

INVESTIGATIONS INTO THE BALANCE OF CALCIUM, PHOSPHORUS AND NITROGEN IN CONNECTION WITH SURGICAL OPERATIONS ON THE SKELETON¹

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Modern clinical researches into the metabolism require access to special wards in which it is possible to follow in detail and to register the supply and evacuation and, as far as possible, the metabolism of the substances it is intended to study. Central metabolism wards of this kind exist in the big American hospitals, being generally responsible to the endocrinological clinics, to which all the departments of the hospital have access for special investigations.

Thanks to the courtesy of the King Gustav V Eightieth Jubilee Fund it became possible for us to set up in the Orthopedic Clinic of the Caroline Institute an experimental department for researches in metabolism.

There have been placed at our disposal one bed, a special kitchen for preparing dietetic food and a laboratory for the analysis of blood, urine and faeces. The laboratory is equipped for carrying out analysis of nitrogen, phosphorus and calcium. The Caroline Institute has provided us with the services of a laboratory assistant who has had special training in the technique of chemical analysis.

The work in a metabolic department differs in many respects from any other clinical and experimental work. The intention is to study the relationship between the supply and evacuation of certain substances by investigating the metabolism; and so the main idea is to be able as exactly as possible to regulate and determine both the supply and the evacuation of those substances.

It is essential to have a *controlled* supply of food. A diet must be

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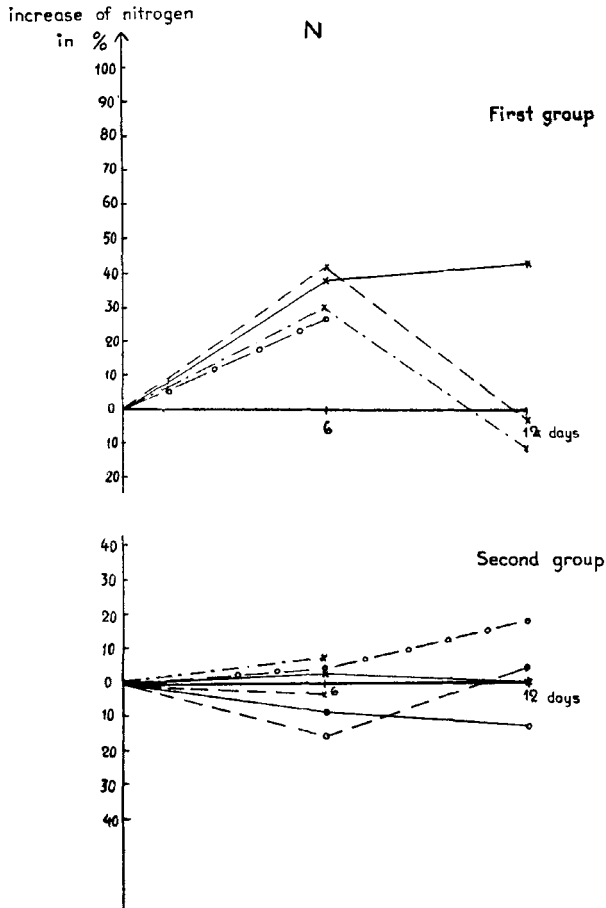


Fig. 1

shows that in the four cases in which a major operation was performed on soft tissues and skeleton, during the first week after the operation a rise of, on an average, 35 % in the secretion of nitrogen was recorded. In the second group, without any operation on the skeleton or with only minor operative action the secretion of nitrogen remained practically unchanged in spite of the fact that the supply in both series was kept the whole time at the same level.

chosen which is suitable for the experiments to be conducted. If, for instance, it is desired to examine the effect on the nitrogen metabolism of a certain action, the supply of nitrogen should be large enough to enable the organism to reach a positive nitrogen balance. If it is intended to investigate the break-down of, for instance, skeletal tissue in the organism, one should prescribe a diet that is poor in calcium. If it is intended to study the calcium metabolism it is preferable to prescribe a diet poor in calcium with the addition of, say, calcium

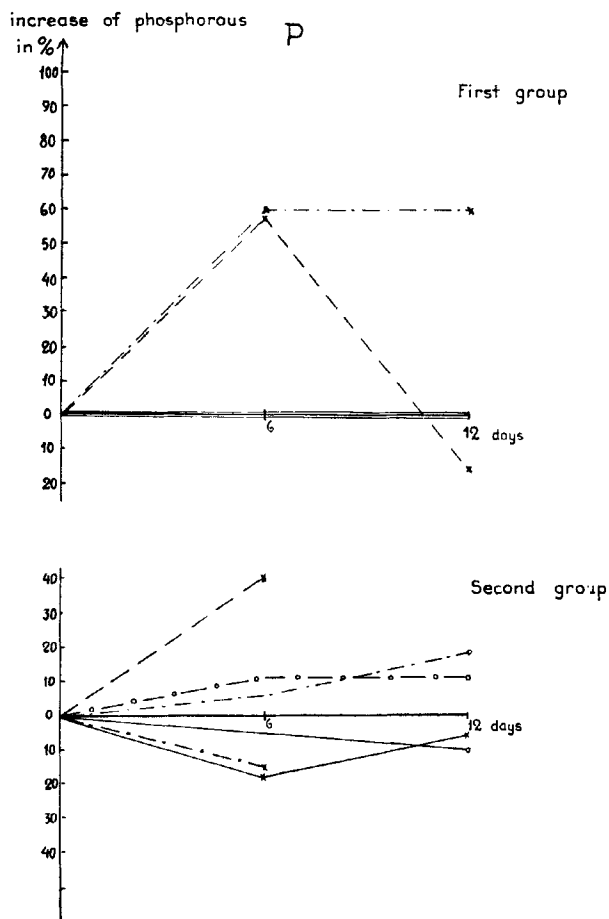


Fig. 2

shows the conditions arising in the case of phosphorus secretion. Here, the situation is in principle the same as for nitrogen, although the differences are not as distinctly marked.

chloride rather than to administer a diet rich in calcium. The basic acid content in the ash of the food must also be kept at a certain level; this is achieved by administering to the patient acid or basic salts.

The duration of the period of investigation is of immense practical and organizational importance. Following the principles practised in corresponding departments at American hospitals, we have employed six-day periods. That is to say, we examine and estimate the supply and evacuation of actual substances for a period of six days. Each investigation comprises at least two such six-day periods. Not until after the lapse of two periods are changes effected in the experimental

conditions, and the effect of each change is followed afresh in the course of two six-day periods.

The composition of the diet may be determined by calculating the

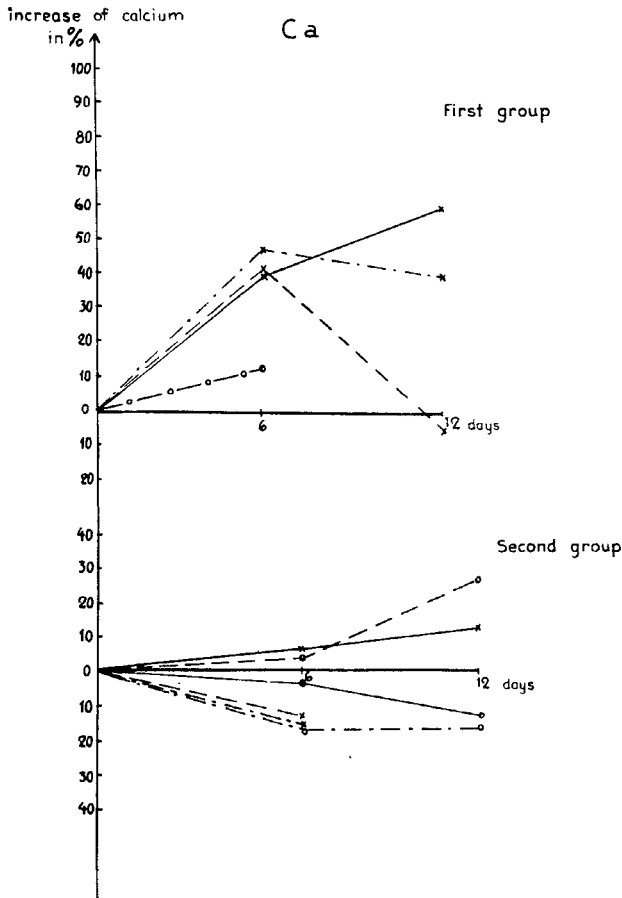


Fig. 3

demonstrates variations in the calcium secretion. A distinct difference is seen between the two groups, with a marked preponderance in that in which the skeleton has been seriously attacked.

composition of the food from standard tables for ascertaining the content of the most important components of the different food substances. Obviously, a calculation of this kind can never be really exact. The composition of the food varies a good deal at different

seasons of the year, so that the difference between the calculated and the true composition may fluctuate considerably. The composition of the diet may also be determined by analysis. We have preferred this method, particularly as during the first stage of our planned investigation we followed the metabolism of only a few substances, viz. nitrogen, phosphorus and calcium. The food analyses have been carried out by the State Institute of Public Health.

The determination of evacuation must be based on the most minute accuracy in the collection of urine and faeces. The quantity of urine in each 24 hours from 6 a.m. in the morning of one day to 6 a.m. on the next day is kept in a special vessel in a refrigerator. The samples of faeces for each 6-day period are kept during the collection time under concentrated hydrochloric acid in the cold-storage room. Each period is marked off with 0.6 gramme of carmine, which the experimentee has to take *per os* at 6 p.m. on the last day of the period. The first carmine-stained evacuation on the next day is included in and terminates the period.

We shall not dwell at length here upon the analytical methods we have employed for determining the nitrogen, calcium and phosphorus in urine and faeces. For the reliability of the technique which we have gradually developed we have to thank Dr. Greta Hammarsten, who at the outset of our laboratory work gave us advice and directives, and who also checked the reliability of the analyses.

We made it our task to ascertain whether operative action on the skeleton and soft tissues influenced the metabolism of the balance of nitrogen, phosphorus and calcium. For this purpose we examined the metabolism of the substances in question before an operation and in the first two weeks after operative action. What we first of all desired to know was whether an orthopedic intervention would at all disturb the metabolism and, further, whether it made any appreciable difference if action were taken on soft tissues alone or on the actual bone-tissue as well. The cases which we present here are our first series of four major operations performed on soft tissues and the skeleton, i.e. an arthroplastic operation on the femoral head according to Judet and three lumbar osteosyntheses, and, further, five cases, of which three are purely soft-tissue operations: one a lumbar retroperitoneal sympathectomy, one a denervation according to Tavernier, and one a medial semilunar cartilage removal, the remaining two are minor operations on bone: an arthrodesis on the thumb and an intercorpal fusion.

DISCUSSION

It may be stated that operative action on the skeleton, in contrast to operative action on soft tissues, is accompanied in our material by a substantial loss of calcium, phosphorus and nitrogen during the period immediately after the operation. We may draw a further conclusion from the material and say that these losses are for the most part confined to the first week after the operation. The significance of these findings is in itself not particularly remarkable. It is a fact proved by many observers that in animal experiments especially different forms of stress induce a break-down of albumen in the body and that at the same time losses of calcium may also arise. It is possible to imitate the condition by treating persons with ACTH and cortisone. Investigations on these lines have been conducted at our laboratory in collaboration with the endocrinological department of the Serafimer Hospital and, generally, it may be said that the characteristic feature is an increased loss of calcium, phosphorus and nitrogen during the period in which the hormones are administered and a return to the initial position at the end of the treatment. What is noteworthy in the cases related here, however, is that operative action on the skeleton differs so strikingly from the values we have obtained after purely soft-tissue operations, in spite of the fact that in several of the cases the size of the soft parts operated on has actually been greater in the aforesaid soft-part group than in the bone group. The reason for this observation is still unknown.

It has merely been our intention to present some preliminary data, being fully aware that a quantity of factors which we are not yet prepared to discuss may conceivably influence the appraisal of our results.

RESUME

Il convient de relever que les interventions chirurgicales qui portent sur les parties osseuses, au contraire de celles des tissus mous, sont accompagnées dans nos observations, d'une perte substantielle de calcium, de phosphore et de nitrogène durant la période qui suit immédiatement l'opération. Nous devons tirer une autre conclusion de ces observations, à savoir que ces pertes sont la plupart constatées dans la première semaine qui suit l'opération. La signification de ces trouvailles n'est pas en soi particulièrement remarquable. Il est un fait, prouvé par beaucoup d'observations, que dans l'expérimentation animale différentes formes d'efforts provoquent une diminution de l'albumine dans le corps et que, simultanément, la perte de calcium

peut aussi s'accroître. Il est possible de retrouver ces faits en traitant les individus par l'ACTH et la cortisone. Des recherches dans ce sens ont été faites par notre laboratoire en collaboration avec le Service endocrinien de l'Hôpital Serafim et on peut dire, d'une manière générale, que le trait caractéristique est la perte accrue de calcium, de phosphore et de nitrogène durant la période pendant laquelle les hormones sont administrées et un retour à la position initiale à la fin du traitement. Ce qu'il convient de noter dans les cas mentionnés ici, c'est que l'action opératoire sur les parties osseuses diffère aussi sensiblement des données que nous avons obtenues après des opérations dans les tissus mous, bien que dans plusieurs de ces cas la dimension des parties molles opérées ait été plus grande pour le groupe de ces malades que pour ceux opérés dans les parties osseuses. La raison de cette constatation reste inconnue jusqu'à présent.

Nous avons plutôt eu l'intention de présenter quelques données préliminaires, car nous comprenons parfaitement qu'une quantité de facteurs, que nous ne sommes pas encore prêts à discuter, peuvent présenter de l'importance pour l'appréciation de nos résultats.

DISKUSSION

Wir können feststellen, dass operative Eingriffe am knöchernen Skelett, im Gegensatz zu solchen an den Weichteilen, in unserem Materiale von einem wesentlichen Verlust von Calcium, Phosphor und Stickstoff während dem der Operation unmittelbar folgenden Zeitraume begleitet sind. Wir können auf Grund unseres Materiales weiterhin die Schlussfolgerung ziehen, dass diese Verluste sich meistens auf den Zeitraum der ersten Woche nach der Operation begrenzen. Die Bedeutung dieser Befunde ist an und für sich nicht besonders bemerkenswert. Es ist eine Tatsache, die von vielen Beobachtern erhärtet worden ist, dass in Tierexperimenten verschiedene Formen der Überbeanspruchung eine Aufspaltung von Eiweiss im Körper hervorrufen und dass zugleich auch Calciumverluste auftreten können. Es gelingt diesen Zustand nachzuahmen, wenn man Personen mit ACTH oder Cortison behandelt. Untersuchungen in dieser Richtung wurden an unserem Laboratorium unter Zusammenarbeit mit der innersekretorischen Abteilung des Serafimer Krankenhauses durchgeführt. Man kann im Allgemeinen sagen, dass die charakteristische Erscheinung eine Zunahme des Calcium-, Phosphor- und Stickstoffverlustes während des Zeitraumes, in welchem die Hormone verabreicht werden, ist und dass weiterhin ein Zurückkehren zu dem ursprünglichen Verhalten nach Beendigung der Behandlung eintritt.

Bemerkenswert in unseren Fällen ist jedoch, dass die Werte, die wir nach Eingriffen am knöchernen Skelett erhalten haben, sich so auffallend von denen nach Eingriffen an den Weichteilen unterscheiden, und dies trotz der Tatsache, dass in einigen Fällen der Eingriff an den Weichteilen in der oben erwähnten „Weichteilgruppe“ grösser war als in der Gruppe mit Eingriffen am Knochensystem. Die Ursache für diese Beobachtung ist zur Zeit unbekannt.

Unsere Absicht ist nur einige vorläufige Daten vorzuweisen. Wir sind uns jedoch des Umstandes voll bewusst, dass eine Anzahl von Faktoren, die wir vorläufig noch nicht in der Lage sind zu diskutieren, die Wertung unserer Ergebnisse beeinflussen können.