The Robert Campbell Memorial Oration

ON

THE SURGERY OF THE BLOOD.

BY

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In selecting a theme for this, the first Robert Campbell Memorial Oration, which the trustees have done me the honour of inviting me to deliver, my object has been to find one that would have interest for physicians and surgeons alike rather than one of purely surgical concern, with its wearisome details of minute technique. I trust that in discussing the surgery of the blood, as allusion must be made to various organic diseases of the haemopoietic system, it would be more correct, and more in harmony with medical nomenclature, to regard the blood dyscrasias as secondary phenomena. I hope to justify my presentation of the blood diseases by viewing them from a different angle, and by pleading that the pathology of the anaemias remains obscure.

Cohnheim's conception of the blood as a tissue consisting of cells and a fluid intercellular substance is attractive, and suits my present purpose, although it must be admitted that its cells differ from those of other tissues in their incapacity to multiply and reproduce their like. This conception of the blood raises its dignity from that of a mere circulating medium, a servant to the more stable tissues, carrying to them the materials for their sustenance and renovation, and at the same time doing all the scavenging they require for the smooth performance of their functions. Such adulteration as these menial services imply may appear to detract from its stability and render it unworthy to rank with the fixed tissues as a constructional entity. But the more its characters are studied the more are we impressed with its marvellous capacity for clearing itself and maintaining a relative constancy or homogeneity of composition and structure.

What tissue allows so many liberties to be taken with it and withal retains its vitality and identity? What tissue can vie with it in rapid restoration after haemorrhage, haemolysis in fevers, and other distempers? What other tissue would survive the insults and abuse of injections into it of copious solutions of salt and soda, eusol, mercurial salts, gelatin, gum arabic, ether, alcohol, aniline dyes, and the homologous blood of other persons, whether freshly drawn or bottled and kept in cold storage for a month or more? Still more the injections of vaccines and serums, often in large volume, at the hands of eager bacteriologists and haematologists—as, for example, in the Argentine treatment of anthrax, or in the treatment of pneumonia and tetanus.

Haemophilia.

Nothing has yet been ascertained as to the essential nature of this strange complaint. We do not know wherein consists the defective coagulation, which may take thirty to fifty minutes to accomplish, as compared with the four to five minutes in normal blood when tested by Sir Almroth Wright's method. Must we accept what seems a counsel of despair? or is it a counsel of perfection when non-sentimental eugenisists forbid the girls of haemophilic families to marry, or, if they marry, to stipulate that they shall not bear children?

Hitherto the surgical rule has been to confine operations upon haemophiles to those of primary surgical urgency. Can we do anything to qualify haemophiles for expediency operations, and render these proceedings reasonably safe? Several experiences of my own in this regard make me think that we can. There are degrees of severity in haemophilia, and if we take the milder forms we may test by Wright's process before and again after a few days of preparatory treatment by calcium salts, haemoplastic serum, or repeated small transfusions of homologous blood at short intervals. Even the subcutaneous injection daily of 40 c.cm. of any mammalian blood, or of human blood not necessarily homologous, may temporarily increase the thrombin elements, and enable us to discriminate those who do not respond, and remain ineligible for operations, from those who do.

Pernicious Anaemia.

In pernicious anaemia the part played by surgery has hitherto been inglorious if we consider the results of splenectomy in the management of the ordinary type; while

in the Addisonian variety the extirpation of the adrenals has been equally unsuccessful. The latest results from the Mayo clinic, however, show some improvement, possibly from improved technique and a careful selection of cases. The Mayo clinic claims now that a couple of years may be added to the life of these patients by a timely splenectomy, combined with transfusions of whole blood carried out after a preparatory treatment by radium, which appears to render the splenectomy much safer. It is doubtful whether the spleen is the seat of the disease, and so accomplished a surgeon as Moynihan, who has recently written so well upon splenic surgery, sums up that the results, having regard to the risks, do not entitle us to urge this operation upon patients with any degree of earnestness or conviction. The nature of the haemolysis is obscure: it seems probable that it is an infection; yet this has not been established, hence a truly rational handling is denied us, and the treatment remains empirical, with arsenical preparations as the leading agents. The surgical demands in many cases may be limited to transfusions of small quantities of whole blood at ten-day intervals, but these seem little better than retarding, not curative, measures. Large quantities of ox serum alone, which appears to have the advantage over horse serum that it does not sicken, may be considered in promoting thrombokinase formation.

Whether Dr. Hurst's method of grafting adrenal gland tissue into the groin—or, better, into the testis—will stand the test of time remains to be determined, but already some encouraging results have been reported.

Haemorrhage.

Turning next to the management of haemorrhage in normal blood we know that the sudden loss of a fourth part of our thirteen pounds' weight of blood may be fatal; but if the shedding be spread over a week or more by recurrent bleedings prodigious quantities may be lost with ultimate survival. We have been told that the extreme age of a single red blood cell is about one month. The speed with which these cells can be reproduced after haemorrhage is wonderful.

The two important indications in haemorrhage are: to restore the blood pressure by ingesting or transfusing fluids copiously, thus enabling the heart to supply the vital centres in the encephalon with a sufficient quantity of blood, however thinned in quality; and secondly, to maintain the warmth of the body by internal and external means, the latter indication being often overlooked when the mind is intent upon the former. Isotonic saline, or 6 per cent. gum solution, may be employed intravenously, but in extreme cases pure homologous blood should be used if available, and warm fluids given by the mouth or rectum.

I have not been impressed by the results of subcutaneous injections of salines for this purpose; I have noted them unabsorbed after a week, and have frequently seen disastrous sloughing follow their use. Dr. George Rea has recently simplified the determination of the homology of bloods. As to apparatus, we have our choice of the hydrostatic method; the multiple Record syringe method; and the paraffin-lined Kimpton-Brown tube. The technique is not difficult if care be taken not to introduce air bubbles. The direct method of connecting the artery of a donor to the vein of the patient by a ten-inch transparent tube with suitable nozzles, which Mr. Fullerton distinguished himself by introducing, has been found inconvenient, and in septic states of secondary haemorrhage positively dangerous to the donor. For anyone not fully familiar with the technique the safest plan appears to be the reception of the donor's blood into a warm vessel containing one-fifth part of a 3.8 per cent. sodium citrate solution, and instilling this mixture into the patient's veins by the gravitation or hydrostatic method. We must make sure that diseased blood—syphilitic, tuberculous, or malarial—is not used. In this connexion the interesting fact has been discovered that blood from an asthmatic donor has caused asthma in the recipient. Does this in any way show that we may revise our views of the pathology of asthma, and regard it as belonging to the category of blood diseases?

Thrombosis and Embolism.

Are we to assume that clotting of blood in varicose veins and in haemorrhoids in apparently healthy persons is an inflammatory process? It is very difficult to prove that it is so; certainly an attempt to demonstrate microbic activity in such simple cases usually fails. On the other hand, when definite phlebitis or arteritis exists, we can readily understand

that changes in the intima due to inflammation cause thrombosis.

The anxieties in phlegmasia dolens and in veins that have been operated on in various ways are common enough, but why detachment of portions to form emboli should be more frequent in the post-operative states as compared with phlegmasia is not easy to explain. In the recent debate in the Royal Society of Medicine conflicting views were expressed as to whether pulmonary embolism and infarctions were commoner now than formerly. My own impression is that they are on the increase, but to what change in technique or nursing this is to be attributed is not clear. The more recent deliverances from America are to the effect that the limbs should be permitted free movements, and no splints applied after operations on veins, in order to promote a freer circulation of blood. The practice hitherto has been the opposite—namely, to keep the limbs at rest in splints for a long time in order to give time for condensation of thrombi, lest bodily movements should detach portions of soft clots, with disastrous embolic excursions. Similarly, long rest has been enjoined for phlegmasia. A close observation of a number of cases convinces me that embolism is commoner in the cases treated by early movement and activity, and I still remain an advocate of prolonged rest. Likewise, in the treatment of acute thrombosis in varicose veins without operation prolonged rest is best. We have had in recent years a fair number of cases where men have refused to lie up and rest; and a fatal pulmonary embolism has been apparently caused by their activity; it has occurred, also, after the too early dismissal of hospital patients.

From a medical point of view we may discuss two rival and diametrically opposite therapeutic methods. Should we give calcium salts to condense the clots that may have formed, or should we give citrates to render the blood less liable to clot? As a matter of experience citric acid is better than its citrates for the latter object. My own view is in favour of the citric acid scheme as opposed to the calcium salts as a prophylactic against embolism.

If we apply to the physiologists for the reason why coagulation does not take place spontaneously in the blood vessels we are told that thrombin, the activating substance, does not exist in the blood. It has to be formed by the interaction of prothrombin and antithrombin which do exist. When these combine we get the thrombin that can convert the fibrinogen of the blood into fibrin. What the exact catalytic process is whereby the calcium salts and kinases react to liberate the thrombin is not clear.

The substance known as antithrombin appears to be formed in the liver as one of the secretions of the liver cells, and it is added to the blood as it passes through that organ. Now the fluidity of the blood in the hepatic veins as it leaves the liver is much superior to that in the portal system entering it. To facilitate coagulation all that is wanted to inhibit the restraining influence of this antithrombin is some thrombokinase, such as is liberated at a wound, bruise, or fracture, or even an internal injury to the intima of a vein, a burst valve, or an overstretch. Antithrombin appears to resemble hirudin, an extract from the salivary glands of the leech, or its more accessible and cheaper substitute albumose of peptone. We do not use this albumose of peptone as a therapeutic agent to prevent clotting because it is a powerful and even dangerous depressor of the blood pressure.

When clotting occurs in a vein after operations, two types of clot are recognized—one the firm white clot at the ligature, and the other a soft red colloidal clot, extending up approximately to the nearest tributary or branch. If the white clot disintegrates, it may be comparatively harmless, for it breaks up into almost powdery fragments. It is the soft red clot we have most to dread. To minimize its formation early movements to reduce stagnation after operations are now recommended. But we may lose as much as we gain by this nursing licence, for, as a soft red clot will inevitably form in some segments, we may by movements facilitate its detachment, leading to embolic developments. It therefore seems to me that the elevation of the limbs, and the foot of the bed, combined with somatic rest, is the safer procedure.

Regarding the matter from the clinical standpoint, we may say that in blood conditions in which thrombosis is the leading feature the coagulability of the blood is already too high. Therefore, in a rational treatment in the prevention of thrombosis and embolism, one would argue that we should endeavour to reduce this tendency by citric acid, or its

citrate, rather than accentuate it by the exhibition of the calcium salts.

The question of the influence of electricity upon thrombosed veins, whether employed as a preventive agent, or to promote absorption or canalization of clots, is interesting. It is well known that the blood of persons killed by lightning remains for a long time uncoagulated, and this has led to the use of electricity in surgery, either as constant, current alone or for the ionization of potassium iodide. We learn from Professor Milroy's researches that other influences, apart from the lightning stroke, may account for the fluidity of the blood. Nevertheless, electric ionization over thrombotic areas appears to do good, and to expedite a restoration of the disabled circulation in post-operative conditions. This action, if we admit it, is probably due to a general effect upon the nutrition of the limb as a whole, for we find that the American experience of electrocution of criminals reveals no specific influence upon the coagulability of the blood, either for or against, from electrical currents.

Polycythaemia Vera.

Erythraemia, also called polycythaemia vera, is a rare disease of the plethoric type in which the red cells may rise to double the normal number. This probably depends upon undue activity of the red bone-marrow. Although the spleen is much enlarged, it is a fatal mistake to extirpate the spleen. This organ is not the source of the disease. Rather is it undergoing functional hypertrophy in its efforts to destroy the excess of red blood cells. Forty years ago the spleen was called "the grave of the red blood corpuscles," and in this disease it justifies its old title. Surgery, therefore, directed to the spleen is quite improper. Whether the suggestion of extirpating every alternate rib to reduce the amount of red marrow at work will bring this disease again within the surgical ambit remains to be seen. For the present the best treatment appears to be radium applied to the long bones, or possibly the deep x-ray therapy of the Erlangen school may have some advantages to offer in the future.

The influence of repeated small bleedings in reducing the plethora in erythraemia must also be borne in mind.

Splenic Anaemia or Banti's Disease.

This form of anaemia furnishes a sharp contrast to pernicious anaemia in its curability by early splenectomy before cirrhotic changes in the liver become too far advanced. The operation may, however, be a formidable one by reason of the parieto-visceral adhesions which abound, and bleed freely in their separation. Possibly a preliminary application of radium to reduce the size of the spleen may help to reduce this risk.

Spleno-medullary Leukaemia.

This myelogenous form of splenomegaly—what used to be called splenic leucocythaemia—causes the pendulum to swing strongly from surgery to medicine, seeing that splenectomy in this form has so gloomy a record. The very few patients that have survived the operation have not permanently benefited by it; at most a very brief retardation has followed, but not sufficient to justify so serious an operation. It will be best to depend upon radium, or the intensive deep x-ray application, when the blood count indicates this particular form of leukaemia. Some remarkably good results have been recorded at the Radium Institute.

Lymphatic Leukaemia.

This is a more rapidly fatal disease than the last mentioned spleno-medullary form, and offers even less inducement to surgical enterprise; its management also must be left in the hands of the radiologists. In this disease it is not so much the increase in size of the lymph glands that strikes one, but the universality of their distribution, rendering surgical extirpation a hopeless task.

Hodgkin's Disease.

On the other hand, Hodgkin's disease reverses this position, and offers in its earlier stages a field for operative surgery. The extirpation of clusters of glands which are very large, discrete, and not adherent through inflammatory changes is not only feasible but useful. The spleen, which enlarges in the later stages, need not be extirpated. At first there are no striking blood changes: the anaemia occurs later on, so that in the early stages the patients are fit to stand operation better than in the anaemias already discussed. Nevertheless, I believe this disease will pass into the hands

of the radiologists, and that surgery will be less and less enlisted in the future for its treatment. The Radium Institute results in this complaint are very encouraging.

Tonsillar Anaemia.

Considerable difference of opinion still exists as to the wisdom of completely extirpating the tonsils, some claiming that an anaemia results from the removal of these haemopoietic organs. There are therefore advocates of the slicing or guillotine operation as against the thorough enucleation. My own experience leads me to adopt the enucleation plan, as less liable to be followed by recurrence of the hypertrophy. Aside from the primary or recurrent haemorrhage at the time of operation, which may be copious and account for a temporary marked anaemia, I have not seen a chronic anaemia result after enucleation that would deter me from ablating these small haemopoietic glands, which are so often removed with manifest advantage to the patient.

Haemolytic Jaundice.

This is a peculiar acholuric jaundice, which may be either congenital or acquired, and which may last for years; it is a slow blood disease, with marked anaemia from destruction of red blood cells. In this disease splenectomy has a high curative value, and may arrest the disease quite promptly and satisfactorily.

Purpura Haemorrhagica.

In this disease, hitherto regarded as purely medical, the intervention of surgery is justified, and may prove curative. The spleen is distinctly enlarged, and its removal by splenectomy has been followed by the happiest results. The exact nature of the disease is ill-understood, and why there should be a deficiency of the fibrin-forming elements is not explained. Though apparently not primarily a splenic disease, still the extirpation of the spleen is very useful. In some way it breaks a link in the vicious circle that underlies this malady. Hence a fair field for surgery in this blood disease may be predicted.

Skin Grafting.

Brief reference may be made to important discoveries of interest to practical surgeons in respect to skin grafting. It is desirable before taking grafts, even from a mother to her child, to determine whether the bloods of both harmonize or are homologous. When they do not correspond there may be failure in grafting—a point of special importance when the larger flaps in plastic surgery are attempted.

Blood-letting.

A word must be said about a practice against which the errors and abuses of former generations have created some prejudice. I refer to blood-letting, either local or general. It is more than possible that we abstain from this too often, and that we should reconsider its value. Anyone who has seen the relief afforded by general blood-letting in the congestion of the lungs in immersion cases, and its recent revival in pneumonia, in apoplexy with high temperature and flushed face, will be willing to admit its potency. Similarly, in chronic kidney inflammation, with uraemia imminent, and in polycythaemia vera, as I have already mentioned.

Artificial Leucocytosis.

The artificial production of leucocytosis has received some attention since Metchnikoff's experiments showed that the resisting power of the peritoneum against the invasions of virulent organisms could be temporarily increased by injections of sterile broths or peptone solutions. This might be utilized in cases where the surgeon dreaded the onset of sepsis in abdominal operations. The same principle has recently been advocated in the treatment of influenza by the injection into the blood of substances capable of producing a general leucocytosis—for example, nucleinic acid or sodium cinnamate—and favourable results have been claimed for this practice.

In passing these various diseases in review it will be apparent that the account of them is necessarily incomplete and discursive. What will emerge, I think, is this, that surgeons in the future will have to be more thorough physicians and physiologists in order to guard themselves against rash or precipitate extirpations of organs which may be temporarily enlarged and apparently inconvenient burdens. These may not be the seat of the disease, though they may constitute its most conspicuous feature. The enlargement

may actually be salutary—of the nature of a functional hypertrophy to protect the patient—as in polycythaemia.

On the other hand, the physicians should see to it that surgical aid should be sought as early as possible after a diagnosis has been made of one of these maladies in which splenic or glandular extirpation has proved of service. In a word, is it not clear that any sharp cleavage between these sister sciences, to which a premature and exclusive specialism is prone, is as unphilosophic as it is unscientific? We should, therefore, condemn an unnatural divorce of surgery and medicine, though both branches must gratefully recognize that only by specialized "team work" in many cases can the necessary diagnosis be laboriously built up.

THE TREATMENT OF INSOMNIA.*

BY

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THE treatment of cases of insomnia is a very large subject, and here only an outline can be given, founded on an attempt to classify the different forms of the affection under two great heads.

Physiologists cannot tell us exactly what sleep is, and it would serve no useful purpose to enunciate here the different theories—or shall I say hypotheses?—that have been advanced as to its nature. A common belief is that the lowering of blood pressure that undoubtedly occurs during sleep is the cause; but if this were so one should find intense drowsiness in cases of low blood pressure, but this is not usual. Sleeplessness is not a symptom of severe haemorrhage, and, on the other hand, I understand that in mania the blood pressure tends to be low. Again, chloralose is a good hypnotic, and yet it raises the blood pressure. A fall in blood pressure is a usual accompaniment, but probably not the cause of sleep.

Sleep and sleeplessness are associated with decrease or increase respectively in the activity of the cells of the central nervous system, and the cause of this decrease or increase is not always the same. Sleeplessness, indeed, is a symptom and not an entity. One might just as well speak of one kind of cough or one kind of pain as of one kind of insomnia. We see it occur in arterio-sclerosis when the arterial blood pressure may be high, and again in anaemia when it is probably low. Usually a cup of coffee will lead to sleeplessness, but I have known people in whom it has the opposite effect. Evidently the essential cause of the symptom is not the same in the two classes.

Sleeplessness is perhaps the most distressing symptom to which human flesh is heir. Every practitioner knows how it wears out his patients and how a few hours of sleep may alter the whole aspect of a case. Sleep is more essential to life than food, in that an animal may go for weeks without eating, but let it be deprived of sleep for four or five days and life becomes impossible. A form of torture said to have been popular in old days was to deprive the victim of sleep, and it must have ranked high as a producer of exquisite suffering, which was the object of the torment. Our patients sometimes undergo this torture, unless we lessen it by therapeutic means.

As sleep is so essential, it follows that absolute insomnia for any length of time is incompatible with life, and yet often one is told by healthy-looking individuals that they have not closed an eye for weeks. I saw an example of this only the other day. A short period of sleeplessness is, strange to say, productive of an increase in weight of the body, but if the insomnia be persistent a loss of weight ensues, and the degree of emaciation is often an index of some value in estimating the amount of insomnia.

A great many classifications have been made of the different forms of insomnia. Perhaps the one most quoted is that of Germain Sée, which is as follows:

1. Dolorous.
2. Digestive.
3. Cardiac and dyspnoeal.
4. Cerebro-spinal and neurotic.
5. Psychic.
6. Insomnia due to physical fatigue.
7. Genito-urinary.
8. Febrile and auto-toxic.
9. Toxic.

* Communicated to a meeting of the Ontario Neuro-Psychiatric Association, September, 1921.