ADRENOCORTICAL RESPONSE IN OPERATIVE PROCEDURES UPON THE BONES AND JOINTS *

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Orthopaedic surgeons are accustomed to think of the responses of their patients to operations upon the bones and joints in terms of surgical reactions and of the success of such procedures as depending chiefly upon the perfection of operative technique and the soundness of the postoperative treatment. They give small heed to the complicated metabolic responses of the body which are set off by these operative procedures and which must to a greater or lesser extent influence their outcome. These metabolic changes are largely the result of the interplay among the hypothalamus, the pituitary, and the adrenal glands [13, 21, 23].

While these endocrinological reactions are being extensively studied by internists and general surgeons, nothing has yet appeared to show that orthopaedic surgeons are awake to their importance. Yet the field of orthopaedic surgery is an interesting one for investigation, because it is quite different from that of surgery of the abdomen and thorax. Its operative procedures are of equal severity, but are performed upon the bones or joints and, because of the slow healing of these structures, often require prolonged immobilization of the parts in plaster-of-Paris encasements or protection by traction or braces. In addition, metallic devices are frequently used for internal fixation, and plastic or metallic appliances may be inserted as artificial replacements for damaged portions of the skeleton. These differences raise questions about the metabolic responses of the body under these special conditions and their possible influence on bone healing [17]. It seemed important to try to answer them by undertaking a study of adrenocortical function following injury or operation upon the skeletal system. As Prof. F. D. Moore of Harvard stated recently in discussing a paper presented before the American Surgical Association: "We, as surgeons, are endocrinologists whether we like it or not. We must discipline our thinking, bring our terminology into harness, and keep our concepts clear as we pilot our way through these next few confusing years of increasing knowledge of surgical endocrinology."

OBJECTS OF STUDY

We set out to study the general adaptation syndrome with relation to orthopaedic surgical procedures and we tried to define our objectives in the form of questions as follows:

1. Is there any evidence of stress from prolonged immobilization or corrective plasters?

2. What are the effects upon the adrenal responses of major multiple-stage operations such as may be required in scoliosis, Pott's disease, or poliomyelitis?

3. May long-continued stress produce metabolic responses which are inimical to wound and bone healing? [9]

4. What are the effects of chronic infection such as tuberculous joint disease or chronic osteomyelitis?

5. Does the operative insertion of metallic appliances or plastic prostheses in the body create a condition of stress?

6. Do bone tumors create a condition of stress and, if so, can the demonstration of this condition be of any diagnostic significance?

7. Is there any evidence that, in cases of prolonged stress, a condition of adrenal refractoriness or depletion may develop in which hormonal replacement therapy may be indicated?

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MECHANISM OF ADRENAL STIMULATION AS A RESULT OF A FRACTURE

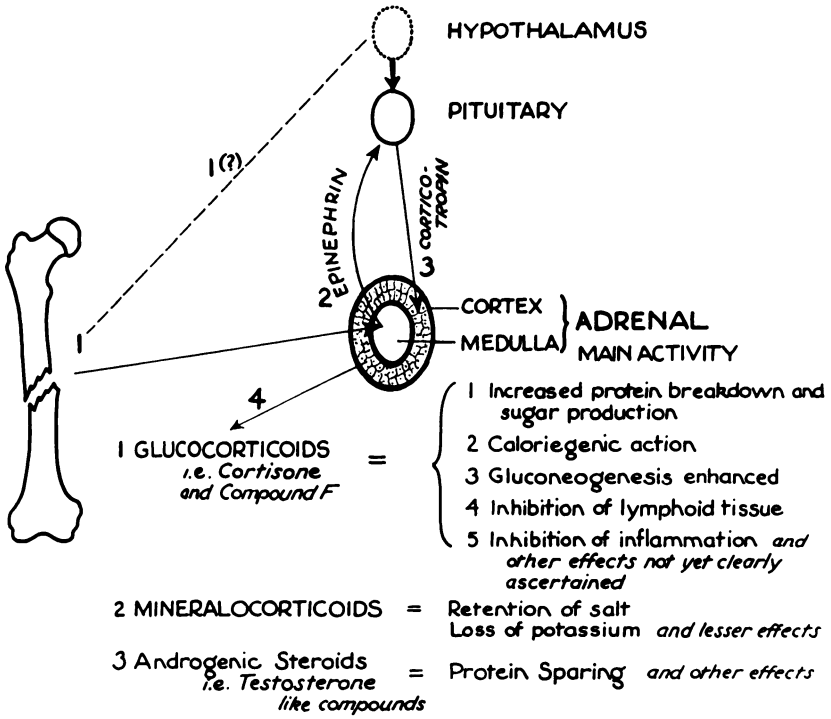

CHART I

Depicts the mechanism which is supposedly invoked following injury.

In summary, our aim was to study the departure from the normal of adrenal function following orthopaedic operations either toward hypofunction, which in the extreme is Addison's disease [4, 19] or toward hyperfunction, which may result in Cushing's syndrome [11].

THE ALARM REACTION AND ADRENOCORTICAL FUNCTION

When sudden stress is thrown upon the body by injury, such as a fracture of the femur or operative trauma, a stimulus is relayed to the pituitary, probably by way of the hypothalamus, and corticotropin (ACTH) is released. This causes adrenocortical stimulation and, as a result, steroids are produced and circulated in increased quantity throughout the body (Chart I). This "alarm reaction" is considered to initiate physiological responses for the conservation of life and to adapt the body to cope more easily with harmful influences. The long-term clinical systemic effects of the action of these corticosteroids constitute what is called the "general adaptation syndrome" [2, 3, 5, 14].

Although there are many classifications of the adrenocortical hormones, probably the simplest is their division into three categories—namely, glucocorticoids, mineralocorticoids, and androgenic steroids. Whether one type of steroid is transformed into three or more hormones, or whether three types of corticoids are separately secreted has not yet been ascertained.

The glucocorticoids, which include cortisone and compound F, exert their effects mainly upon glucose metabolism, but they also have many lesser effects. Their action is chiefly catabolic and anti-anabolic; for this reason they are of importance to the surgeon because of their effect upon elements which play a part in wound repair and bone healing. Among their effects the following have been noted [7, 14, 23]:

1. Increased gluconeogenesis (sugar production);
2. Increased breakdown of protein;

3. A calorigenic effect which provides an increased amount of energy to meet the increased metabolic requirements created by stress [8];

4. An anti-inflammatory response;

5. An antihyaluronidase effect which is believed to aid in decreasing the exudative response to trauma;

6. A drop in the level of vitamin A and vitamin C circulating in the blood stream;

7. A drop in the level of circulating eosinophils. This has been shown to be due chiefly to the action of cortisone and hydrocortisone (compound F);

8. Regression of lymphoid tissue;

9. Lesser effects on mineral metabolism.

The mineralocorticoids exert powerful effects upon electrolyte balance and especially cause sodium and chloride retention and increased potassium excretion. Little is yet known of their effects on the metabolism of calcium.

The exact role of androgenic steroids is not quite clear; their action is thought to be anabolic or anticatabolic and somewhat similar to that of testosterone.

More is known about the effects of cortisone than those of any of the other cortical steroids. It has been shown to exert powerful immunological, metabolic, and other physiological effects. Prolonged stress causes the liberation of increased quantities of cortisone and hydrocortisone (compound F) and other glucocorticoids which may exert significant effects upon the healing of wounds and of bone.

Sufficient alarm produces a general adrenocortical response. The presence of increased quantities of glucocorticoid, mineral corticoid, and androgenic steroids can be determined by various chemical analyses of different substances in the blood and urine. For example, the amounts of sodium, potassium, and chloride can be measured in the blood and urine and give an indication of the mineralocorticoid response. Determinations of blood and urinary nitrogen and sugar, together with nitrogen-balance studies, show the activity of the glucocorticoids. It is believed that measurement of the ketosteroids in the urine gives an indication of androgenic-steroid response [14] and that quantitative analysis of the oxysteroids shows the glucocorticoid response [1, 10].

To make the large number of complicated chemical determinations which would be required to follow a large number of patients through the preoperative, operative, and postoperative phases in studying adrenocortical reaction would be prohibitively time-consuming and expensive. Fortunately, an easier method is available which has been shown by Thorn, Evans, and others to be an excellent indicator of adrenocortical activity. This is the level of eosinophils circulating in the blood [16, 18, 22].

EOSINOPHIL LEVELS

When cortisone or hydrocortisone (compound F) are administered, a rapid drop occurs in the level of circulating eosinophils and the decrease bears a rough relationship to the quantity of hormone given. Of the various adrenal hormones tested, only the two mentioned above produce this result. After the hormonal effect ceases, the level of eosinophils returns to normal or temporarily above normal. The administration of twenty-five milligrams of adrenocorticotropin (ACTH) also depresses the eosinophil level, usually by at least 50 per cent. within a period of four hours. Thorn used this as a test of adrenocortical reserve and considered a response of less than 50 per cent. as indicative of dangerously lowered function.

It was observed before the turn of the century that the appearance of eosinophilia following illness often coincided with the patient's clinical improvement. Injury or operative trauma is followed by eosinopenia, which is evidently the result of excitation of the pituitary with liberation of adrenocorticotropin (ACTH) which in turn stimulates adrenal secretions. Failure to develop eosinopenia following trauma is thought to be indicative of some disorder either at the adrenal or pituitary level [21, 24]. Rud, following a study of 525

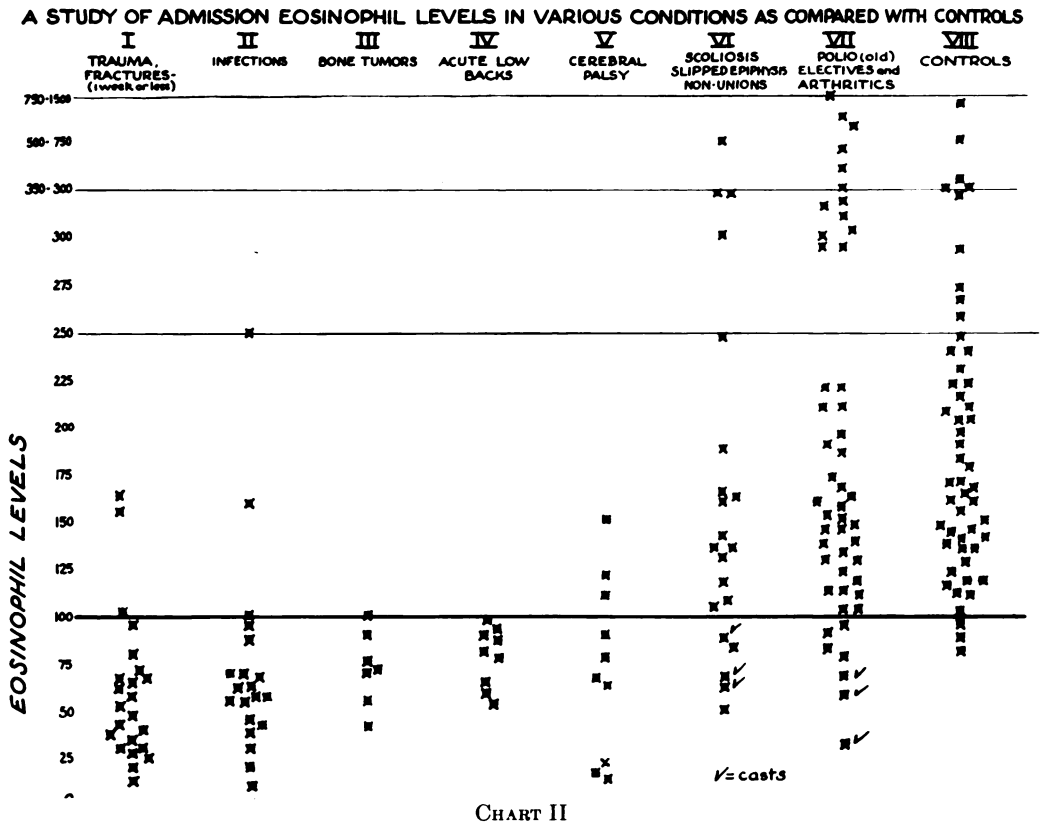

CHART II

The influence of stress can readily be seen in comparison of the columns.

subjects, noted that the eosinophil level behaved characteristically in health and mental disease.

It is recognized that this is a new field of study in which much remains to be learned, and it is also admitted that the determination of eosinophil levels is only a limited method of testing complete adrenocortical activity. Nevertheless, there is sufficient evidence in the literature to show that consecutive eosinophil counts, when done accurately and according to proper standards, may yield important information. It was because of this conclusion, reached only after careful study of the literature, and because of the ease and rapidity with which this method could be utilized frequently and consecutively in many patients, that we adopted it for study of our patients both before and following orthopaedic surgical procedures.

METHOD OF STUDY

In an attempt to eliminate common sources of error, we adhered rigidly to several specifications in our technique. We used standardized pipettes and chambers and used the same pipettes on the same patients. The stains were frequently filtered. We drew two cubic centimeters of venous blood and always counted four chambers. If a difference of over ten cells in any chamber from another was noted, the count was repeated until satisfactory spread was obtained. Since there is a slight variation in the morning and afternoon counts in the same patient, we made it a point to draw the blood at the same time each day. Also we made use of Randolph's method. Finally, the counts were made always by the same team, one physician and one technician.

A group of fifty-two control cases composed mainly of hospital personnel who were free from illness and known tension were first studied. They were divided into two groups of twenty-six each; the first group had morning counts and the second had afternoon

counts. The counts were performed on from six to eight separate days on each person and always at the same time of day. The results obtained were consistent and served to prove that our technique was accurate. To corroborate further our control study, we compared these counts with those made on a group of patients who underwent elective operations for the correction of various types of deformity which had been incurred in childhood, but who were free of disease at the time of operation. The results here were identical with those in the controls.

The material for study was made up of 125 patients suffering from various types of skeletal injury or orthopaedic disease. Serial eosinophil counts were made from admission, during and following operation, and during convalescence, often many weeks after discharge from the hospital. Thorn tests were often carried out before operation and also at different stages of recovery when indicated. The patient's clinical behavior was carefully observed preoperatively, during operation, and postoperatively. A rating system was devised by means of which the patient's vital signs and clinical course could be evaluated. These were recorded objectively, as were the amounts of sedations, medication, and other supportive treatment. Wound healing was observed and all complications were recorded, such as sloughing, separation, drainage, or marginal necrosis. The wounds were not rated as complicated unless their treatment prolonged the patient's hospital stay. Wound complications which occurred within plaster casings, where pressure might have been a factor or where an obvious physical element accounted for it, were not included.

RESULTS OF STUDY

Comparison of Eosinophil Levels of Newly Admitted Patients with Those of Normal Controls

The results of a study of admission eosinophil levels in various orthopaedic conditions compared with a group of normal controls are shown in Chart II. As we recognized that there may be considerable variability in the eosinophil counts at different times, serial counts were done on different days when possible and many of the patients had repeated counts. It was observed that low counts varied only slightly, while counts above 200 varied considerably. Many showed a range of only plus or minus 10 per cent. of the initial level. This indicated a marked consistency of eosinophil levels in our series.

The last column on the right in Chart II indicates the average results in the fifty normal controls collected over a twenty-month period. The counts ranged between 100 and 250 in 74 per cent., which is the range that Thorn considers normal. Only 6 per cent. of the counts were below 100 while 20 per cent. had counts above 250. As a result of these observations, we are inclined to feel that the upper limit of the normal range should be increased to 300 or 350. The fluctuation of counts did not exceed plus or minus 20 per cent. in 90 per cent. of the cases, while in 65 per cent. it did not vary over plus or minus 10 per cent.

When the other groups of cases shown in Chart II are studied, some interesting differences can be noted in comparison with the control group. Patients with recent fractures of bone, infections, or acute low-back pain and tumors with a few exceptions showed eosinopenia. Patients who were admitted for elective surgical procedures, such as correction of deformity in poliomyelitis or scoliosis, had counts which compared with the control group. In Groups VI and VII of the twelve counts which averaged below 100, plaster casings were being worn by six of the patients; this may be considered as an adequate cause of stress. Cerebral-palsy patients generally had low counts. Only six patients with fractures or infections showed eosinophil counts over 100. In three of these the Thorn test was below 50 per cent., indicating adrenal refractoriness.

Our findings on this part of the study therefore substantially agreed with Thorn's finding that 100 is the lower limit of normal; the upper limit, however, is probably higher than he thought, perhaps even up to 350. It appears that the eosinophil level can serve as a fairly reliable method of showing response to stress and adrenal stimulation; hence it

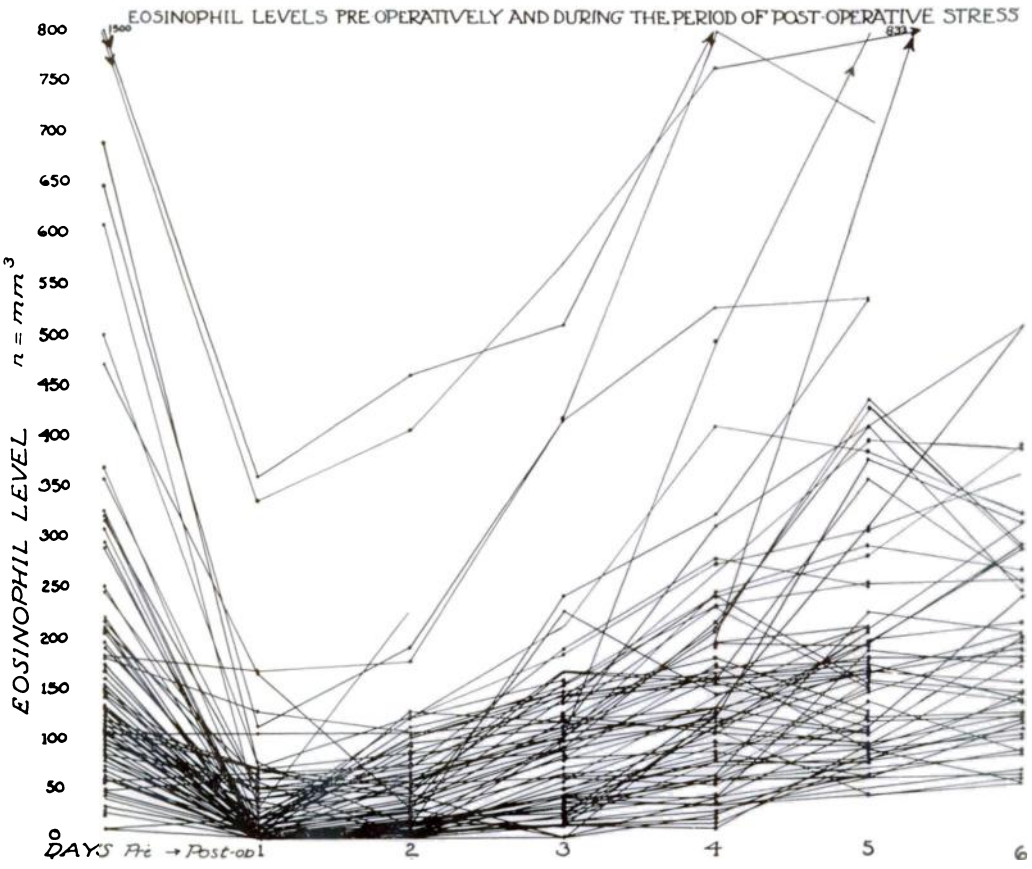

CHART III

Showing the sharp postoperative drop within twenty-four hours and the subsequent pattern.

can serve as a diagnostic and prognostic aid in conditions producing prolonged eosinopenia, such as bone and joint infections, hematomata, or in acutely painful states, such as acute low-back pain and herniated discs. By the same token it may help to differentiate the malingerer from the true sufferer in medicolegal and other cases where this question may be raised.

It is of interest to note that in a case of extensive caseous tuberculosis of the knee in which the sedimentation rate of the erythrocytes was within normal limits the eosinophil count was depressed to 50 and was therefore a truer indication of active disease than the former. Following knee fusion and into convalescence, the eosinophil count rose and leveled off at 400. In other cases we have noted that a rising eosinophil count parallels a falling sedimentation rate.

Behavior of Eosinophil Levels after Surgery or Trauma

We have broken down our study of these consecutive eosinophil counts into two periods: the first, the stress period which represents the first five days after injury or surgery, and the second, the convalescent period.

The counts during the stress period are shown in Chart III and it can be seen that the changes are profound and almost uniform. Marked eosinopenia lasting from seventy-two to ninety-six hours is followed by rapid rise to normal levels. This indicates strong adrenal-cortical stimulation as a normal result of stress. Failure to respond in this manner would indicate either failure of normal stimulation or impairment of adrenal function.

During the convalescent period the counts showed considerable variability and it

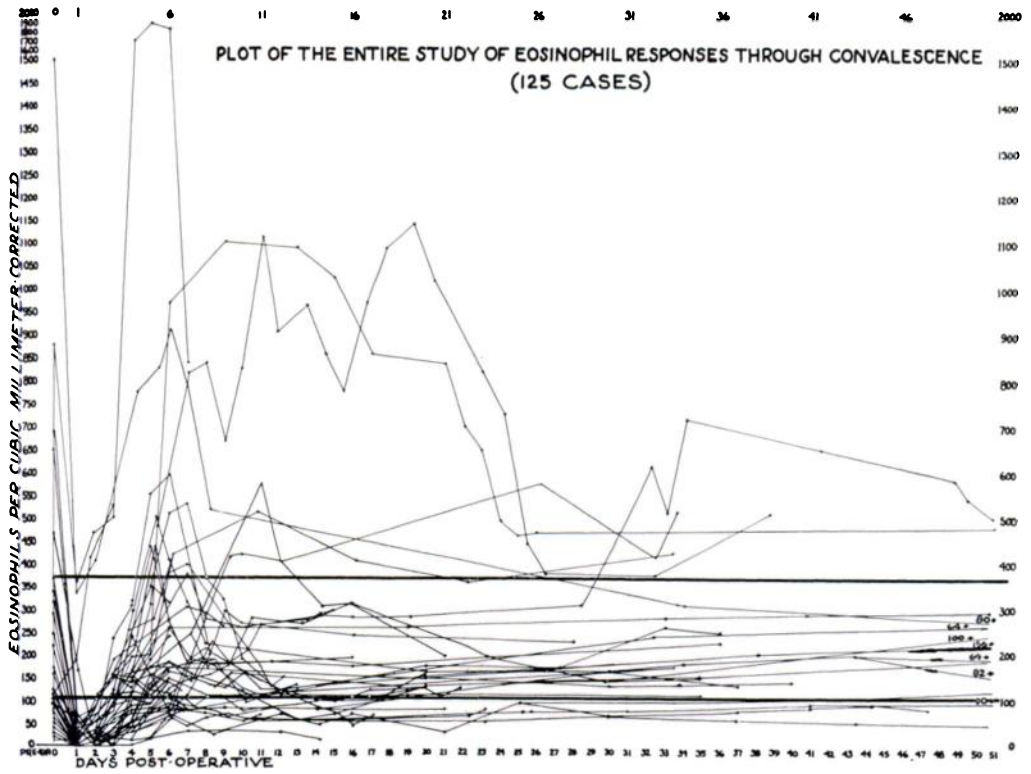

CHART IV

Although in most of the cases there is a return to preoperative levels, some cases are eosinopenic and others are eosinophilic. Cases with hematopoietic or other stimulant therapy are not depicted.

was difficult to draw conclusions. Nevertheless, two types of variation were noted which are worthy of further investigation (Chart IV). It was noted that high levels of eosinophilia developed in some patients while severe eosinopenia developed in others. These cases will be considered later in this paper.

It should be noted that all patients were eliminated from this part of the study in whom sensitivity to drugs existed or to whom hematopoietic stimulants had been administered, such as liver, folic acid, or iron, as these are known to produce eosinophilia through their stimulating action on the bone marrow.

Eosinophil Level with Relation to Clinical Course of Patient

Clinical observation of the patients from day to day revealed that rising eosinophil counts following periods of stress corresponded with clinical improvement. The patients felt better, their appetite improved, fever declined, urinary output increased, and there was lessened need for analgesics. It was noted in the postoperative course of most patients that, following a severe depression lasting two to three days, the eosinophil level rebounded rapidly to normal and even above normal, but eventually returned to the normal preoperative level.

Low counts persisted in patients who were ill following operation. There were two exceptions. These patients, although quite ill, showed eosinophilia. In one of these patients bronchopneumonia developed forty-eight hours after operation, with elevated temperature. A Thorn test was carried out with negative response and was interpreted as indicating adrenal refractoriness. She was given cortisone in therapeutic doses for five days. After thirty-six hours the fever subsided and her reactions became normal. This test, however, is inconclusive, because at the same time she was treated with antibiotics; and it is more likely that she improved as a result of this treatment rather than as a result of cortisone.

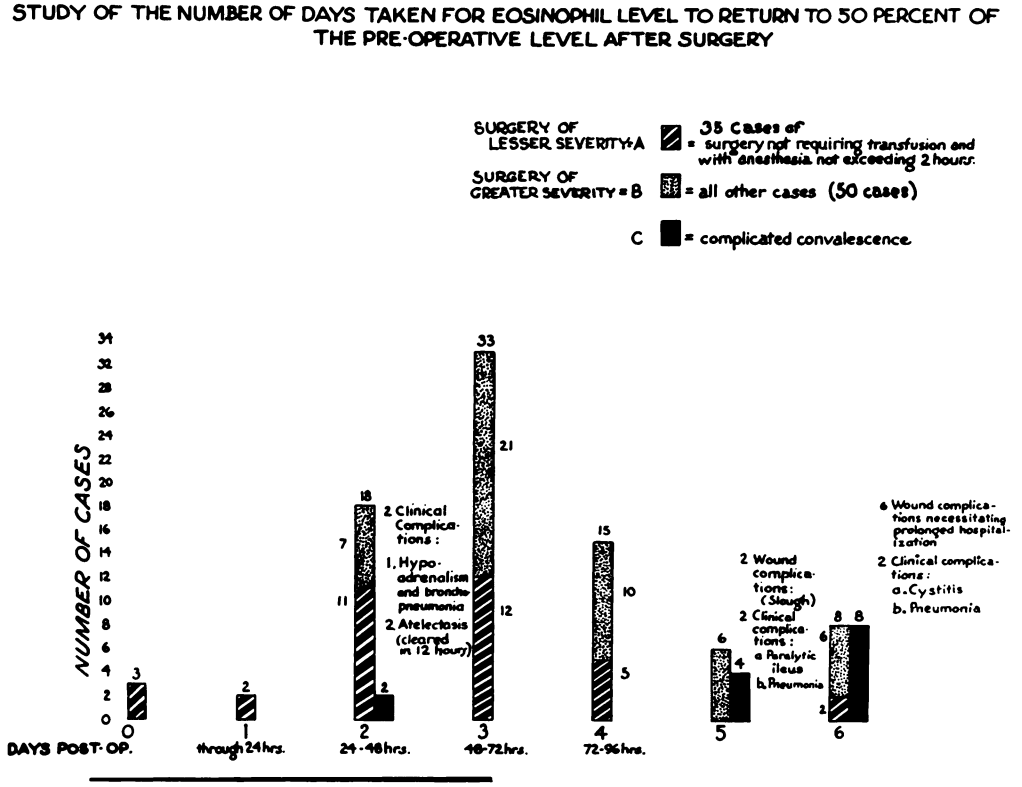

CHART V

Illustrates how the greater the intensity of surgery, the longer the eosinopenia, as well as the rising incidence of complications with prolonged eosinopenia.

We do think that the administration of cortisone contributed to her recovery. In the second patient high eosinophilia developed one month postoperatively. This corresponded with the development of a draining sinus. Her Thorn test too was negative at this time, although she had shown an excellent response when it was done preoperatively.

The rebound phenomenon of the eosinophils generally did not occur when postoperative complications developed. In these cases, with the exceptions noted above, the counts remained depressed until the complicating condition was relieved. A study of the cases in which the eosinophil counts were depressed to a level of less than 50 per cent. of the preoperative level for a longer than average period of days is shown in Chart V. An effort was made to divide these cases into two classes according to the severity of their operations. Procedures of lesser severity were considered to be those requiring less than two hours of anaesthesia and no blood replacement. Those of greater severity either required more than two hours of anaesthesia, or blood transfusion, or both. From this graph one may note that the greater the severity of the surgery, usually, the longer the eosinopenia. Nevertheless the phenomenon of rebound was remarkably consistent.

It is of great interest to note that complications had occurred in all of the eight patients in whom the count remained depressed to below 50 per cent. of the preoperative level for six days and in four of the six patients in whom it was depressed for five days. Of these complications, four had been recognized early and included two pneumonias, one cystitis, and one paralytic ileus. The other eight patients had complications of wound healing such as skin slough, infection, hematoma, or wound separation. In six patients the wound complication was severe and prolonged the patient's hospital stay. In none of these cases was the wound complication discovered until later, at the time the sutures were removed. In two cases the complication was not evident until the eighteenth and

GRAPH DEPICTING FOUR DIFFERENT PATIENTS WITH INITIAL EOSINOPENIA — THEIR RESPONSE AFTER OPERATIVE TREATMENT — THE USE OF THE EOSINOPHIL LEVEL AS A PROGNOSTIC INDEX

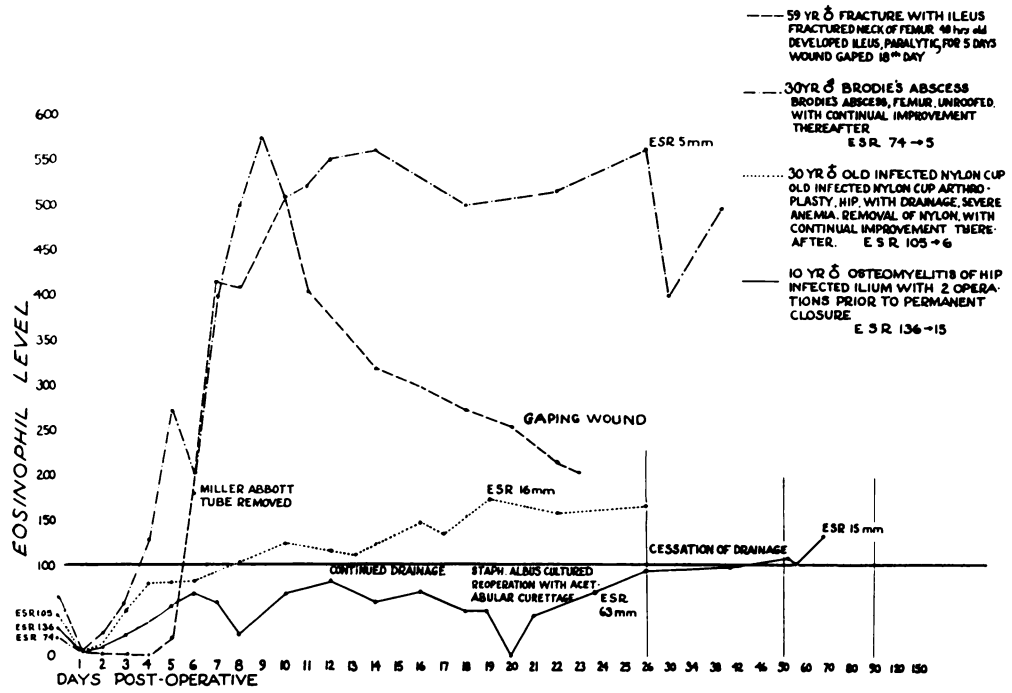

CHART VI

Illustrating how removal of stress releases the patient from eosinopenia.

twenty-third postoperative days. A prolonged depression of the eosinophil count following operation is, therefore, of considerable prognostic importance and certainly calls for careful and repeated check-up on the patient. It may also be argued from the frequency of wound complications in these cases that the environment for good wound healing is produced within the first three to four days following operation.

Use of the Eosinophil Level in Prognosis

In Chart VI are illustrated the consecutive eosinophil counts of four patients who showed severe eosinopenia upon admission to the hospital. The first patient had incurred fracture of the neck of the femur forty-eight hours prior to admission. She was operated upon the following day, the fracture was reduced, and a Smith-Petersen nail was inserted for fixation. Paralytic ileus developed following operation and the patient was in serious condition. A Miller-Abbott tube was inserted and she was given supportive therapy. Although she showed profound eosinopenia, the tube was removed. Vomiting recurred and it was necessary to reinsert the tube. Thirty-six hours later, after the eosinophil count had begun to rise, the tube was removed and the patient had uneventful progress.

The other three patients exhibited eosinopenia because of infection. One had a postoperative infection following nylon-cup arthroplasty of the hip and the other two had osteomyelitis. All had elevated sedimentation rates of the erythrocytes upon admission. In two of these cases, the eosinophil level rapidly rebounded to above normal upon surgical eradication of the infection. In the third case the eosinophil count remained depressed after the first operation and a second operation was later required. After recovery from this with cessation of drainage the eosinophil level rose to normal. It is particularly interesting to note that the high sedimentation rates in these patients dropped to normal as the eosinophil levels returned to normal or above normal.

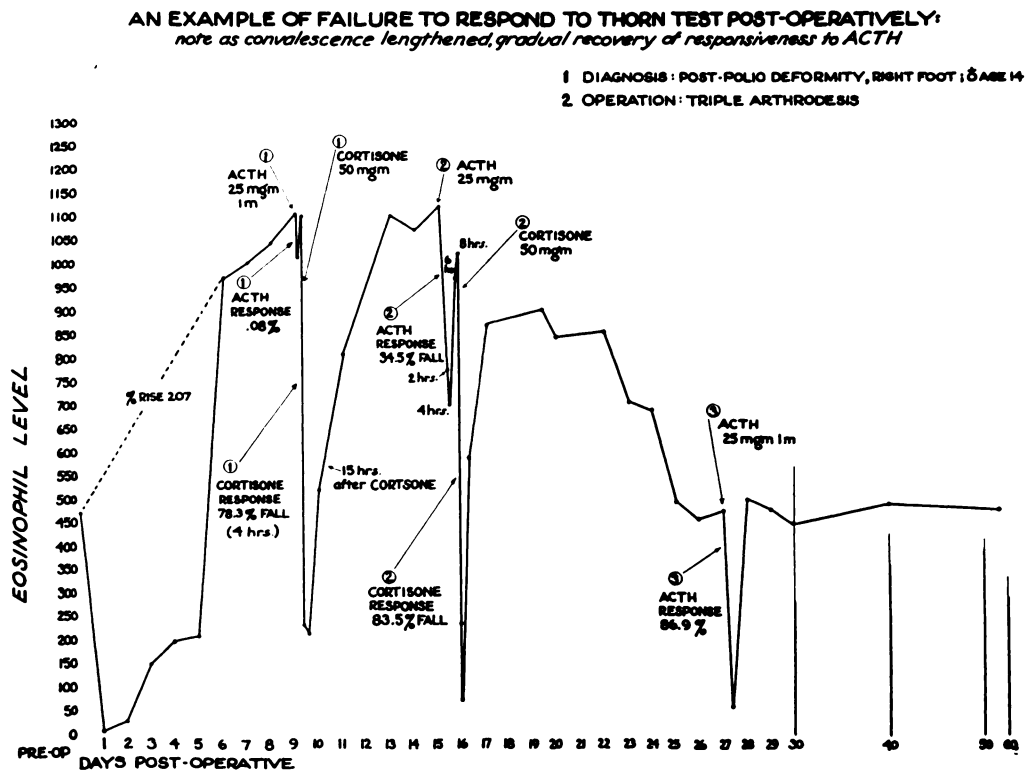

CHART VII

Showing the gradual return of responsiveness to ACTH postoperatively.

It appears from this study that the eosinophil level may be of use as a prognostic guide in recovery from any stressful situation. Patients with acute fractures of the hip consistently show eosinopenia and evidence of stress. In aged patients who are not in good physical condition, this seems to offer a good argument for early operation and fixation of the fracture in order to relieve stress. More evidence bearing on this point will be accumulated.

Evaluation of Results of the Thorn Test

As was stated previously, the administration of twenty-five milligrams of adrenocorticotropic hormone (ACTH) will ordinarily depress the eosinophil level by at least 50 per cent. within four hours. Thorn considered this to be a good test of adrenocortical function and thought that a response of less than 50 per cent. was indicative of lessened adrenocortical reserve. This has come to be known as the "Thorn test" and it has been used extensively for experimental purposes. We were also interested in studying this reaction to determine whether or not it was of valuable prognostic importance in operative cases.

Twenty patients were subjected preoperatively to the Thorn test. Of these, two showed no change in the eosinophil level, four showed a drop of less than 50 per cent., and the remaining fourteen showed the predicted response of over 50 per cent. Of the six patients who showed poor responses, only one had a postoperative complication. This was the patient mentioned previously who incurred pneumonia. She was subjected to a second Thorn test with negative result, whereupon she was given cortisone. Concomitantly, she was treated also with antibiotics and recovered. She showed eosinophilia at a time of stress and we believe she had lowered adrenocortical function. The other patients progressed through operation and convalescence without incident.

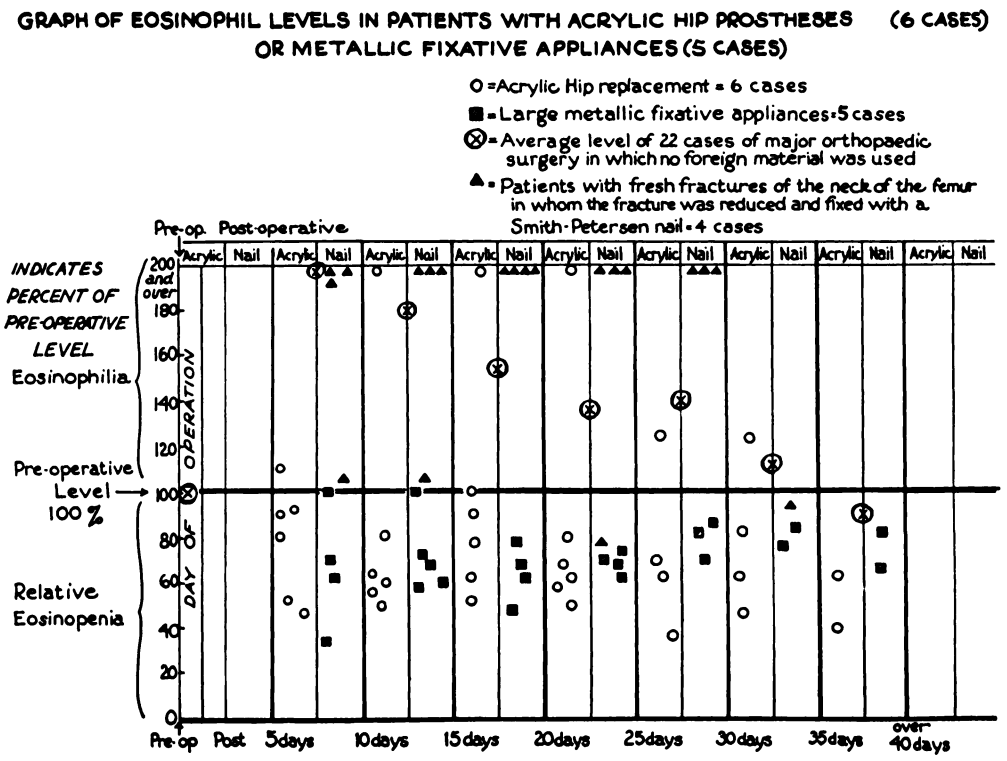

CHART VIII

Illustrating the prolonged mild eosinopenia in convalescence which occurs in patients with acrylic or metallic fixative appliances. The cause is unknown.

When the preoperative response to the Thorn test was good, the patients withstood major surgical trauma well. Two patients, both over eighty years of age, with excellent ratings in the Thorn tests preoperatively had postoperative courses marked by complete freedom from any disturbance.

Thirty patients were subjected to Thorn tests during convalescence; of these nineteen showed normal responses of 50 per cent. or more. The consecutive eosinophil counts of one patient who showed a negative response to the Thorn test postoperatively are shown in Chart VII. The patient was a girl of fourteen years who was suffering from residual effects of poliomyelitis, with deformity of the right foot. A subtalar and mid-tarsal arthrodesis was performed. She showed a normal drop of eosinophils for two days following operation and then showed marked eosinophilia. This interested us and she was given a Thorn test, in which she showed inadequate response. She was then given fifty milligrams of cortisone; this was followed by a marked drop of eosinophils. This seemed to prove poor adrenocortical response. Nevertheless she made progress without complication and, when again tested on the sixteenth postoperative day, showed a better response, and on the twenty-seventh postoperative day, a normal response. Of ten patients who underwent consecutive Thorn tests, nine ultimately showed good responses, although at one time or another six showed poor responses.

From our observations, we believe it is impossible at this time to draw conclusions about the value of the Thorn test. In our hands a poor response did not preclude a good postoperative course. It is possible that a standard dose of ACTH does not stimulate the same adrenocortical response in all patients. Perhaps the dose should be based on body weight and some patients may require more of the hormone than others to produce the same result. When the response to ACTH is a drop of the eosinophil level of more than 50 per cent. we feel we have definite evidence of good adrenocortical reserve.

Eosinophil Response in Patients with Acrylic Hip Prostheses or Metallic Fixative Appliances

In patients in whom acrylic hip prostheses or large metallic appliances for internal fixation of the bones were employed, it was noted that there generally occurred a significant depression of the postoperative eosinophil levels in comparison with the preoperative levels. Although this depression was not profound, it appeared to be significant, as it was present in nine out of eleven cases in this group, and lasted as long as six to seven weeks. Furthermore, in four patients in whom the metallic appliances were removed the eosinophil levels rose. It should be remembered, however, that the appliances were generally removed because of pain.

The results of our studies in these cases are shown in Chart VIII. It is to be noted that an effort has been made here to reduce all of the cases to a common denominator on a percentage basis. The eosinophil levels on admission were taken arbitrarily as 100 per cent. and the subsequent counts at stated intervals of five days were expressed in terms of percentage of these admission levels. Therefore, levels below 100 per cent. represent relative eosinopenia and those above represent eosinophilia. In order to obtain a mean for comparison, we have taken, as a control, a group of twenty-two patients who were subjected to operations of equal severity, such as hip fusions or spine fusions, in whom no foreign materials were employed and subjected them to the same mathematical procedure.

We have also included in this study a group of patients with fresh fractures of the neck of the femur in whom the fracture was reduced and fixed by the insertion of a Smith-Petersen nail.

The results may be analyzed as follows:

1. *The Control Group* (twenty-two patients): The counts on these patients conformed to the usual pattern previously described. After operation there occurred the usual short period of eosinopenia followed by a rebound to eosinophilia. The levels at five days were nearly 200 per cent. or more compared with the admission level of 100 per cent. Thereafter there was a gradual tapering off of the levels so that they reached normal after forty days.

2. *Patients with Acrylic Hip Prostheses* (six cases): In this group, following the period of postoperative eosinopenia and the rebound, the counts quickly became depressed below the admission level even as long as thirty-five days. Most of these patients did well from a clinical standpoint and there was only one complication in the group. Note that one patient did not conform to this pattern.

3. *Patients in Whom Large Metallic Appliances Were Employed* (five cases): These patients had chiefly complicated fractures for which large metallic appliances were used, such as Küntscher nails or large trochanteric plates. It can be noted from the graph that the eosinophil levels in these patients conformed closely to the pattern seen in the patients with acrylic hip prostheses. They remained depressed below the admission level for approximately five weeks.

4. *Patients with Fresh Fractures of the Neck of the Femur Treated by Reduction and Internal Fixation* (four cases): While the number of patients in this group is too small to be conclusive, the pattern of the eosinophil levels is uniform and therefore suggestive. Upon admission these patients showed eosinopenia as would be expected from the stress of their injuries. Following reduction and internal fixation, there occurred a rapid rebound and persistent eosinophilia at a level of 200 per cent. or more compared with the admission level of 100 per cent. and lasting as long as four weeks. This indicates complete relief of the stress from injury.

All of these observations are based on small groups of cases and are presented only because the findings are suggestive. We have no explanation of these findings and more patients must be studied and for longer periods before they can be considered conclusive.

SUMMARY

We have presented the results of a study of eosinophil levels in 177 patients. Of these, fifty-two were healthy persons used as controls and 125 were patients who were suffering from various disabilities or injuries of the skeletal system and who underwent different surgical procedures. We have described the important metabolic effects taking place in the body, which depend chiefly upon the response of the adrenal gland to the stimulus of injury, and have pointed out the significant findings. We have employed the eosinophil count only as an indicator of these activities.

Finally, it should be pointed out that the metabolic processes we are trying to observe are multiple and complicated. The study of eosinophil levels, which is the method we have employed, may be likened to the opening of one small window through which may be obtained only an imperfect glimpse of the many activities going on within. Many other avenues of approach must be explored before we can penetrate to a point where we can obtain a clearer understanding of these complex mechanisms. We believe that a greater knowledge of them is important to orthopaedic surgeons and will promote the welfare of their patients.

CONCLUSIONS

1. Our studies confirm previous observations that following operation there normally occurs a profound drop in the eosinophil level which is generally followed by a rise to normal or above normal within three or four days. During the period of eosinopenia the patient is ill, and improvement parallels the rising eosinophil counts.

2. Persistent eosinopenia beyond the usual stress period is suggestive of developing complications, either of wound healing or of a general nature.

3. Infections, whether due to pyogenic or tuberculous organisms, cause stress and resultant eosinopenia. As infection is overcome, the counts rise toward eosinophilia. A rising eosinophil count generally parallels a falling sedimentation rate.

4. Eosinophilia when the clinical course of the patient is unsatisfactory is indicative of adrenal insufficiency and should be checked by the Thorn test. A negative result confirms this diagnosis and calls for a trial of cortisone in therapeutic doses.

5. Patients with fresh fractures uniformly showed eosinopenia or evidence of stress. When the fractures had been reduced and fixed there was a rapid rebound to eosinophilia.

6. Immobilization in plaster encasements did not produce evidence of stress. When plaster jackets were employed for correction of deformity, as in scoliosis, the patients showed eosinopenia.

7. Patients with painful conditions, such as acute low-back pain, exhibited signs of stress.

8. Decrease in the eosinophil count did not occur during anaesthesia.

9. Patients in whom acrylic prostheses or large metallic appliances were employed showed persistent eosinopenia lasting as long as five or six weeks.

10. Patients with deformities of congenital origin or with deformities due to poliomyelitis who were admitted for elective surgery showed normal eosinophil levels. Patients with cerebral palsy or neoplasms of the bones or joints showed eosinopenia upon hospital admission.

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