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SPLENOMEGALY*

BY

E. ROCK CARLING, F.R.C.S.

SURGEON TO THE WESTMINSTER HOSPITAL

Splenomegaly affords the surgeon some of his most striking trophies, and very big spleens look imposing when mounted with their colour preserved; but the symptom of which the patient complains at the outset of his disorder may take him, with or without the concurrence of his own doctor, to the exponent of almost any specialism: to the dermatologist for bronzing of the skin, or for lymphomatous masses in and under the skin of hands or face, for purpuric rashes, and so on; to the ophthalmologist for thickening of the conjunctiva, for retinal changes, for intraocular haemorrhages, or for proptosis; to the gynaecologist, the proctologist, or the urologist for haemorrhages from the orifices in their respective territories; to the laryngologist for glossitis, pharyngitis, or gingivitis and spreading oedema; to the neurologist for combined degeneration or for cramps; to the psychiatrist or the psycho-analyst for depression; and of course to the internist for indigestion, haematemesis, cirrhosis, ascites, and, in particular, anaemia. Icterus, exhaustion, and aching back, haemoglobinuria, an acute abdominal emergency, such as a torsion (and that may fall to the gynaecologist), obstruction, cholelithiasis with colic—all these and many more may necessitate an investigation of the palpability of the spleen.

Specialism and Over-elaboration

The specialist in any department ought to be first a good general physician; although he may well know more and more about less and less, he ought not to know less and less about the whole, but it is a temptation to which many succumb, and it is perhaps because he is not exposed to this danger that the good general practitioner remains the salt of the profession. Those who concentrate their work, who specialize—even so little as that increasingly rare bird the "general surgeon"—cannot do the best for the patient except by combined effort. No man who has "specialized" is a safe guardian of a patient's health if he act alone. The burden of "information" is such that no average brain will digest and absorb all the known facts of more than one small field abstracted from the vast domain of possible modes of departure from health. The more recondite become the tests and investigations elaborated by those who specialize, the more difficult becomes the task of integration. The biochemist alone has introduced so many figures and curves offering opportunities of error that with much elucidation he has sometimes darkened counsel. Many of us are unable to appreciate the factor of error permissible in his work, and lack the courage, in the face of statistics and percentages, to check them against the factor of error in clinical observation. Of what use are four places of decimals in one part of an equation which has a sign of uncertainty or approximation elsewhere?

* Part of the Ramsay Memorial Lecture delivered at Bournemouth on June 6th, 1936.

Two hundred and fifty years after the demonstration of the splenic corpuscles and their relation to the arteries by Malpighi we are still in uncertainty as to the functions of the spleen in health. We know that it is not indispensable for health—but even Pliny knew that, at least as regards animals. We know that its functions before birth are different from those in separate existence, though the former may be resumed in abnormal adult states. We have gone very little beyond the old description of the organ as "the birthplace and graveyard of the red blood cells"—chiefly in the direction of eliminating the "birthplace" half of the dictum; we begin to have some suspicion of the biochemical relations of the organ, and we have arrived at a conception of the spleen as but an important part of the reticulo-endothelial system which links it with the liver, the bone marrow, and the capillary and the lymphatic glandular systems.

If our knowledge of the proper activity of the spleen is so lacking in precision it is little surprising that the departure from normal which constitutes "disease" should be ill understood. Enlargement of the spleen, despite all the efforts of the specialists, remains a clinical problem. There are cases which conform in their whole aspect to certain well-known classifications, but since there are more than twenty surnames applied to abstracted syndromes it must be admitted that it is difficult to confine individual examples within the limits of general categories.

Splenic Function

If physicians were able to control the progress of these disorders there would be no place for the surgeon at all. It is but recently that pernicious anaemia has been taken successfully and satisfactorily out of the surgeon's hands. The plain fact is that despite an immense volume of animal research we are still in doubt even as to the place held by the spleen in the group of organs or parts that constitute the reticulo-endothelial system. It is still a matter of controversy whether the spleen functions by the local activities of its cells or by the elaboration of hormones or similar bodies which exert their influence elsewhere. There is no doubt at all as to the dual functioning of spleen and liver, though the linking mechanism is still in question. There seems little doubt that in some young animals growth may be retarded by splenectomy, gonadal development may be upset, some of the endocrine organs may be disturbed in function, and effects upon nitrogen excretion, upon cholesterol mobilization, and lipid storage are to be observed and measured. It may be that some similar effects are exerted in human beings, but here as elsewhere it is easy to fall into the assumption that what has been proven for laboratory animals is true also for men and women. In cold fact splenectomy—that is, removal of the normal organ—may be performed without any detectable, or

certainly with only transient, alteration of bodily functions. One explanation is simple—namely, that spleniculi may be overlooked by the operator (as many as four hundred have been observed in a single body) and may assume the functions of the excised major organ. There is, however, another explanation of much more subtle character. More and more evidence is forthcoming of the interrelation of many organs and mechanisms of the body and of potential substitution.

The reason why gross ablation of parts of the autonomic system is sometimes followed by a tardy return of symptoms is that the system functions dually; besides the direct stimulation of nerve impulses, substitute agents are available via the blood stream, the plasma of which is maintained in the optimum condition for continued function of all contributors to general well-being, despite local failure. Similarly, all parts of the endocrine system may combine to make good defects in an individual part; and all parts of the reticulo-endothelial system, of which the spleen forms an important but not indispensable part, react to make good deficiencies in its components.

Biochemical Confusion

For the purposes of this lecture the records of twenty cases in which splenectomy was performed have been studied, and in their small degree they illustrate a very common crux of diagnosis. Looking back at any collection of cases it is feasible to divide them into groups: to generalize and to draw a composite picture suitable for selection of types; and thus, no doubt, the textbook diseases arise. But consideration of a particular case may present so much conflicting evidence that it may be very difficult indeed to assign it to any accepted niche in the classificatory pigeon-hole or to feel certain that the known results of treatment—in this case splenectomy—can be anticipated for this particular patient.

The opportunity for reconsideration of these twenty cases only confirms the difficulty which many presented at the time of operation. Not only was the diagnosis at the bedside in doubt, or at least the occasion of differences of opinion, but even when the spleen was in the hands of the histologist it sometimes remained a matter of uncertainty as to how the case records should be indexed. The results as regards diagnosis show the great difficulty that confronts ordinary people like myself in the complexity of the tests used and the variations in them that occur from time to time even within a few days. Reticulocytes appear and disappear. Fragility varies rapidly and may be absent for considerable periods in a disorder of which it is characteristic. The shape and volume of the red blood cell (a difficult and delicate observation) may be differently estimated by different observers or vary on successive days. Tests such as those for mean corpuscular volume and haemoglobin concentration are well-intentioned refinements that help but little to decide whether or not to remove the spleen. Blood ureas, blood sugars, blood cholesterols; auto-agglutinations, auto-haemolysins; coagulation and bleeding times; free acid estimations; bilirubin, urobilin, urobilinogen quantities in the urine; Fouchet's and van den Bergh's tests, liver function tests, and not a few others present a complex in my records that confuse almost as much as they clarify the problem.

The labours of the clinical pathologist have hardly simplified the question of jaundice for the clinician. It is true that the conception of Kupffer cells fulfilling or failing in the task of dealing with the pigment brought to the liver, and of the possibility of distinguishing obstructive from non-obstructive jaundice is useful, but there is so much overlap that sometimes it is simpler and more satisfactory to look at the stools than at the laboratory reports.

The haematologist, too, is rather a burden. The great number of different cells, the same cells differently named, the multitude of tinctorial minutiae; the fearsomely named changes of size and shape of red blood cells; the permutations and combinations of them which have led to so many christenings of types of anaemia, all these have done little to facilitate, even if they have lent precision to, diagnosis.

Study of the extirpated spleen throws little light on what has happened. The fibrosis in the capsule and trabeculae seems to be no more than a strengthening of the structure to sustain increased weight. Fibrosis of the pulp on the other hand may be effective in preventing the free passage of cells into the sinuses and thence into the venules and the portal circulation. It may be responsible for the blockade of cells in the spleen, for the failure of transmission of cell contents, and that may mean not only of pigment but also of hormone-like bodies, to the liver; but histology tells us little as to the reasons for proliferation, now of one set now of another, of the cell constituents of the spleen.

Decision to Operate

What claims, then, can the surgeon put forward in the matter of splenomegaly? If we do not know what is the significance of enlargement; if the haematologist cannot always classify precisely the type of anaemia; if the biochemist's reports are open to equivocal interpretations; if patients, as is well known, sometimes live long lives with a large spleen and are seemingly none the worse for it, where does the surgeon come in? Many spleens are removable with impunity, but in certain circumstances the operation is deadly. Whose shall be the responsibility for deciding on operation? The surgeon, the physician, the general practitioner, or the patient? In my humble opinion the advice finally tendered should be voiced by the general practitioner after full discussion with the specialists in equal council assembled. The decision should be as to what the individual patient's departure from health demands to restore him to some normality. Each man's "disease" is his own.

I have had the opportunity of testing the experience first formulated at the Mayo Clinic with regard to the operability of myeloid leukaemia, formerly almost invariably fatal. The danger has been reduced to reasonable limits. What were at one time surgically hopeless cases are now treated by preliminary irradiation, partly by radium teletherapy, and partly by high-voltage x -radiation. It is not possible, I think, at present to name a dose. The irradiation should proceed until the shrinkage in bulk of the spleen is at least one-half its maximum, but the progress of the blood picture must be closely watched, since arrest of improvement in the anaemia and leucocytosis may occur before the desired decrease in size has been reached. Choice of the optimum moment for operation should be made after consultation of surgeon, physician, and radiologist. It goes without saying that blood transfusions should be employed, either repeatedly or even continuously for two or three days immediately before operation. In these conditions the spleen may be removed, and with it all spleniculi discoverable, without fear of a catastrophe. Operation should be followed immediately by further transfusion.

Effects of Splenectomy

It remains a little uncertain how great is the gain from splenectomy. It is sometimes a notable advantage to rid the patient of a considerable weight pressing upon the stomach, colon, kidney, and suprarenal. The immediate betterment, whether or not in part psychological, is gratifying to patient and doctor alike. The question is: how long will it last? My experience is small, and my

first operation for myeloid leukaemia only four years since, but the charts of the blood are, though by no means without remissions, certainly striking, and the present state of both patients, under very careful medical attention, very satisfactory. There certainly seems no reason any longer to dismiss the possibility of betterment after operation as entirely out of the question. That attitude was quite justified in the past, still generally prevails, and is only now worthy of reconsideration.

In adults acholuric jaundice, which may or may not be of the familial type, may be improved immensely, but though icterus may be abolished, removal of the spleen will not necessarily lead to repair of damage in other organs or arrest completely the progress of a mode of ill-health. It used to be said that "fragility" of the corpuscles was always a feature of the familial form, but that in the sporadic cases in adults fragility was absent. Either fragility may be no part of the picture in adult familial cases or our test—the osmotic one—is apparently inadequate, for the rest of the clinical evidence may be complete yet the corpuscles withstand saline of standard percentage.

Although there are considerable differences between cases of haemolytic icterus, and the decision to operate or not may be long held in abeyance, fortunately there is one complication which decides the question. Whenever blood destruction attains a certain degree of intensity pigment stones may be formed anywhere in the biliary passages, and obstructive jaundice thus be added to the haemic; in these circumstances biliary colic may appear and recur persistently.

Justification for operation is then clear, and the procedure involves clearance of the stones and "mud" both from the ducts and from the gall-bladder. To prevent further recurrence the spleen should be removed. In most cases a "cure"—that is, permanent freedom from either type of jaundice—results. Since, however, it is difficult to be certain of removing all splenic tissue and impossible to prevent assumption of splenic action by other parts of the reticulo-endothelial system, it is rational to drain rather than to remove the gall-bladder and to drain the common duct also. It is also possible that intervention may come too late, since after splenectomy and disappearance of jaundice it may be found that the liver functions are below par or that the harmonious action of the pancreas and other endocrine organs is permanently disturbed.

In familial cases it may well be that only one among many members of a family may suffer so much in general health as to justify operation. Here again it is for the general practitioner to stand between his patient and the enthusiasm of physicians and surgeons over a rare type of disorder.

Thrombocytopenic Purpura and Splenic Anaemia

Thrombocytopenic purpura is also the occasion for heart-searching among surgeons. If it were true that splenomegaly with deficiency of platelets was a clear indication for splenectomy it would be easy, in the face of such distressing symptoms as uncontrollable haemorrhages, to decide upon operation. Unhappily the platelets fluctuate widely in number almost from day to day—from 11,000 to 250,000 per c.mm. in one of my cases—and it can but be guessed whether the case be indeed one of deficiency and likely to benefit. In one of this series no lasting benefit resulted, though the decision to operate was supported by a Section of the Royal Society of Medicine. The bleeding time and clotting time test do not at present permit of conclusive deductions. On the other hand, in the most favourable cases nothing can be more dramatic than the immediate cessation of bleeding from all mucous surfaces and from all over the body.

When we come to the case of splenic anaemia—Banti's disease—the literature is a nightmare. There are so many variations on the theme. Even in Italy, where naturally the claims of Banti have been treated with respect, the abstraction of the particular clinical picture he first described is regarded now as artificial. A conception of the disorder is now formulated in accordance with current views of the reticulo-endothelial system. The disorders of the blood are of the most various types, with now one and now another and now none of its cellular constituents dominating the picture; with leucopenia generally, but occasionally leucocytosis with gross or no anomalies of the erythrocytes; but in association therewith is an affection of the liver that ends in cirrhosis and eventual perishing of the liver cells proper. In the interim there has been enlargement with infiltration of this or that element of the hepatic complex with cells from the haemo-lymphopoietic system; eventually there is ascites. The difficulties of diagnosis are enormous when details are studied: the broad picture is so clear that nowadays whenever hepatic enlargement otherwise unexplained is encountered the tendency is to fill in the rest of the syndrome from the anticipated future, and to remove the spleen, however little at present it may be enlarged. The attitude is perhaps justified if it be true, as asserted, that for the inevitable end of cirrhosis there is no help unless perchance a gross breach in the lino-hepatic relations be effected by splenectomy. The toxin of splenic origin, which must be postulated if the whole scheme is to be rationalized, has not yet been found.

Polycythaemia and Tuberculosis

Polycythaemia vera would seem to be an ideal opportunity for the surgeon, and even the radiotherapist, to leave the spleen severely alone, so that it may get on with the good work of destroying red corpuscles; but it is of interest that irradiation of the marrow with the object of stopping production is not a simple matter. It would seem that the marrow may be stimulated as well as inhibited by irradiation, and that normal and abnormal marrow may react differently, so that at present the best method of irradiation is not certainly known. It is of interest, too, that, although contrary to theoretical anticipation, irradiation of the spleen may in fact be of some slight value. It is in any case safer than the use of phenylhydrazine, which is cumulative in action and must be watched with great care. One thing is clear: we do not know the whole inwardness of polycythaemia, and splenectomy has no place in its treatment.

With regard to tuberculosis, which is responsible for some of the extreme examples of splenomegaly, there was at one time a hope that, since in these cases it is sometimes impossible to demonstrate any other tuberculous lesion in the body, removal might permit complete recovery. I have operated on two such cases—one under a mistaken diagnosis, and one deliberately—but both eventually succumbed to other tuberculous lesions; one after a year, and one about two and a half years or thereabouts.

In lymphadenoma the spleen is a minor site of the lymphomatosis. There is, I fear, but little advance in the irradiation treatment of the disease; perhaps the combination of gamma rays with x rays has slightly prolonged the period of expectation of life, but even this thought probably has a volitional parentage.

Splenic Miscellany

The thrombotic form of splenomegaly certainly calls for removal of the organ, but while most splenectomies can now be performed without undue operative risk,

the danger in this condition is too considerable; it is unfortunate that the splenic vein runs into the portal, but so it is.

Of malarial spleens, of kala-azar, and of Egyptian splenomegaly, which some people think is bilharzial, I have no experience, but in the latter the practice of splenomegaly is well established. Gaucher's disease is now well recognized as a metabolic fault, a lipoidal dystrophy, in which the spleen is involved, and no hope of affecting the fundamental disturbance by splenectomy would be held out if that were the whole story. It may, however, be associated with a critical haemopathy. In one of my cases there were attacks of haemoglobinuria in which the haemoglobin fell as low as 17 per cent. Blood transfusion in that case was of no help, for it precipitated a lysis and determined haemorrhages that threatened death. It is now some years since that patient's spleen was removed and, though at times blood crises of minor severity have occurred, she remains in what she considers good health and leads an active life.

The von Jaksch type of splenic anaemia that occurs in childhood has been supposed to have a toxic or specific infective origin and to be recoverable, but in my small experience it has not been possible to demonstrate any source of poisoning, and the duration of the disorder—even though much improved by splenectomy—makes it improbable that the disease is different in origin from other forms of splenic anaemia.

In lymphatic leukaemia nothing at present is to be gained by operation.

It is perhaps permissible to say this in defence of splenectomies that do not cure the underlying disease: that the patient when asked is always ready to state that he or she would not willingly return to the pre-operative state.

The Diagnostic Arch

So far as my personal experience goes I can say that I have been called in at some crisis and that splenectomy has enabled the crisis to be surmounted. It is a resource that obviously cannot be repeated, but it has prolonged life. It has been my good fortune to have no operative death in any of my Westminster cases, though the record is spoilt by a fatality that occurred in an outlying hospital. Follow-up inquiries have been, I suppose one may say, satisfactory; but my physician colleagues rightly claim the credit for that, because in most instances there has been continuous or at least intermittent medical treatment.

In conclusion, I want to make one short generalization. In this particular case the problem is to judge amidst a multitude of test reports from laboratories, which are vital and which insignificant. But in other cases it is to decide which amongst the various opinions of specialists carries most weight. I offer a simile that is easily to be borne in mind. Diagnosis may be compared to an arch while under construction. The individual stones, though themselves of the finest quality, even when in position do not afford dependable support; they must themselves be continuously supported until the keystone is placed in position; and even then need abutments. The stones are the contributions of individual specialists, worthless in isolation; and, even when properly assembled, needing the master stone to fit them for bearing a superstructure of treatment. The entire galaxy of symptoms and the whole of the test data must be held resolutely in suspension until the man responsible for treatment can effect a summation. I suggest that the old plan of making that man the patient's own family adviser is still the best, and that the aim of the medical curriculum should be to fit him so to act.

THE ROLE OF THE SYMPATHETIC IN SENSORY CONDUCTION AND CERTAIN NEURALGIAS*

BY

WILFRED HARRIS, M.D., F.R.C.P.

PHYSICIAN TO THE HOSPITAL FOR NERVOUS DISEASES, MAIDA VALE;
CONSULTING PHYSICIAN, ST. MARY'S HOSPITAL

For nearly forty years Langley's statement that the sympathetic system was entirely efferent has been mostly accepted without dispute, and as recently as 1933 Carmichael and Woollard¹ agreed that the cervical sympathetic contained no afferent fibres. Yet it is known that many sympathetic nerve trunks contain afferent fibres, some medullated and others not, which arise in the spinal posterior root ganglia, enter the sympathetic by the white rami communicantes, and are distributed to various viscera without making any synaptic connexion with sympathetic ganglion cells. These fibres doubtless carry afferent impressions from the viscera and peritoneum to the central nervous system, sensations usually not rising above the threshold of consciousness. The viscera, like the skin and other structures, are supplied with the special sensory mechanisms adapted for dealing with those stimuli to which they are liable to be exposed. Thus the exposed gut or stomach may be cut, pinched, or burnt without any sensations of pain being perceived, and the martyrs of old who, after being disembowelled, had their entrails seared with hot irons probably suffered much less pain than they are generally given credit for.

Distension of the stomach or gut, intestinal cramp, and biliary or ureteric cramp may arise above the normally high threshold of consciousness by stimulation of afferent nerves in the unstriated muscle and may set up intense pain. Stimulation of efferent sympathetic fibres is said to produce its effects by the elaboration at the periphery of the fibre of an adrenaline-like substance, thus causing vaso-constriction, while stimulation of the parasympathetic fibres in the cranial and lower sacral nerves produces a dilator effect through the production of a substance resembling acetylcholine. Gastric and duodenal pain from ulceration and the acute pain of perforation are also suggestive evidence of sympathetic afferent conduction. Experimentally many American observers, Frazier,² Max Peet,³ Davis and Pollock,⁴ and also Foerster,⁵ have produced pain in the face by stimulation of the superior cervical sympathetic ganglion. Adson⁶ has shown that compression of the first and second lumbar sympathetic ganglia, the coeliac ganglion, and the three splanchnic nerves caused pain in direct ratio to the force used, the pain being very severe, sharp, and lancinating, and referred from the shoulder to the lower abdomen according to the nerve stimulated, the lesser splanchnics radiating pain to the lower abdomen and the coeliac ganglion to the shoulder, the pain promptly disappearing after injection of procaine to the splanchnic nerves. Adson considers that his results are proof of the conduction of afferent impressions along the splanchnic nerves.

Stimulation of the Stellate Ganglion

With Dickson Wright I stimulated the branches of the right stellate ganglion—that is, the combined inferior cervical and first dorsal sympathetic ganglion—in a young man of 22, who was suffering from recurrent severe right hemicrania alternating with profuse sweating from the forehead on that side. After exposing the ganglion by the anterior route above the clavicle under local

* A paper read before the Association of British Neurologists, June 13th, 1936.