Conclusions

1. Medical and surgical treatment of peptic ulcers give approximately the same late results, judged by the frequency of failures and relapses and subsequent working capacity.
2. The operative mortality is considerable and is higher than has been generally believed, especially in the case of gastric ulcers, in which it may be between 10 and 20 per cent. under favourable circumstances.
3. The immediate results of gastro-enterostomy for duodenal ulcer are appreciably better than those of medical treatment.
4. The incidence of gastro-jejunal ulcer after gastro-enterostomy for duodenal ulcer is not less than 10 per cent.
5. Evidence is lacking to support the view that cases which are medical failures will in general do better permanently after operation, or will do sufficiently better to counterbalance the operative mortality and the risk of gastro-jejunal ulcer.
6. Cases which relapse after a first course of medical treatment may be successfully treated by a second.

7. Grave cases of haemorrhage from peptic ulcer have so high a mortality that operation is indicated to check the bleeding point. There is no indication for operating when haemorrhage has ceased.

8. The medical treatment of haemorrhage should not involve prolonged starvation.

9. The medical treatment of active peptic ulcer should be based on the principle that the stomach is not left for more than two hours without treatment.

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INFLAMMATION: HUNTER'S VIEWS AND MODERN CONCEPTIONS*

BY

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There is probably no subject of the present day that is so dominated by Hunter as is his work on inflammation. He came to the conclusion that it was a process of activity, while Lister, working fifty or sixty years later, believed it to be a loss of function and vital activity.

Since these opinions are so directly opposed I thought that it might be interesting to dwell upon notions so divergent, in order to determine which of the two views is better adapted to the requirements of present knowledge. I shall not have time to discuss more than one point upon which Hunter based his view, and then I will take up Lister's work.

Increased Vascularity

Hunter regarded the increased vascularity he observed in inflammation as being the direct and primary cause of repair. The morphological appearances of a healing ulcer serve to illustrate Hunter's conception. There is a decided increase in the number of blood vessels supplying the base of the ulcer compared with the parts around. Their existence is maintained until the granulation tissue becomes finally covered by epithelium, whereupon they atrophy and disappear, leaving an almost avascular cicatricial tissue. Finally the amount of cicatricial tissue itself diminishes to such an extent as to become almost imperceptible in old wounds that have healed by first intention.

One thing is perfectly obvious here. All the time the tissues are undergoing the growth of repair they are supplied by an increase in the number of blood vessels. Is this increase of blood supply the master of the process as Hunter thought, or is it merely a servant? If it be the uncontrolled master, then why is it that the epithelium and granulation tissue remain on a level? What is there to prevent these tissues from growing to form epithelial and connective tumours?

It is a wonderful and inexplicable fact that when the epithelial cells have completed their function of covering the exposed surface of granulation tissue their superficial spread ceases, and their future activity is devoted to keeping intact the covering layer they have made. The blood vessels have diminished in number sufficient only for that purpose. Is the definite performance of these epithelial cells the result of the accomplishment of a function? Everything that is happening points to the fact that all the events are under a co-ordinating general control, and that no single one of them can be regarded as a master of the process of healing. In fact it appears that the blood supply and the behaviour of the epithelial and connective tissue elements that compose a healing ulcer are all alike under a predominating control, which regulates the total and combined events, ending in orderly growth.

Healing Processes

The same considerations arise with even greater potency when the orderly sequence of events occurring in the more complicated and still controlled stages of growth in a healing fracture is observed. The same orderliness can be seen in the new formations that occur in an artery after its ligation. In all these events the processes of new formation are different, and depend upon the function they are intended to fulfil.

I hope I have given sufficient reason to doubt whether the increase of blood supply is either the sole factor in controlling repair or even its incentive. There can be no doubt that an increased supply of blood cannot alone induce growth. I admit that the existence, growth, and repair of tissues could not be maintained without an adequate blood supply. I know of no instance which can be quoted as an example of growth being stimulated or incited solely by a more than adequate supply of blood.

The healing of varicose ulcers occurs after sympathectomy, when all other attempts have failed. Recently obstinate varicose ulcers have been induced to heal by diathermy in some instances and by short-wave therapy in others. The healing in these instances could be explained by the delivery of an adequate blood supply that was inadequate prior to the sympathectomy. Supposing this explanation to be correct, the subsequent events of the healing process are under an all-powerful control, and they cannot be regulated only by alterations in blood supply.

* Part of the Hunterian Oration delivered before the Hunterian Society of London, February 24th, 1936.

In this respect the increase in size of a rabbit's ear, when it has been deprived of its sympathetic nerve supply, has to be considered. Reginald Smith, Norman Freeman, and James White of America have recently shown that a part deprived of its sympathetic nerves is rendered more sensitive to the action of epinephrine, and for that reason vaso-constriction is apt to recur. So it may be that the increase in size of a rabbit's ear, and the repair of the varicose ulcer I have just mentioned, may depend upon other factors and not upon vaso-dilatation as the result of sympathectomy.

Experimental Work

In order to prove that a tissue is incited to grow merely because it is granted an increase of its blood supply, Hunter performed his well-known experiment. He transplanted the spurs of cocks into their combs, assuming that the former would receive there a greater blood supply than they were accustomed to in their normal situations, and that therefore they would grow larger. As Hunter expected, larger growth resulted. The spurs grew to enormous sizes, and, not so expectedly, in most abnormal shapes. I repeated these experiments, and besides transplanting spurs into the combs, I transplanted them into the avascular tissue between skin and fascia in the birds' necks. There they grew as fast, as large, and as abnormally as they did in the combs.

This control experiment does not support the deductions Hunter made as a result of his experiment; it destroys his conception. I am not at all sure what the combined experiments do prove; they may assist in proving that the uprooting of a spur and placing it in an abnormal environment upsets and violates all the laws that govern its growth and function in its normal situation. You see here that Hunter regarded his experiment as being the control of his preconceived notion. The control really required was a control of his experiment. The result of a control experiment by transplantation of a spur in the most avascular tissue I can imagine does not confirm the notion which Hunter intended to prove.

Let me go a little further into this matter. A cock's comb contains blood vessels which become engorged when it is erect, but during quiescence it is not the highly vascular structure it looks. It does not bleed when incised in an undisturbed state, and its chief mass consists of a myxomatous tissue.

It is interesting to observe that if a spur in its normal situation be protected by a thimble it grows to an enormous length in a normal way, and becomes a most formidable weapon for cock-fighting purposes. These protected spurs are beautifully formed and dangerous-looking tools of offence, and certainly do not assume the abnormal shapes and sizes seen in transplanted spurs. Moreover, Hunter did not go more deeply into the problem that arose if he believed all his assumptions and deductions were true. The problem is this: if a cock's comb possesses such an abundance of blood vessels that they alone are able to incite excessive growth in another structure, why, with all this reserve of blood supply, does the comb itself stop growing?

The thimble experiment I have just mentioned suggests an explanation of the fact that the spurs grow so large in a comb and in the control experiment—namely, that here they are not subjected to the same wear and tear as that to which they are exposed in their normal situation. The explanation receives some support when it is realized that the hair of scalps and beards, and finger nails, grow to great lengths if they are not cut. Certain fakirs in India keep their fingers permanently doubled up into the palms of their hands, through which their finger nails pierce, to appear on the dorsal surfaces.

As a matter of fact this explanation is not so simple as it at first appears. The hairs of the eyebrows, eyelashes, and pubic region remain constant in their length. They do not require cutting, and they are not exposed to an abnormal wear and tear of life, nor are they deficient in blood supply. The appearance and the incitement to growth of beards and pubic hairs at adolescence is much more complicated than a mere dependence upon an acquisition of a greater vascularity than they received during boyhood.

From these examples it cannot be claimed that the mere amount of blood supply delivered to a part either limits growth in some instances or incites it in others. On the whole, therefore, we are obliged to conclude that Hunter's experiment on the cock's spurs and combs, and his observations upon them, do not confirm his opinion that inflammation is a process of activity.

Definition of the Term "Inflammation"

In all these considerations it has to be realized that when the term "inflammation" was first applied to describe a painful, hot, red, and swollen part it was a descriptive picture of the clinical state under observation. When certain changes occurred immediately following these signs and symptoms they were naturally described as "chronic inflammation." In those days men knew nothing of micro-organisms, of infection and immunity, and of the laws that govern growth. Some evidence that growth was a complicated process certainly existed, and was available for observation in Hunter's time—the controlled growth of hair, for example. I have omitted allusion to the fact that a comb develops in an ovariectomized hen, and that its psychology is also altered. The knowledge of endocrinology on which this experiment is based had not been discovered when Hunter lived.

About 1870 Burdon-Sanderson attempted to define inflammation. His definition was apparently based on Hunter's notions, in spite of the fact that Lister had published his classical treatise on inflammation in 1856, and that vitally important fresh knowledge had begun to accumulate. Burdon-Sanderson's definition was as follows: Inflammation is the succession of changes occurring in a part as the result of injury, provided that the injury be not so excessive as to destroy the vitality of the part. Valy Menkin of Harvard University, as late as 1935, stated: "Inflammation, broadly defined, is the complex vascular, lymphatic, and general tissue response to the presence of an irritant."

For obvious reasons these conceptions are too comprehensive; they include too many completely different processes—the repair of tissue, for example. Many pathologists to-day are beginning to doubt whether repair of tissues should be included in the subject of inflammation. I agree with them, but at the same time I also see that the removal of so important a keystone from the more general and popular conception of inflammation so weakens its fabric that it begins to totter.

There are other matters to be considered in this respect. Burdon-Sanderson's and Valy Menkin's definitions also include the problems of infection and immunity, and, in addition, the suppuration that is met with in ordinary surgical practice. Suppuration is not a local process only; the bone marrow is actively manufacturing polynuclear leucocytes, and I cannot see that this evidence of activity can be held as occurring in an inflamed bone marrow. It is a protective property, and concerns the establishment of immunity.

The definitions also include the subsequent development of benign and malignant tumours when they occur in parts as a result of injury. In this respect the recent

experiments of Lacassagne on young male mice are of intense interest. He injected oestrin into their bodies; the animals developed breasts in which carcinoma appeared in the majority of instances. There is no suggestion of inflammation to be observed in the microscopical sections he made of the succession of changes that ended in carcinoma.

Lister's View

This question now arises: If the process of inflammation be deprived of all changes except loss of function, as I think it should be, what is there left to consider as being, in truth, inflammation? The answer brings me to Lord Lister's work on the early stages of inflammation. His observations and his experiments led him to believe that it was a process of diminished activity and loss of function as a result of injury—quite the opposite of Hunterian conceptions.

He demonstrated that the injured parts contained blood vessels dilated in a state of paralysis, and that the red and white corpuscles tended to adhere to each other, and to the blood vessel wall. The red blood corpuscles formed rouleaux, and stasis occurred as the result of the exudation of plasma. But when the corpuscles escaped from an injured into a normal blood vessel they immediately behaved naturally. Lister also showed that injury stops the movements of the cilia of ciliated epithelium, and the movements of pigment granules within pigment cells are arrested.

As a result of his researches Lister taught that the signs of inflammation were pain, heat, redness, swelling, and loss of function. Repair of tissue, the change of a lymphocyte into a macrophage and into a fibrous tissue cell, and the inclusion of a micro-organism within a polynuclear leucocyte are examples of co-ordinated and successful efforts of function. The adoption of Lister's teaching sinks inflammation into comparative insignificance. On the other hand it removes from the subject all the matter that now confuses the prevailing attempts to describe what is meant by the terms "acute" and "chronic" inflammation.

Deductions

The point is not merely academic and needing clearness only for the sake of the medical student. To all whom it concerns the term "inflammation" should have a definite meaning and limitation. To take only one example of this statement: in all breasts of male and female infants at birth the developing ducts are surrounded by many layers of new connective tissue, among which lymphocytes are commonly seen. These normal breasts cannot be conceived to be in a pathological state of "chronic mastitis." Yet when exactly the same morphological appearances surround the epithelial elements of adult breasts they are usually described as being in a state of chronic inflammation. Indeed, many observers regard the condition of what is called "chronic mastitis" as being a precursor of cysts, and in other instances of carcinoma.

The study of whole serial sections of normal and abnormal breasts does not warrant these conclusions. For some reason these particular breasts seem to be in a state of activity when they should be at rest. I have never seen the epithelial elements of these cases develop into cyst formation, nor have I discovered any form of neoplastic growth, except the fibro-adenomata of puberty type: Cyst formation and carcinoma belong to a different category.

I do not believe the so-called "chronic mastitis" to be inflammatory in origin or dangerous in prognosis. If the subject of inflammation had not reached us by

gradual descent from early days I doubt if the term would be called into existence in the present conception of disease and of the active efforts of nature to keep the body alive.

Finally, I hope I shall not be accused of treating Hunter with disrespect. Nobody realizes more than I the stagnant state of surgery into which Hunter was plunged. He appears to me to be an outstanding man of his time whose disposition was shaken by thoughts beyond the reaches of his soul. His reputation is as high to-day as it was in the eighteenth century, and justifies the annual homage that is paid to his memory.

URINARY TRACT COMPLICATIONS IN THE PROLONGED IMMOBILIZATION OF CHILDREN

BY

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During the treatment of certain orthopaedic conditions by prolonged immobilization there is a tendency for urinary tract complications to occur, especially renal calculus formation. Many textbooks on orthopaedic surgery make little or no mention of the subject, although most surgeons who have experience in the treatment of surgical tuberculosis, for example, can give instances of urinary tract complications.

Urological surgeons recognize their incidence. Swift Joly,¹ also Ball and Evans,² record the liability to nephrolithiasis of patients who have to lie in the recumbent position over a long time. In a recent paper Lee Brown and Earlam³ consider theories of the mechanism of renal calculus formation in general. They also consider the relationship of prolonged immobilization thereto, reviewing the literature, and reporting six of their own cases. The influence of urinary tract infection, coincident with prolonged immobilization, on nephrolithiasis is also discussed.

The subject seems to merit rather wider appreciation than it receives at present, especially from the standpoint of adopting suitable prophylactic measures. At the least, early diagnosis and treatment are desirable. Many cases of nephrolithiasis or renal tuberculosis, for example, occurring in recumbent patients are asymptomatic over long periods, and are only brought to light by routine radiography of the urinary tract or by periodical microscopy of the urine. When symptoms do arise it is still not infrequent to find the patient's troubles labelled with diagnoses such as "haematuria" or "albuminuria," no reasonable attempt having been made to elicit the pathology of the underlying condition.

Incidence of Complications

With the object of determining the incidence of urinary tract complications in children undergoing prolonged recumbent treatment, I investigated 200 unselected cases at Princess Mary's Hospital for Children, Margate. This hospital is intended principally for the treatment of surgical tuberculosis, but cases of other orthopaedic conditions are also admitted, and tables of the clinical material examined are subjoined. A number of the patients (principally those with tuberculous cervical lymphadenitis) were not confined to bed for any appreciable length of time, but these serve to some extent as controls.

The number of cases treated by immobilization for a period of three months or longer was 162. In them urinary tract complications, to which a definite diagnosis