Calcium Metabolism after Injury

It has been pointed out above that mere confinement to bed can produce a negative nitrogen balance. Reifensstein (1942) also showed that under like conditions the urinary calcium output may be doubled and the faecal calcium increased by one-third. In fracture cases the increased urinary calcium excretion reaches much higher levels. It then becomes a potential danger, for if conditions within the urinary apparatus are favourable the calcium may be precipitated as calcium phosphate and give rise to renal calculi. Shorr (1942) has shown that calcium excretion in the urine is balanced accurately in normal persons by the excretion of citrate. If enough of the latter ion is not available precipitation of calcium phosphate may occur. Investigations by Shorr and others have led to three possible methods for preventing calcium phosphate precipitation. The first is to use substances which can act as precursors of urinary citrate. No fully adequate material, however, has yet been found. The second method is to increase the output of urinary citrate by the use of oestrin; but such a method is not always desirable on account of other effects. The third method is to reduce urinary phosphate excretion by increasing faecal phosphate excretion. This Shorr (1943) accomplished by giving aluminium hydroxide by mouth. That substance forms an insoluble precipitate of aluminium phosphate in the bowel and leads to increased passage of phosphate into the bowel lumen. The value of these methods has not yet been fully explored.

Summary

In well-nourished persons subjected to injury the urinary nitrogen output increases to reach a peak by the end of the first week after injury. This high output gradually declines until in less severe injuries it reaches the normal level by the end of two to three weeks. Thereafter the level of output may decline further, but by the end of two to three months it returns to normal. The high nitrogen output may be diminished but not abolished by high-protein diets during the first seven to ten days. Continuation of such diets, however, leads to a positive nitrogen balance during the latter half of the period of high urinary nitrogen output and during the subsequent period. In this way the depletion of body nitrogen is compensated. The magnitude of the nitrogen loss in the urine depends on the nutritional state of the individual and on the severity of the injury. Some of the loss is due to the effects of immobilization in bed, but this part is relatively small. Poorly nourished individuals show either no metabolic response or a diminished one after injury. There is evidence that the severity of the injury conditions the magnitude of the nitrogen loss in the urine. The source of the nitrogen lost in the urine during the period of high output is the body cells. These apparently can yield up protein without affecting their viability.

The mechanisms involved in these metabolic disturbances are unknown. It has been shown that the urine during the period of high nitrogen output contains large quantities of corticosteroid material presumably derived from the adrenal cortex. It is not certain how an increased output of such material is related to the increased urinary nitrogen output.

After injury the body requirement for ascorbic acid (vitamin C) is apparently greater. Some of the increased demand may be due to an increased utilization in the adrenal cortex and the liver and some to the needs of the tissues at the site of injury.

The increase in calcium output in the urine after injury is a potential danger, as insoluble calcium phosphate may be precipitated, leading to the formation of calculi. Various methods of treatment to avoid precipitation have been advocated, but these are still in the experimental stage.

I wish to thank the many surgeons who permitted observations to be made on their patients and the dietitians who co-operated in this work. My thanks are also due to Mrs. P. H. Herbert, Leverhulme Scholar, and to my technical staff—S. P. Steward, L. S. Drewell, and R. D. Chambers—for their assistance in the analytical

work. Dr. J. S. L. Browne has permitted me to quote freely from the reports of his group which have been recorded in the minutes of the Conference on Bone and Wound Healing.

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SYNCHRONOUS COMBINED TOTAL GASTRECTOMY

BY

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Since the introduction of transthoracic total gastrectomy in 1938 there has been an appreciable improvement in the results of surgery in carcinoma of the stomach. The work, among others, of Churchill, Sweet, Garlock, and Phemister testifies to this admirably and has altered the whole outlook, but even now the figures leave a good deal to be desired. The five-year cure rate is depressingly low, though it is early to assess it, and the mortality rate far too high. Finney and Rienhoff (1929) quoted a 53.8% mortality in 67 cases, Waugh and Fahlund (1945) 44.2% in 77 cases, and Clagett (1945) 16.6% (five deaths in 30 operable cases of malignant disease of the stomach). These figures illustrate the progressive improvement in surgical treatment of an otherwise fatal disease, and a great many factors are responsible—earlier diagnosis, better pre-operative preparation, an increasing resectability rate, advances in anaesthesia, and the introduction of chemotherapy and antibiotics.

This communication is essentially a preliminary one, recording a new method of approach which we have found useful, and clearly some time must elapse before any instructive figures are available or there are results from which deductions can be drawn.

FIG. 1.—Diagram showing position of personnel and apparatus during operation.

In an attempt to reduce the time of operation we conceived the idea of two surgeons working synchronously, in a manner parallel to that employed in excision of the rectum (Morgan and Lloyd Davies). The position of the patient on the table has therefore been adjusted to make it possible for one surgeon to work in the chest at the same time as the other works in the abdomen (Fig. 1). A tilt of approximately 30 degrees (Fig. 2) has made this feasible, and it has been found easier for the abdominal surgeon to sit down and work through a transverse incision. This divides the left rectus muscle and just crosses the midline. Each surgeon has his assistant opposite him, though we have tried the alternative of having the assistant on the same side of the table. A Mayo table is placed at the head of the table and another at the foot, and an instrument trolley is provided for each of the two sisters; thus confusion or competition in the use of instruments is avoided. Finally, we pay particular attention to the position of the arms, avoiding the use of an arm rest, which was found to impede the thoracic surgeon. The illumination of the two wounds presents no difficulties provided that separate lights are employed. Additional spotlights can be used on either side if required.

The usual thoracotomy incision, with resection of one rib, has been made to approach the lower oesophagus, but we have not found it necessary to cut across the costal margin and join the thoracic and abdominal wounds. Experience of thoraco-abdominal wounds with and without damage to the costal margin has

convinced us that its division is not only unnecessary for exposure but undesirable for the patient's convalescence. The thoraco-abdominal wound employed by surgeons such as Wookey and Tanner is therefore replaced by a thoracic and an abdominal wound separated by the width of the costal margin.

The lymphatic drainage of the stomach is so disposed (Fig. 3) that excision of the cardia and 2-3 cm. of oesophagus is essential if ablation of a growth is to be radical. Submucosal spread in the oesophagus and even enlarged lymph glands above the diaphragm occur often enough to commend this step. It is, moreover, an abnegation of surgical principles to remove only part of the lymphatic field in a disease so fatal as carcinoma of the stomach. We would go even further and say that the operation of partial gastrectomy for carcinoma of the stomach is lamentably conceived as a radical method of extirpation of malignant disease in this area. It should surely be replaced by total gastrectomy if and when this operation can be done with a comparable mortality.

Division of the jejunum and end-to-end or end-to-side oesophago-jejunostomy have been carried out, with an anastomosis of the Roux type to complete the operation, but these are details outside the scope of our present theme. Jejunostomy likewise seems to be a matter of individual preference, adaptable to certain patients but not invariably required.

The time of operation should, in our view, be two to two and a half hours in an uncomplicated case—the abdominal surgeon doing the division of the duodenum, lower stomach mobilization, and Roux anastomosis, and the thoracic operator the mobilization of oesophagus and cardia and the oesophago-jejunostomy. It is pertinent to add that the thoracic operator does not begin until operability in the abdomen has been decided by his colleague.

FIG. 2.—Tilt of the table.

FIG. 3.—The disposition of lymphatic drainage of stomach.

We believe this to be easier than abdominal total gastrectomy as practised by Lahey and others. Decrease in the time of anaesthesia alone would seem to justify it, because patients with this disease tolerate anaesthesia badly. Our preference is for inhalational anaesthesia with endotracheal intubation, and if controlled respiration is employed the lung should be inflated at half-hourly intervals to minimize the risk of post-operative collapse. Bronchoscopy at the end of operation may in some instances be a wise additional measure.

Conclusions

The present position of surgery in relation to carcinoma of the stomach is unsatisfactory.

Immediate mortality from total gastrectomy for malignant disease is too high.

A reduction in the time of operation might help to reduce morbidity and mortality.

Synchronous combined excision through a thoracic and an abdominal wound is suggested as a means of attaining it.

We are indebted to Dr. John Hunter for his skill and care in anaesthetizing the patients, and to the staff of St. Andrew's Hospital, Dollis Hill, for much valuable help.

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EFFECT OF PENICILLIN ON BACTERIAL FLORA OF THE MOUTH

BY

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Many of the organisms present in the mouth as part of the normal flora or as pathogens have been known, since Fleming's original paper in 1929, to be penicillin-sensitive, but it was not until 1944 that the possibility of treating oral infections with penicillin was fully appreciated. Basing his observations on the bacteriological findings in a series of patients treated by Mowlem (1944) for infection of the mandible, Garrod wrote:

"The great majority of the very numerous bacterial species found in the mouth are penicillin-sensitive. This is of far-reaching practical importance, since it means that infections derived from or connected with the mouth are in general susceptible to penicillin treatment, just as those connected with the bowel are insusceptible owing to the prevalence there of resistant species. The flora of the mouth is highly complex and has been imperfectly studied; the following observations are therefore perforce of an elementary nature. In plates, both aerobic and anaerobic, inoculated with material from osteomyelitis of the jaw, from infected compound fractures of the jaw, and from infected gums, or with saliva, the only organisms ever found markedly resistant to penicillin as judged by the cup method have been *Monilia albicans*, an occasional *Neisseria*, and *Haemophilus*. Whole groups of bacteria which are thus sensitive in doubtless varying but apparently adequate degrees are aerobic streptococci (including various types of *Str. viridans*), anaerobic streptococci, anaerobic Gram-negative bacilli (*F. fusiformis* and many others unidentified), and various Gram-

positive bacilli. The mixed and predominantly anaerobic flora often found in infections derived from the mouth is thus in general sensitive to penicillin, and the results of treatment are as would be expected from this."

These findings were confirmed by MacGregor and Long (1944, 1945a), who incorporated penicillin in a slowly dissolving pastille for use in the mouth; the patient was instructed to insert another when the previous one had disappeared. By this means the saliva could be kept fully bacteriostatic throughout the day. Promising results were obtained in a variety of infectious conditions of the oral cavity and in prophylaxis against infection secondary to surgical or dental trauma in the mouth.

Since then penicillin has been applied to the mouth by numerous workers, using many different techniques; the whole subject has recently been reviewed by Hutchinson and Cranston Low (1946). It is not proposed to discuss these various techniques, but to describe the bacteriological findings in a series of patients who were treated with penicillin during the years 1944-6. These patients were classified as follows:

A. Patients Receiving Local Penicillin Treatment (Penicillin Pastilles).—(1) Patients with acute gingivo-stomatitis (Vincent's type); (2) patients with acute and chronic tonsillitis; (3) patients under the care of the Maxillo-facial and Plastic Units at Hill End Hospital, St. Albans, while receiving treatment for a variety of traumatic, surgical, and dental conditions. The total number of cases was 500.

B. Patients Receiving Systemic Penicillin Treatment.—(1) In a dosage of 500,000 to 1,000,000 units of penicillin in 24 hours:—(a) Patients treated under the scheme sponsored by the Penicillin Trials Committee of the Medical Research Council for the investigation of the penicillin treatment of subacute bacterial endocarditis; (b) patients treated for severe diphtheria and scarlet fever; (c) patients treated for actinomycosis. The total number of cases in Group B 1 was 30. (2) In a dosage of less than 500,000 units of penicillin in 24 hours:—(a) As Group B 1 (a); (b) patients receiving routine penicillin treatment for a variety of conditions. The total number of cases in Group B 2 was 30.

Excretion of Penicillin in the Saliva

Changes can be produced in the bacterial flora of the mouth by the administration of penicillin either locally as already stated (Garrod, 1944; MacGregor and Long, 1944) or systemically if sufficiently large dosage is employed (Long, 1946a, 1946b, 1947). It is probable that in the latter case the changes are caused by penicillin excreted in the saliva, though attempts to demonstrate this have either been unsuccessful (Rammekamp and Keefer, 1943) or have detected it only in small quantities (Florey *et al.*, 1941; Struble and Bellows, 1944; Fleming, 1945). No simple relationship has been shown to exist between the penicillin content of the saliva and the penicillin content of the blood. Herrell (1945), reviewing the evidence, is unable to be dogmatic, and states: "I am inclined to believe that fairly adequate amounts of penicillin do reach the saliva following systemic administration." The persistence of highly penicillin-sensitive organisms in the mouth of patients receiving less than 500,000 units of penicillin systemically in 24 hours, combined with failure to demonstrate penicillin in their saliva, suggests that the threshold for penicillin excretion in the saliva is attained only by a dosage of this magnitude. However large the dosage employed systemically, penicillin will be demonstrable in the saliva only in the initial phases of treatment, for as soon as the organisms of the *Bacterium* group establish themselves in the mouth penicillinase is produced in sufficient quantity to destroy it. Further work on the concentration of penicillin in the blood, the excretion of penicillin in the