immunity (Krumbhaar - Physiolog. Rev. 1926. vi. 160).

It has a relative affinity for bacteria, it fixes toxins and produces anti-bodies. In this function also the spleen co-operates with other tissues which can assume its function after removal.

Its frequent involvement in infection is a clinical demonstration of this relationship (e.g. typhoid and malaria), and the serious lesions that may result are examples of the common biological phenomenon that on sufficient provocation an organ may become the chief victim of the very process which it is designed to combat.

5. The spleen has a relation to tumour-growth (Krumbhaar - *ibidem*). Growths "take" less readily and are smaller in the spleen than elsewhere and intra-splenic inoculation is most successful in raising resistance to tumour growths elsewhere in the body.

It is on this principle that Dr. Todd founds his method of treatment of inoperable growth; all the different measures he adopts are taken with the single object of stimulating the reticulo-endothelial system.

There is some experimental evidence (*Krumbhaar ibidem*) that removal of the spleen stimulates growth already present elsewhere.

6. The spleen has a role in the metabolism of fat.

After splenectomy the blood cholesterol is always increased.

Gaucher's disease is an example of the storage of a protein - lipoid substance in the reticulo-endothelial cells; the substance is stored in the spleen and in some cases in the bone marrow. It is not known whether the disease is due to an abnormal metabolism which presents an unusual lipoid to the reticulo-endothelial cells, or whether these cells take upon themselves an unusual type and degree of storage capacity.

7. Finally the spleen may or may not have some hormonal action.

In old text books of Physiology (e.g. Kirke's Handbook 1872, p. 418) the spleen is compared with the thyroid and thymus glands as having some "higher but not yet understood function."

The modern representative of this view is Dr. F. Parkes Weber (Proc. Roy. Soc. Med. 26. Feb. 1933) who suggests that in acholuric jaundice splenectomy "not only removes excessive destruction of red cells but also removes some subtle influence of the spleen on the bone marrow owing to which the marrow produces abnormal erythrocytes."

Krumbhaar in the article from which quotation has already been made would appear to subscribe to this view and Pepper and Farley's "Practical Haematological Diagnosis," p. 339, mention it with approval.

As yet, there is no proof of such hormonal influence.

The Physiology of the Blood Platelets.

In the chick embryo, Sabin claims to have demonstrated the blood platelets as early as the fourth day. They are probably formed from the megakaryocytes of the bone marrow, though Schilling believes that the platelet is the entire modified nucleus of the young erythrocyte, partly detached and becoming free in the circulation. In this connection, Watson (Edinburgh Medical Journal 1932. 39. 311) has found that fragments of effete erythrocytes correspond in every detail to platelets. Nevertheless, the almost unanimous opinion of physiologists is that the platelets are formed from megakaryocytes. These are very large cells with a single large nucleus divided into lobes, with a complex retiform arrangement of the chromatin. No nucleoli are seen; the protoplasm is basophilic and contains many irregular granules. These cells are actively amoeboid, with long pseudopods which seem to extend into the blood channels. Bits of these pseudopods are pinched off to form the platelets.

The platelet is smaller than the red cell, and like it has no nucleus. Abnormal platelets cannot be recognised by their appearance, and there is as yet no criterion of their maturity or size. Their number in the circulating blood is variously stated at from 200,000 to 400,000 per c.m.m:

different methods of isolation seem to result in different estimates and no doubt the number varies very considerably from one time to another.

The most important function of the platelets is to cause blood coagulation. Cramer and Bannerman (Lancet 1929. 1. 992) say tersely that no coagulation of blood occurs without disintegration of platelets; everything that retards or prevents disintegration of platelets retards or prevents coagulation.

When blood has coagulated normally the clot shrinks. There is said to be a definite quantitative relationship between clot retraction and the number of blood platelets; the minimum number of platelets for the formation of a firmly contractile clot is said to be 100,000 per c.m.m.

The bleeding time is in direct proportion to the number of platelets; coagulation time may be normal in the presence of prolonged bleeding time; in such a case, however, the clot is usually of poor quality and retracts badly.

The blood platelet lives only three or four days and is destroyed in the spleen and reticulo-endothelial system. Platelet phagocytosis by leucocytes has been described, and in anaphylactic shock there appears to occur a massive agglutination and destruction of platelets in the viscera (Pepper and Farley, p. 173).

In addition to its destructive function, the spleen seems to act as an emergency reservoir for platelets. Binet and Kaplan (Ann. de physiol. 1928. 4. 671) working with

dogs found in acute asphyxia an increase of platelets in the peripheral blood of no less than 200,000 per c.m.m. This result seems confirmed by Field (Am. Journ. Physiolog. 1930. 93. 245).

The Etiology and Pathology of certain blood disorders.

Splenectomy has been performed for a wide variety of diseases associated with splenomegaly, but its chief use has been in the treatment of three diseases:-

1. Acholuric Jaundice.
2. Splenic anaemia.
3. "Essential Thrombocytopenia."

Before discussing these conditions for which splenectomy seems the treatment of choice it may be well to review briefly some other conditions in which splenectomy has been practised.

(1) Splenectomy for normal spleens and blood.

Spleens have been removed for cystic disease and for rupture. Shortly after the operation there occurs a temporary anaemia of variable degree; after a short period the red cell count and haemoglobin tend to return to the normal, or even slightly above normal. During this period there is an increased number of immature forms in the circulating blood in the form of normoblasts and reticulated cells. There is nothing characteristic of splenectomy in this picture except the high number of cells which contain Howell-Jolly bodies.

In the white cells, there is the usual post-operative increase in the number of neutrophil leucocytes, though this increase persists longer and perhaps rises higher after

splenectomy than after a comparable operation. Thirty thousand is not an unusual figure.

After the primary post-operative increase of granular leucocytes, a true lymphocytosis and eosinophilia appear to keep the total count high for at least a month. The blood platelets show a greatly increased count during the period of bone marrow activity which follows splenectomy, but no permanent increase in the numbers occurs. It is during this period of platelet increase that the well-recognised danger of thrombosis after splenectomy arises, and probably the two are related.

(2) Splenectomy for Addisonian anaemia.

Before liver or stomach extracts became the routine treatment for "pernicious" anaemia, splenectomy was practised not infrequently. It almost always initiated a remission of symptoms, but this remission was usually the last. There can be little doubt that the temporary improvement was due to the stimulus to the bone marrow applied by removal of the organ chiefly concerned in destruction of red cells and platelets. Since the introduction of liver therapy splenectomy has been abandoned, though it might be worth consideration again in those rare cases described by Wilkinson and Israëls as Achresthic Anaemia (B.M.J. Jan 26th and Feb. 2nd. 1935).

(3) Splenectomy in Gaucher's and Niemann's Diseases.

Splenectomy has been performed several times in Gaucher's disease. It removes a large tumour and may improve cases with haemorrhages due to thrombocytopenia, but it has no effect on the progress of the disease; in fact, in children a relatively early skeletal infiltration has followed splenectomy (Well, Rosenthal and Oppenheimer. Journ. Amer. Med. Assoc. 1929. xcii. 637).

The one case of Niemann's disease in which a record of splenectomy has been found was followed by fatal pneumonia. The patient was an infant of twenty months. (Schmidt and Thoemes, quoted by Rolleston).

(4) Splenectomy in various chronic infections.

Splenectomy has been performed for chronic enlargement of the spleen from tuberculous disease and from syphilis, especially, in the latter case, when an added infection has prevented the success of anti-syphilitic measures.

Egyptian splenomegaly due to schistosomiasis is best treated by splenectomy; otherwise it is followed after an interval of five to fifteen years by hepatic cirrhosis and ascites, thus resembling the sequence of events in Banti's disease. It is probable that not all cases of Egyptian splenomegaly are really due to schistosomiasis; some may be syphilitic or malarial; dysentery and bilharziasis have

been suggested as the causes of others.

In all the conditions of disease mentioned above, the splenic involvement is a comparatively minor part of a more general disorder and splenectomy cannot be expected to produce a cure; its performance is largely dictated for the removal of a tumour whose size is a source of discomfort. They differ entirely from the three conditions now to be discussed in which splenectomy is performed with the direct object of producing clinical cure. These conditions are acholuric jaundice, splenic anaemia and "essential thrombocytopenia."

Acholuric Jaundice.

Acholuric jaundice is a rare disease of which two forms are described; the common form is familial and congenital, the rarer is acquired. The two forms differ only in the degree of blood changes present, except for the familial history, and even in these acquired cases a series of family blood counts may reveal a microcytosis in certain of the members.

Aetiology. The disease was first described in 1900 by Minkowski, who considered it a primary disease of the spleen.

In 1907 Chauffard (Semaine Medicale Jan. 1907. 25) pointed out its connection with microcytosis and increased fragility of the red cells. Since that time there has been

division of opinion as to whether the fault lies primarily in the bone marrow's production of poorly resistant cells, or in the spleen's phagocytic activities compelling the marrow to produce cells rapidly.

In 1930 A.G. Gibson (Mycosis of the spleen) reported the discovery of a streptothrix of the genus nocardia in various chronic splenomegalies, and in the Lancet (August 5th 1933) he reported the finding of this organism in the spleens of four cases of acholuric jaundice. He reports especially the finding of this organism in a patient with extremely slight evidence of the disease, but with a family history of the disease, and draws the inference that it may lie dormant and yet produce the slight signs that have been taken to be the hereditary factor.

Other pathologists have not been able to demonstrate the streptothrix, and some regard it as purely an accidental contamination, but Tidý (Synopsis of Medicine p. 714) regards it as a possible cause of some cases of Banti's disease.

Morbid Anatomy. As acholuric jaundice is usually compatible with long life, few cases have come to post-mortem observation. The accepted morbid appearances may be summarised as:-

1. Splenomegaly is invariable. There is great vascularity of the pulp, with hyaline changes in the arterioles. The Malpighian bodies are scanty and usually slightly

atrophied, the atrophy spreading out from the degenerated central arteriole in a manner comparable to the fibro adenia described by Banti in the disease called after him.

The changes in the pulp are the most important. Normally in the spleen pulp the numbers of red cells and nucleated cells are about the same; in acholuric jaundice the red cells are much more numerous than any other type.

2. The bone marrow is enormously hyperactive, the hyperactivity being chiefly of the erythropoietic marrow.
3. The liver shows little or no change.

Clinical Course. The congenital and familial nature of the disease is well established; the sexes are equally affected and the tendency to the disease passes equally with both sexes.

Jaundice, which is the most striking feature, is present at or soon after birth; it is rarely delayed till after infancy. It is of all degrees of intensity, the colour deepening after cold or prolonged strain, mental or physical. Crises of abdominal pain may occur, in which the jaundice may be increased. These attacks may be due to peri-splenitis or to gall stone trouble, for gall stones are very common in acholuric jaundice, presumably from the bile becoming inspissated.

The jaundice is of the dissociated type, giving usually an indirect positive Van den Bergh reaction, and is

not associated with pruritus; the urine also does not usually contain bile salts, and the faeces are normally or even excessively coloured.

The liver is not usually enlarged, and if it is, the enlargement is due not to cirrhosis but to congestion or fatty changes.

Anaemia is almost invariably associated with the incessant blood destruction, but it appears as if the patient often remained in a state of compensation until some additional factor, intercurrent infection or trauma, caused a break in compensation, with an increase in the anaemia. An average count might be R.B.C. 3000,000, haemoglobin 60%. The character of the red cells rather than their number is the determining factor in the blood picture. They vary in size, but there are enough small ones, measuring from 5.9μ to 6.4μ to justify the term microcytosis, while vital staining will show up to 15% reticulated cells.

The other characteristic, on which a diagnosis may have to depend, is the increased fragility of these red cells to hypotonic salt solution. Normally corpuscles begin to break up in saline of about .44% and haemolysis is complete at about .34%; in this disease haemolysis starts as early as .7% and is often complete by .4%.

The course of the disease is very chronic, but is often marked by repeated periods of rapid blood destruction,

during which there is fever and deepened jaundice. Following such a period the red cells are often below 1,000,000 and the haemoglobin down to or below 20%. Very active red cell formation is stimulated and the young cells may number 60% of the total. With the severe anaemia irregularity in size and shape of the red cells may appear and nucleated reds are common. An occasional megaloblast may appear. Nevertheless microcytosis and increased fragility persist and may even become more evident. At the height of a crisis the urobilin output is greatly above normal and the Van den Bergh test reveals the high pigment content of the plasma.

It remains to add that there are all grades of severity of the disease; in some families where the third generation is known to suffer from acholuric jaundice there is a family history of father and grandfather living to advanced ages (70+) though known always to suffer from jaundice and a big spleen. The main danger to life lies in the haemolytic crises, though the frequent occurrence of gall stones may also cause danger and much disability. Atypical forms occur (Proc. Roy. Soc. Med. 26. Feb. 1933) in which the diagnosis may depend purely on increased fragility of the cells, and a very rare case has been described by Thomson (Lancet Nov. 18th. 1933) in which increased fragility appeared only after

splenectomy. To explain this case Thomson puts forward the theory that before splenectomy, the destruction of immature cells by the spleen just balanced their production; after splenectomy these immature forms with increased fragility appear in the circulation.

The treatment of the condition is firstly by liver, which is sometimes successful; in acute haemolytic crises blood transfusion is required and if the crises recur often or are severe splenectomy should be performed. The mortality is low and the results very good, but in the milder grades it is unnecessary.

Though the clinical results of splenectomy are good, the results on the fragility of the red cells are by no means so good; in at least one half of cases the fragility is unaltered. In spite of this, the red count becomes normal and the size of the red cells becomes or approaches normal. Lord Dawson reports a case in whom splenectomy was originally performed for a splenomegaly diagnosed as splenic anaemia.

Later studies seemed to justify the view that the case had been one of acholuric jaundice from the beginning. Twenty-seven years after splenectomy the red cells show increased fragility.

Splenic Anaemia and Banti's Disease.

Splenic anaemia is a group of clinical manifestations of unknown cause; the demonstration of a cause such as syphilis, malaria or haemolytic jaundice automatically removes the case from the category.

The features of this chronic syndrome, which occurs in children as well as in adults are:-

1. Chronic splenomegaly.
2. Secondary anaemia.
3. Absence of leucocytosis or more usually some leucopenia.
4. Absence of enlarged lymphatic glands.
5. Periodic gastro intestinal haemorrhages.
6. Prolonged course, with no tendency to spontaneous cure.

When the condition becomes complicated by portal cirrhosis of the liver it is known as Banti's disease. According to Banti and Naegeli all cases of splenic anaemia end in cirrhosis of the liver; this is correct of many cases, but there are certainly very chronic cases in which hepatic cirrhosis does not supervene.

Pathogeny. The infecting agent is unknown, but there is every appearance of a low grade infection of the spleen. Gibson's claim to have demonstrated a streptothrix has already been noticed, and in 1926 Nanta in Algiers and in 1927 Emile-Weil, Gregoire and Flandrin (Bull. et mem. Soc.

Med. d. hop. de Paris 1927. 3ieme series li. 713) ascribed the condition to an aspergillus-like fungus. On the other hand, the appearances described as a mycelium have been regarded as the deposit of crystals of iron and calcium on fibrin filaments, (Langeron. Presse med. 1928. 481. Lancet 1931. 1. 1063) or on degenerated elastic and white fibrous tissue (McNee. Glasgow Medical Journal 1929. cxi. 65). Thrombosis of the splenic vein has been suggested as a common cause of the condition in children (Wallgreen Acto Paediral. 1927. vi. Supplem.), the thrombosis being ascribed to such causes as umbilical infection, abdominal trauma and spread of inflammation from tuberculous glands.

Morbid Anatomy. The spleen is enlarged; the capsule is thickened and there may be perisplenic adhesions containing dilated veins. The spleen retains its form, is tough and may show infarcts. The common histological finding is diffuse fibrosis; different writers vary as to other findings. The Malpighian bodies show no constant change, but excess of fibrous tissue round the central arteriole is common. The walls of the splenic vein show endophlebitis and often areas of calcification. The vasa brevia veins and the anastomoses between the gastric and oesophageal veins are dilated, and in the lower end of the oesophagus there may be varices which tend to gastro-intestinal haemorrhage.

The bone marrow is often hyperplastic, though hypoplasia is also described.

The Clinical Picture. The onset is gradual and the course chronic, often probably beginning in childhood, though first diagnosed in adult life. The initial symptoms are those of anaemia: weakness, debility and dyspnoea on exertion. The enlarged spleen may precede other manifestations. The cardinal features are splenomegaly, anaemia and periodic haemorrhages. The splenic enlargement is slowly progressive, but its size is never so great as in myeloid leukaemia or Gaucher's disease.

The anaemia may be due to gastro-intestinal haemorrhages and may improve in the interval between these periodic attacks, or it may be due to the inhibitory effect on the bone marrow of toxins produced in the spleen. It is of secondary type, with a low colour index; the red count may fall to 2,000,000, or even lower and the colour index falls to 0.6 or lower. Nucleated red cells do not appear except after severe haemorrhages. The fragility of the red cells is normal, or sometimes slightly diminished. Rosenthal (Journ. Am. Med. Assoc. 1925. lxxxiv. 1887) divides the cases into two classes according to presence of thrombocytopenia or thrombocythaemia and suggests that only cases with thrombocytopenia are suitable for treatment by splenectomy. In

cases of increased platelet count he considers the risk of thrombosis after operation an absolute contra-indication, on the ground that the splenomegaly deprives the body of the means of inhibiting the formation of platelets.

This view is questioned by Bryce (Lancet 2. 1423. Dec. 31st. 1932) who records two cases of splenectomy. In the first there was thrombocytopenia in a patient who was regarded as a good surgical risk, yet death followed splenectomy and the post-mortem findings were of extensive thrombosis of the splenic and portal veins. In the second case there was a patient desperately ill, with previous attacks of venous thrombosis, and a moderate platelet count, yet recovery followed splenectomy, even though a fine cirrhosis of the liver was reported at the operation. It would appear that the relative numbers of platelets cannot be regarded as an absolute indication for or against splenectomy.

The leucocyte count may be normal at first, but characteristically there is a leucopenia even to 2,000 per c.m.m., with a diminution in the polymorphs, the lymphocytes being relatively increased. Myelocytes are absent.

Gastro intestinal haemorrhages occur at irregular intervals of weeks, months or even years; in the intervals the subsequent anaemia may pass away, and in rare cases, a normal or above normal red count (anaemia splenica sine anaemia) has been recorded. The haemorrhage is probably

due to failure of the compensatory mechanism of dilated veins to relieve the engorgement of the splenic venous system, for other haemorrhage (epistaxis, bleeding from the gums or purpura) is decidedly exceptional.

The skin is usually pale, but there may be pigmentation, especially of the abdomen; this may be caused by sympathetic irritation from the enlarged spleen; oedema of the feet from the pressure of the spleen and perhaps from cardiac dilatation may also occur.

The liver is not enlarged unless cirrhosis supervenes, but ascites may occur from preisplenitis.

The treatment of choice is splenectomy; spontaneous cure does not occur, though the disease may remain so far stationary that life is prolonged for many years, with intermittent gastro-intestinal haemorrhages.

Splenectomy is followed by cure or improvement; Krumbhaar (Modern Medicine, Osler, McNae and Funk 1927. v. 147) records 315 cases, some of which were cases of Banti's disease. Of these improvement followed splenectomy in 187 and cure in 14, with an operative mortality of 45 (14%).

Banti's Disease.

In several papers between 1883 and 1911 Banti of Florence described the disease which bears his name. He divided its course into three stages:-

- (i) The pre-ascitic stage with the symptoms of chronic splenic anaemia, lasting 3 - 5 years.
- (ii) The intermediate stage of 12 - 18 months with enlargement of the liver, digestive disturbance and sometimes slight jaundice.
- (iii) The terminal stage (6 - 12 months) of a cirrhotic liver becoming smaller, with wasting, ascites, oedema and cachexia.

Pathogeny.

Banti believed that bacteria and toxins in the spleen produce changes in the centre of the Malpighian bodies via the pulp, thus causing anaemia, endophlebitis of the splenic vein and ultimately hepatic cirrhosis.

Chauffard (Semaine med. Paris 1899. xix. 177) supported him in the view that portal cirrhosis might be due to poisons produced in the spleen.

The prognosis in Banti's disease is worse than in uncomplicated chronic splenic anaemia, and the results of splenectomy less favourable. Chaney (Am. Journ. Med. Sc. Philadelp. 1925. clxv. 856) records a mortality of 13% in 39 cases of chronic splenic anaemia and of 23% in 30 cases with hepatic cirrhosis. Nevertheless splenectomy is the only real form of treatment, for no other known treatment is anything but symptomatic. It is certainly the case in this disease that "if 'twere well done, 'twere well done quickly;" the less advanced the liver cirrhosis the better the prospect of cure, or real improvement.

Purpura Haemorrhagica.

The third disease in which splenectomy is the treatment of choice is that which has been known by a variety of names since Werlhof described it in 1735 as the "morbus maculosus." It is now most commonly known as "purpura haemorrhagica", a name derived from its most prominent clinical sign, which is not, however, invariably present, or as "essential thrombocytopenia" from the haematological fact demonstrated by Frank in 1915 that the platelets are deficient in number.

The disease is rarely either familial or hereditary; it is marked by periodic haemorrhages into or from the tissues; the course may be intermittent or chronic, the attacks of haemorrhage occurring at periods of thrombocytopenia. The essential feature is haemorrhage for no detectable reason, the haemorrhage recurring in days, weeks or months. In the intervals the patient may be well and the changes in his blood disappear; though typical, this is less common than a failure of restoration to normal of the blood picture. A still more severe form is associated with a constant tendency to haemorrhage, slight or severe.

Purpura is not essential to the diagnosis, but can almost always be demonstrated by venous congestion of the arm for 10 minutes by the arm-band of a sphygmomanometer. This

"Capillary Resistance Test" is so constantly positive that in its absence the diagnosis is open to doubt.

The pathogeny of this disease has given rise to much difference of opinion, and is still not determined.

Kaznelson (quoted by Piney "Recent Advances in Haematology") in 1919 considered the disease to be a primary hyperfunction of the spleen, giving as his reasons:-

- (a) The not infrequent occurrence of splenomegaly, which he regards as being due to excessive functional activity.
- (b) Excessive numbers of megakaryocytes have been seen in the marrow in such conditions of symptomatic purpura as streptococcal septicaemia. He describes megakaryocytes in the splenic pulp also in this condition. Similar appearances are invariable in purpura haemorrhagica, and he supposes that their presence indicates a myeloid compensatory reaction so vigorous that even the parent cell of the platelets appears in the circulation.
- (c) The great rise in the platelet count after splenectomy can only be attributed to the removal of the chief thrombolytic organ.

Frank (1925) believed that the disease is due to a real defect in the production of platelets, which he attributes to the action of some noxa on the megakaryocytes alone. Normally after splenectomy, as after a big haemorrhage, there is a vigorous reaction of the whole bone marrow tissue, but Frank describes cases where following splenectomy the white and red corpuscles increased in number without a corresponding increase in the platelets.

In this connection, Seeliger has described pathological changes in the protoplasm of the megakaryocytes in a case of purpura haemorrhagica; about 90% of these cells in the marrow showed no granules; 6% were only partially granular and the remaining 4% appeared normal.

The non-granular megakaryocytes may be poisoned cells or may be megakaryoblasts, but in either case it is clear that there is some defect in them which will pre-dispose to defective platelet formation. Of this defective formation the giant thrombocytes are taken to be evidence, on the presumption that each giant represents several platelets which have separated from the parent megakaryocyte as a mass instead of individually. There can be no doubt that the platelet-forming mechanism is very delicately balanced, for Duke (Journ. American Med. Assoc. 1910. lv) caused practically complete thrombocytopenia by administering benzol without altering the white or red cell count.

Although thrombocytopenia appears to be the major defect leading to haemorrhage bleeding sometimes does not appear even with marked depression of the number of platelets. Accordingly Morawitz in 1930 suggested that a capillary defect must also play a part in the tendency of the disease to haemorrhage. When a break occurs in the capillary endothelium it is normally sealed promptly by the platelets; if the platelets are few purpura results.

Sampson Wright (Applied Physiology 221) states that the thrombopenia alone cannot be responsible for the haemorrhages, because bleeding may cease in a severe case several days before the platelet count rises and platelets have been known to disappear from blood without haemorrhage recurring. A somewhat parallel condition will be described in the original case whose history is given later.

Bedson has shown that injection of agar serum into an animal reduces the platelets to a low figure, but does not cause haemorrhage. But if an anti-red cell serum is injected four hours earlier, subsequent injection of agar-serum produces rapid purpura. Bedson suggests that the anti-red-cell serum injures the capillary endothelium, which is closely related to the red cells. Normally the platelets would be deposited on such an area and prevent haemorrhage, but the destroyed platelets leave the endothelium unprotected.

He suggests, therefore, that abnormal capillary permeability may be the initial disorder; the platelets are used up secondarily in the defence of weak areas. If the endothelial damage is widespread all the platelets may be used up without supplying adequate protection and haemorrhage results. As a further support to this view Bedson showed that in the normal guinea pig splenectomy protects against the production of experimental purpura only so long as an increase in the platelets is present.

H.L. Tidy (Lancet 1926 ii. 365. Brit. Med. Journ. 1930. ii. 1073) has accepted the theory of capillary permeability and has argued that the different forms of purpura are manifestations, varying in degree, of the haemorrhagic diathesis, the initial defect being abnormal permeability of the endothelium. He states that the factors concerned in capillary haemorrhages are:-

(a) Capillary permeability; this being increased permits the escape of the blood constituents. He quotes Dale and Laidlaw as showing experimentally that the capillaries are dilated and the blood current not slowed; the defect is probably in the inability of the capillary wall to contract; precisely as in urticaria (where the plasma escapes without cells) or after histamine injections.

(b) The Blood Platelets.

Thrombocytopenia may arise (1) primarily from lack of formation as in aplastic anaemia, (2) secondarily by massive destruction in an attempt to defend weak capillary endothelium. He suggests that in this case the bone marrow, under pressure, produces defective platelets which are readily destroyed by the spleen.

(c) The Bone Marrow, which forms the platelets.

(d) The spleen, which normally destroys effete platelets.

He summarised his views thus:-

Increased capillary permeability is the essential factor; its cause is unknown, but a histamine effect is suggested. Thrombopenia is a contributory factor arising from:-

- (1) Destruction of platelets in an attempt to protect the vessels.
- (2) Increased destruction of defective platelets by the spleen.
- (3) Defective and deficient formation of platelets by the marrow under excessive demand.

Pepper and Farley ("Practical Haematological Diagnosis" 1934. p. 309) state that it is impossible to explain every case of the haemorrhagic disease. "Some arise clearly from disorders of the platelets, others from deficiency of calcium or fibrinogen; some present no recognisable abnormality; in some of these the fault lies in the capillary endothelium."

Two isolated observations of the platelet count should be mentioned here. V. Giudiceandrea (Rass. di Clin. Ter. e Sci. Affin. July 1934. 223. Quoted in the B.M.J. 16.2.35. p. 27) points out that many substances are known which have an effect on the platelet count.

Pyridine, trypan blue and Congo-red increase the platelet count; this observation may serve to explain the recent acclamation of Congo-red as the treatment for haemoptysis. Platelets are increased also by Lead, Mercury and Arsenic and by artificial pneumothorax and X-ray therapy.

The platelet count is decreased by benzol, repeated blood-letting, splenic extracts and fatigue states.

Stimulation of the vagus decreases the number, of the sympathetic increases the number, of platelets.

The other observation is quoted from Sampson Wright "Applied Physiology" p. 222 - "The platelet count is diminished in vitamin A deficiency, where the platelets may serve as agglutinins to clump invading organisms."

To the writer, the theories and arguments of H.L. Tidy appear convincing, except for one defect. He does not seem to explain how splenectomy is so valuable a therapeutic measure as undoubtedly it is in purpura haemorrhagica. If the essential lesion is in the capillary endothelium the role of splenectomy would appear to be on the same level in purpura haemorrhagica as, for instance, in Addisonian anaemia - at the best - or leukaemia, at the worst. That is, the operation removes the main thrombolytic organ and so allows a remission which can only be temporary, or alternately fails altogether. To this, the reply might be that splenectomy does not invariably cure the disease, and that cases are known where no improvement follows the operation and others where temporary improvement is followed by relapse, especially in the form of severe menorrhagia occurring at puberty.

It is true that such cases are known, but their rarity

is such that it does not appear to invalidate the argument that normally splenectomy cures purpura haemorrhagica. Other explanations are easily possible for the rare failures; accessory spleens may have been overlooked at the first operation and actually cases have been described where a⁽¹⁾ second operation has removed an accessory spleen with resultant cure. Similarly cases of temporary improvement only may be due to the reticulo endothelial system taking upon itself the (? perverted) function of the spleen.

To the writer it seems the most probable view that all three diseases in which splenectomy is so valuable are primarily diseases of the spleen, probably of an infective nature, and possibly due to variations of Gibson's fungi. Banti's disease and splenomegaly are almost universally thought to be infective; acholuric jaundice might easily be due to a splenic toxin acting on the red bone marrow, and purpura haemorrhagica to a similar but different toxin acting on the megakaryocytes in patients who were predisposed to such capillary disturbances as urticaria. This hypothesis would at least explain the undoubted value of splenectomy in these cases, and it would cover the fact that quite a number of cases have now been described in which the cardinal signs of all three diseases have been found - splenomegaly, purpura and excessive fragility of the red cells.

(1) Marison, Lederer and Fradkin. Accessory Spleens and their significance in Purpura Haemorrhagica. Am. J. Med. Science. 176. 672. (Nov. 1928)

No account is given here of the clinical picture in purpura haemorrhagica as a detailed account of an original case is given later.

The treatment of choice is splenectomy, though it may not be needed in some of the milder chronic intermittent forms. In the severe chronic forms and in acute forms the results are excellent. Elrason and Ferguson (Amer. Ann. Surg. 1932. 96 - 801) report 113 recent cases; the operative mortality was 7% and the results excellent.

The Indications for and Results of Splenectomy.

A symposium on the indications for splenectomy at the B.M.A. Centenary meeting is reported in the Lancet (Sept. 1932. 516).

At this meeting of experts, there was unanimous opinion that splenectomy should be performed in all cases of splenic anaemia and Banti's disease; Lord Moynihan's views may be quoted as summarising the general opinion:

"Since the condition was always fatal if the patient lived long enough, he believed operation should be undertaken at all stages, though early operation was desirable. The presence of ascites and cirrhosis of the liver he did not think contra-indicated operation. The greatest technical difficulty of the operation was the presence of adhesions. He emphasised the necessity, however, of careful preparation of the patient. Splenectomy for this condition should never be performed as an emergency. Two or three months were well spent in reducing the size of the spleen by radium or X-rays, and in raising the red blood count by transfusions. He had reduced his mortality in this way from 12% to 6%."

No real difference from this opinion appeared in the subsequent discussion, though both Prof. S.P. Davidson and Dr. Dorothy Hare emphasized the necessity for caution in diagnosis and the difficulty of diagnosis in some cases. Prof. Sheen regarded the results as being much worse in the presence of cirrhosis, but also agreed that splenectomy should be performed.

Statistics of the results are difficult to find; we have already quoted Krumbhaar's 315 cases, of which 201 were reported cured or much improved and 45 died, and Chaney's statement of 30 collected cases of Banti's disease, with a mortality of 23%. We have personal knowledge of only one case; an advanced case of Banti's disease with ascites died eleven days after removal of a spleen weighing 5 pounds.

The indications for splenectomy in acholuric jaundice are at least as strong; in the symposium already quoted Lord Dawson said that other things being equal, splenectomy should be performed in all cases of acholuric jaundice, but that the operation should not be done before the age of 12. In his opinion, cases might appear to be well, but they were only well at the expense of the bone marrow, which was kept continuously in a state of hyperactivity to supply the needs of the circulation. In acholuric jaundice he did not favour preliminary blood transfusion, on account of the possibility of disaster from the unduly fragile red cells, even with the most careful typing of the blood.

With the last opinion we are in hearty agreement; we have knowledge of one patient who died of excessive haemolysis with haemoglobinuria following a blood transfusion

done for a blood crisis in a patient with acholuric jaundice. Lord Moynihan thought that splenectomy in acholuric jaundice should be performed especially for the prevention of complications, of which the greatest were haemolytic crises and gall stones.

We have personal knowledge of a young man of 18 and of his father, aged 56, both of whom suffer from acholuric jaundice. Neither has had, as yet, any acute blood crises, but the father has begun of late to suffer from attacks of gall-colic. So far, both refuse to consider surgical treatment, though one is hopeful that a few more attacks of gall-colic may serve to alter their views.

The results of splenectomy in this condition are good, and the mortality is apparently lower than in splenectomy either for splenomegalic anaemia or for purpura haemorrhagica. Krumbhaar (Physiolo. Rev. 1926. vi. 160) states that the mortality has fallen below 3% and adds "Even this low death rate should suffice, however, to prevent surgical intervention if the patient suffers little or no inconvenience." The difference between his attitude and that of Lord Moynihan will be obvious, but as gall stones complicate acholuric jaundice in a very large proportion of cases sooner or later, and as the mortality of cholecystectomy

is certainly greater than 3% this would seem to the writer a case in which "prevention is better than cure."

Splenectomy is followed by disappearance of the jaundice, an increased feeling of well-being and a cessation of the haemolytic crises which led to abdominal pain. The red blood corpuscles return to the normal in number and even in size; reticulocytes diminish to the general average of about 2%. Haemoglobin percentage rises. The fragility of the red cells could hardly be expected to diminish, and it has generally been found to remain at a high level.

Splenectomy has been regarded as the treatment of choice in purpura haemorrhagica of the chronic type since Williamson (Arch. Dis. Children 1926. i. 36) collected 58 cases in 1926 of which 50 were free from symptoms two years later. In the same year Whipple (Surg. Gyn. and Obstet. 1926. xlii. 329) reported 7 fatal cases out of 8 acute cases with severe haemorrhage, and for a time splenectomy was regarded as contra-indicated in the acute condition. Lord Moynihan, in the symposium from which quotation has already been made, divided cases into acute and chronic, the latter giving no anxiety at operation.

Since their time, however, there has been a steadily increasing record of success in the treatment of acute cases by splenectomy. Thus Myers (St. Bartholomew's Hospital

Journal. Dec. 1933) records five successful cases of splenectomy for purpura haemorrhagica. Of these two at least were acute, and a third, in a girl aet 10, had severe symptoms for nine months only.

H.S. Le Marquand (The Royal Berkshire Hospital Reports 1933) reports splenectomy in three cases, two of which were extremely acute, with very severe haemorrhage. All three cases achieved cure, although one had a nearly fatal post-operative collapse.

Another acute case successfully treated by splenectomy is recorded in this paper.

The most important precaution in advising splenectomy is to be quite sure that the condition is purpura haemorrhagica and not some other disease with similar symptoms.

Askey and Tolland (Archives of Surgery 26. 1933. p. 103) record several cases in which the symptoms were those of purpura haemorrhagica but in which splenectomy either had no effect or was disastrous. In all these cases, however, there was some departure from the essential picture as it will be described; either thrombocytopenia was absent, or both the bleeding and coagulation times were prolonged; the diagnosis would appear to be haemophilia or an atypical aplastic anaemia in these cases. They say "The most careful scrutiny of all patients with haemorrhagic disease is indicated before splenectomy is resorted to. Many cases

are not typical and the differential diagnosis is most difficult. In borderline cases with no improvement, splenectomy is perhaps justifiable if the haemorrhage is unrelieved by transfusion and death seems otherwise inevitable. In the chronic type of bleeding with ecchymosis, bruising and moderate anaemia we believe it is better to postpone splenectomy unless the following requisites are met:-

- (i) Splenomegaly.
- (ii) Thrombocytopenia.
- (iii) Prolongation of the bleeding time.
- (iv) Non-retractility of the clot.
- (v) Positive capillary resistance test.
- (vi) Normal coagulation time.
- (vii) Normal or slightly increased leucocyte count.

, According to Piney, there are three groups of cases, divided according to their response to splenectomy.

1. Those in which a rapid and persistent rise of thrombocytes occurs to normal or more. There is usually a fall later, but symptoms of purpura do not recur.

2. Cases where the thrombocyte figures rise to normal for a few days after operation, but fall below the critical value soon. The platelet count, however, varies rapidly above and below the critical value; thus a persistent case may become a case with remissions and exacerbations.

3. Cases in which there is more or less no change in the platelets.

In Piney's opinion the indications for splenectomy are:-

1. All children with chronic anaemia from loss of blood.
2. Adults with continuous or frequent attacks, especially such as menorrhagia.

He advises a preliminary blood transfusion in all cases where the red cells number less than 2,000,000.

The contra-indications to splenectomy, when once the diagnosis of splenomegalic anaemia, acholuric jaundice or purpura haemorrhagica is established, are the contra-indications to any surgical operation performed for a reason other than the direct saving of life. Splenectomy, on the whole, is as safe an operation as cholecystectomy, for instance; like cholecystectomy it may occasionally be imperative for the saving of life - and again like cholecystectomy, under such circumstances it is fraught with more than average risk. Under ordinary circumstances the earlier splenectomy is done the better, partly because the patient's blood is not too worn down by exhaustion of the bone marrow and partly because the infection - at least in splenomegalic anaemia and perhaps also in the other two diseases - has not become widely diffused, with consequent injury to other organs and tissues.

Much discussion has occurred as to the advisability of transfusion before splenectomy in purpura haemorrhagica; one school of thought, ably represented by Dr. Le Marquand argues very strongly in favour of transfusion; the other thinks that in a condition where one of the three main risks

is post-operative thrombosis the addition of blood platelets even for the two or three days in which the transfused platelet is known to survive, is full of danger. Individual opinions probably depend on isolated personal experience, and the rule expressed by Piney - transfusion should be performed if the red count is less than 2,000,000 - is a sound compromise between the two opposing schools of thought.

There is no evidence that removal of the spleen - many sided as are its functions - is followed by any prolonged injury to the body; the blood count, especially the white count, is longer in returning to the normal than after a comparable abdominal operation, but there is no evidence of any ill effect from this fact. There is no evidence of any lowering of resistance to infection, nor of any alteration in the lipoid metabolism. Theoretically the most important defect should be the loss of the reservoir for red cells and platelets; in fact, after a reasonable interval, there seems to be no defect.

If the requisite conditions of accurate diagnosis and reasonable surgical risk can be satisfied, there would therefore appear to be no contra indication to splenectomy.

Case of Acute Purpura Haemorrhagica, successfully treated by
Splenectomy.

H.L., a girl of 5½, was seen in the Out-patient Department of the Bradford Children's Hospital on 19th June, 1934.

The history given was that six weeks previously the child had two teeth extracted under gas at the School Dental Clinic. There was no excessive haemorrhage at the time, but from two days afterwards purple spots appeared in crops on the skin, bruising followed the slightest touch, and for four days the urine had been dark brown to black in colour. There had been no blood in the stools and there was no history of melaena.

The family history was quite negative; the mother and father were both healthy; the child was one of seven children, all of whom had always been healthy. Her past history included measles, whooping cough and chicken pox, from all of which she had made a satisfactory recovery. It may be significant that she lived in a poor quarter of the town, and that her father was out of work; the family income - to support nine persons - was stated to be just under £2. a week. Her dietary was grossly lacking in proteins and in Vitamines, an average day's food being thus:-

Breakfast: one egg and bread, sometimes with butter: tea.
Dinner: potatoes and gravy: bread or milk pudding: tea.
Tea: one or two buns: tea.

Jam and oranges were rare luxuries; she had a little meat usually once a week; milk was used to flavour tea, but was never used as a beverage.

Physical examination showed a child of normal size and development, but very pale. There were two large bruises on the right cheek, one bruise on the right lower costal margin, several on the right thigh and a huge bruise in the middle of the back. A purpuric rash was seen chiefly on the chest and round the ankles. There were a few carious teeth; the gums were not bleeding, but there was recent haemorrhage from the nose and lips.

No abnormal findings were made in the throat, heart, lungs or abdomen; the liver and spleen were not palpable and there were no enlarged glands.

The urine was dark red in colour and contained much blood.

The child was admitted to the Ward immediately, the provisional diagnoses being (1) purpura haemorrhagica, (2) acute leukaemia.

On the 20th, the day after admission, there were two attacks of epistaxis, and some swallowed blood was vomited. The urine still contained much blood.

On the 21st the urine contained less blood, and there was no epistaxis, but slight bleeding occurred from the gum

about a carious tooth.

On the 22nd there was no bleeding during the day, but the upper lip bled at night.

On the 23rd there was no obvious blood in the urine, but microscopic examination showed a few red cells and some small oxalate crystals.

On the 25th there was another slight attack of epistaxis.

On the 27th and 28th there was smart haemorrhage from a tooth socket.

On 3rd July there was slight bleeding from the gums.

On 4th July there was severe epistaxis from the right nostril, the face was swollen and bruised and fresh purpuric spots appeared on the chest.

On 14th July the child scratched some of the spots on her face and lips, infected them and had an inflamed gland under the chin.

On the 24th, 25th and 26th there was a recurrence of haematuria, though the condition was not so severe as on admission.

On 1st August bleeding recurred from the gums.

On 7th August the spleen was just palpable; the tourniquet test which had been negative on two previous occasions, was positive this day.

On 11th August two large bruises appeared on the back.

On 18th August an enormous bruise appeared on the chin, following a trifling accident.

On 25th August the blood was typed and found to belong to Group II.

On 6th September, on which day her platelets numbered 700 per c.m.m., it is recorded that for the first time there were no bleedings and no bruises; during the night epistaxis occurred.

On 7th September Mr. H.H. Stewart, the Senior Surgeon to the Hospital, performed splenectomy.

On 8th and 9th her condition was entirely satisfactory; no further bleeding or bruising occurred and a catheter specimen of urine showed no red cells on microscopic examination.

On 6th October, as a therapeutic test, five carious teeth were extracted under gas; no unusual bleeding followed.

On 13th October she was discharged from the Hospital in good health.

The Blood Counts, for which I am indebted to Dr. C.J. Young, pathologist to the hospital, showed as follows:-

20th June	22nd August	6th Sept.	10th Sept.	14th Sept.	19th Sept.	
60%	68%	68%	58%	62%	66%	Haemoglobin.
2,487,000	3,437,000	3,700,000	2,987,000	3,100,000	3,200,000	Red cells.
1.21	1	.92	.97	1	1.03	Colour Index.
10,000	10,700	10,000	14,600	14,800		Leucocytes.
8,100. 81%	6,377. 59%					Polymorphs.
1,600. 16%	3,957. 37%					Lymphocytes.
300. 3%	257. 2.4%					Monocytes.
None.	86. .8%					Eosinophils.
9,000	5,000 Basophils. 4%	700	497,000	968,000	514,000	Platelets.
244,000. 8.9%	41,000 1.2%	81,000 2.2%	84,000 2.8%			Reticulocytes.
Weak indirect.	Negative	Negative.				Van den Bergh.
	At least 10 minutes	13 minutes	1½ minutes			Bleeding time.
	Poor.					Clot Retraction.

Splenectomy = Sept. 7th.

Dr. Young's reports added the following information:-

On 20th June, the film shows slight irregularity only in the size of the red cells.

On 22nd August, the film showed slight irregularity in the size of the red cells. There was no toxic granulation of the polymorphs.

The Arneth Count was 7/27/45/18/3%. 283%.

"Although the other blood elements do not give a clear cut indication on the point, the evidence is slightly in favour of excessive platelet destruction, rather than aplasia."

The treatment before splenectomy was largely symptomatic. The child was kept in bed on full normal diet, which included Cod Liver Oil three times a day. Bleeding was controlled by adrenalin, applied on gauze, and by the injection of Coagulen (Ciba), as much as 10 c.c. being used every third day.

Livogen (3i) was administered daily throughout the whole period. In August a trial was made of Collosol Calcium (3i. t.d.s.) for the first fortnight, and for the second fortnight Calcium Gluconate was given intramuscularly every 4th day, 5 c.c. of a 20% solution being used.

As there was little or no improvement at the end of August either in the clinical or haematological picture, Mr.



Stewart was asked to see the child with a view to splenectomy. He agreed that the operation was indicated and that the necessary conditions were all fulfilled, and it was decided to operate on 7th September. A blood count on the 6th showed that the platelets had now fallen to 700 per c.m.m., though on that day there were no bleedings and no bruises. The patient was transferred to the Surgical Ward, and the question of transfusion was carefully considered. The ultimate decision, chiefly on the ground that the red cells numbered about $3\frac{3}{4}$ millions, was against transfusion though a suitable donor was obtained for use if necessary.

The operation itself was performed under open ether anaesthesia, after a preliminary injection of Atropine, gr. 1/150. It occupied about 50 minutes, for the last 10 of which Chloroform was administered on account of the excessive formation of mucus in the naso-pharynx. Apart from the inconvenience of this mucus the anaesthetic caused no anxiety at all.

The incision was made with a cutting scalpel, since we had no diathermy knife, to the use of which Dr. Le Marquand pays tribute. There was considerably more bleeding than normal, the bleeding being not only an ooze but actual free bleeding from vessels. The rectus muscle was noticed to be

of a peculiar brick red colour, and from its surface also there was a good deal of bleeding. The haemorrhage was controlled as well as possible by ligaturing all the bleeding points and by firm pressure with swabs dipped in saline to which adrenalin had been added. The spleen was found to be protruding about an inch below the rib margin; it was free from adhesions but quite sessile and the pedicle had to be ligatured in situ; this formed the only difficulty of the operation. A search was made for accessory spleens, but none was seen. The abdomen was then closed, and it was noted in contra-distinction to the first case reported by Dr. Le Marquand, but as in his second case, that the oozing of blood still continued during the closure of the abdomen.

The child was put back to bed in good condition; four rectal glucose salines (3 vi) were given during the next twenty four hours and were well retained.

On the day after operation the pulse rose from its average of 90 to 136, but was of good volume, and the temperature which had never previously since admission been above 99° rose to 101°. Next morning it was normal and the pulse 112; thereafter the child's condition gave rise to no anxiety whatever for a week. A blood count then showed a platelet count little short of 1,000,000 and for a

day or two we had anxiety in regard to a post operative thrombosis. Five days later the platelet count had fallen to a little over half a million, and all our fears were ended.

A month after the operation, as a test of recovery, five carious teeth were extracted under gas; there was no undue haemorrhage at all, and as the patient seemed quite well, she was discharged a week later to report monthly at the Out-patient Department. She has remained quite well clinically and a blood count made at the beginning of March 1935, six months after operation showed:-

Haemoglobin	81%		
R.B.C.	4,150,000	per c.m.m.	
Colour Index	0.98.		
Leucocytes	12,000	per c.m.m.	
Polymorphs	5,160	per c.m.m.	43%
Lymphocytes	5,760	" "	48%
Monocytes	780	" "	6.5%
Eosinophiles	240	" "	2%
Basophiles	60	" "	0.5%

Platelets 638,000 per c.m.m.

Film: red cells appear normal. Arneth shift to the right in the polymorphs and eosinophiles.

"The leucocytosis is not due to increased output, but to delayed removal, the polymorph output being normal, but abnormally old forms are present. Presumably this is due to the absence of the spleen."

This report is in close accord with all such reports except for the unusual persistence in the rise of the blood platelet count. It seems clear that as yet the reticulo

endothelial system is not very active in destruction of the blood cells.

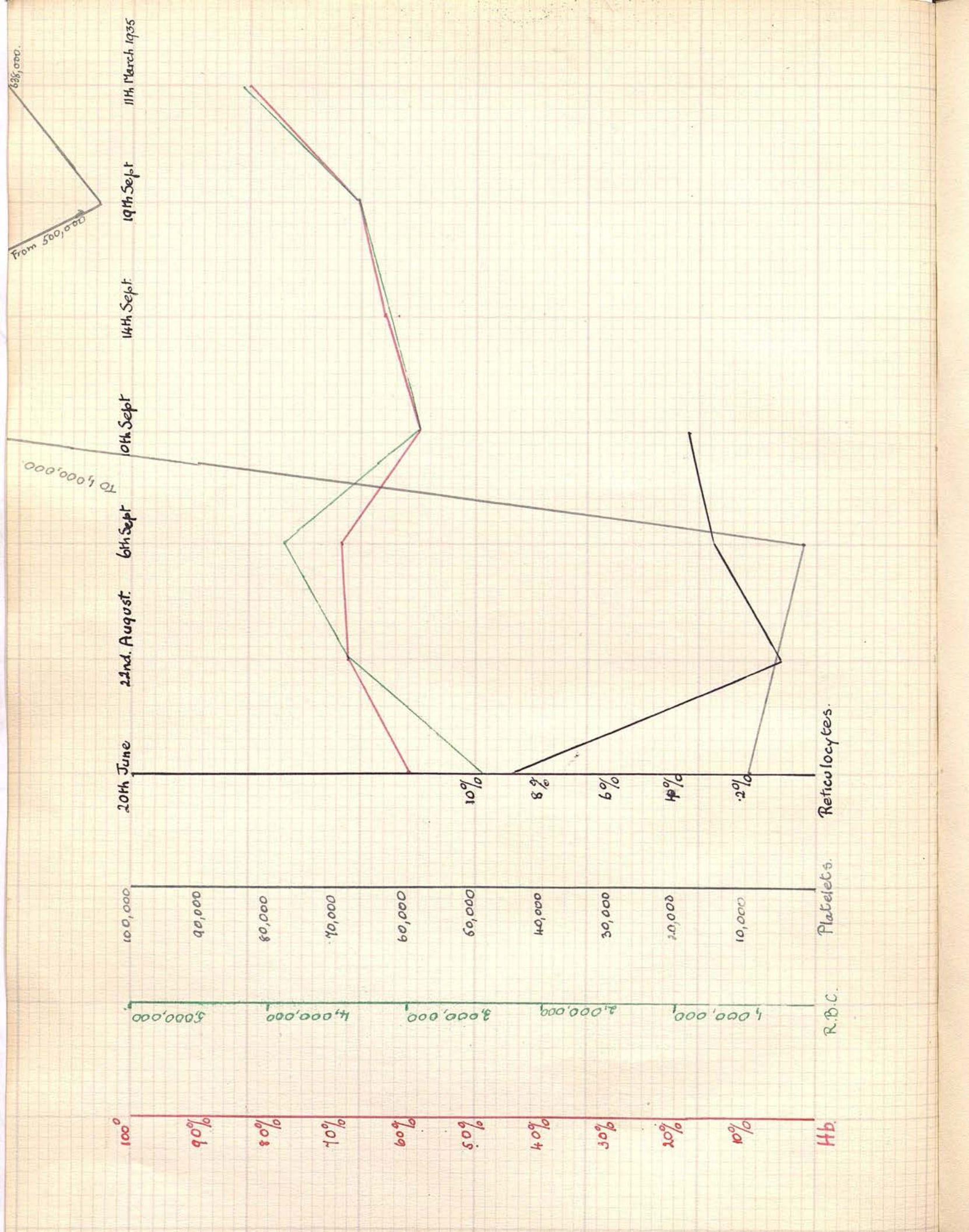
A curious clinical fact is that the abdominal scar is already very decidedly keloid; in all other respects the child is clinically in excellent health.

The histological report on the removed spleen reads:-

"The weight of the spleen when received was 53 grms. This is probably within the normal limits as the normal range, calculated from the relation of normal body weight for age to adult weights, would appear to be 50 to 70 grms. Blood may, however, have been largely spilled at operation.

Microscopic examination shows no marked abnormality. The pigment deposits usually associated with excessive blood destruction were not found, which is in agreement with the blood findings. Malpighian bodies are present in about the usual numbers, are not unduly widely separated by pulp and show no enlargement, being perhaps rather small for a child.

The sinuses contain very little blood, which may be due to its expulsion at operation, so that there may be some increase in the pulp, especially as this appears to be somewhat cellular. No haemorrhages or infarctions were found. The findings are quite compatible with those of the blood, which suggested a selective destruction of platelets, alone, of which well marked histological evidence is hardly to be expected."



Discussion of the Pre-operative Treatment.

Livogen was given throughout the pre-operative period. This was in deference to the case reported by Jacob and Clapperton (Brit. Med. Journal 1930. 1. 823) in which recovery occurred in an acute case under the administration of liver. We did not observe any benefit; possibly the dosage was too small: Livogen (3i) contains active principle of 4 oz. of liver.

Iron was not administered: the Colour Index on admission was 1.2, and continually ranged about 1, so that there seemed no indication for iron.

Coagulen Ciba was given with the direct object of controlling the bleeding; we are of opinion that its use and adrenalin packs were the only two methods of treatment which really had any effect on the haemorrhages.

Various forms of Calcium were administered in the hope that some Calcium deficiency might be at the root of the poor contractility of the clot; there was no evidence of any improvement.

Though the actual haemorrhages were much less severe than on admission by the beginning of September, after 10 weeks of medical treatment, the platelet count had sunk to 700 per c.m.m. This, and the fulfilment of all the

postulates, was really the deciding point in favour of operation; as far as could be seen, the child was certain to have some big haemorrhage before long which, by reducing her red cells, could only make operative interference more dangerous.

We considered irradiation of the spleen, but the recorded cases seemed to suggest that any benefit derived is temporary, whereas the reports of splenectomy suggested the probability of permanent clinical cure.

I have to record my thanks to Mr. Stewart and to Dr Young for their invaluable help in the diagnosis and treatment of this case.

A graphic representation is added of the changes in the Haemoglobin, Red Cell Count, Platelet Count and the Reticulocyte Count - the last until operation only.

S U M M A R Y.

1. The physiology of the spleen and blood platelets is reviewed.
2. A short account is given of the various conditions for which splenectomy has been performed, and the aetiology and pathology is discussed in detail of the three conditions for which splenectomy is regarded as the treatment of choice.
3. It is suggested that splenectomy should not be regarded as a last resource of treatment, but should be practised promptly in these three conditions, providing that the diagnosis is established, and the patient a reasonable surgical risk.
4. A case of acute purpura haemorrhagica is described in detail, with a note of the operative treatment and its results clinically and haematologically.

B I B L I O G R A P H Y.

The following text books have been consulted:

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Farley | "Practical Haematological Diagnosis" (1934). |
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