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EARLY RECOGNITION OF HETEROTOPIC CALCIFICATIONS BY MEANS OF ALKALINE PHOSPHATASE.

By E. NECHWATAL, M.D.

Rehabilitationszentrum der Allgemeinen Unfallversicherungsanstalt Tobelbad bei Graz, Austria.

INTRODUCTION

THIS paper deals with the avoidance of heterotopic calcifications in traumatogen paraplegia. On the one hand it is necessary to provide the periarticular and paraosseus calcifications by means of the alkaline phosphatase (ap) and on the other hand to determine the impaired metabolism of calcium and phosphorus in the early phase of paraplegia and to interpret its causes in order to derive an appropriate therapy.

METHODS AND RESULTS

At the Rehabilitationcenter Tobelbad the following metabolic investigations have been made:

1. Alkaline Phosphatase (ap).
2. The level of calcium and phosphorus in serum.
3. Renal function by examining urea and creatinine in the serum.
4. In the early phase it is very important to recognize a metabolic acidosis, which nearly always has a nephrogenic cause.

In 169 patients with spinal cord injury the urea and creatinine of the serum was checked 508 times from May 1971 until May 1972. At the same time, the serum-ap was investigated 533 times. The ap level was of particular interest, because the investigators had already noticed its increase before any signs of manifest heterotopic calcifications could be seen on X-ray. In 121 patients studied from October 1971 until May 1972 the level of inorganic phosphorus in serum was controlled 269 times while determining the usual electrolytic values at an interval of 1-4 weeks. Twenty patients of this group were non-paraplegics, and 101 mostly recently injured patients had a spinal cord injury. Fifty per cent. of the paraplegics admitted with 2 weeks of injury had a transitional renal insufficiency; probably a sign of renal shock. The following were the highest values measured 11 days after injury and laminectomy.

356 mg. per cent. of urea in serum.
10 mg. per cent. of creatinine in serum.

Apart from this there was a severe, non-compensated acidosis as a sequence of renal insufficiency (fig. 1). In six of seven paraplegics, admitted within one week after injury, urea was initially more than 50 mg. per cent and creatinine increased more than 1·1 mg. per cent. This transitional elevation of urea and creatinine in serum was only demonstrable up to four weeks after injury. Nevertheless, the

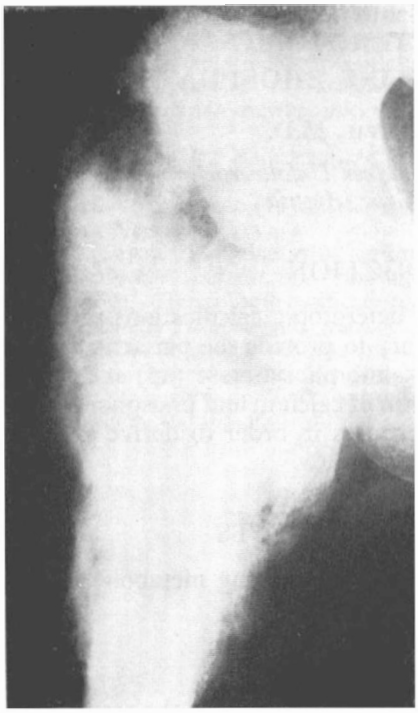
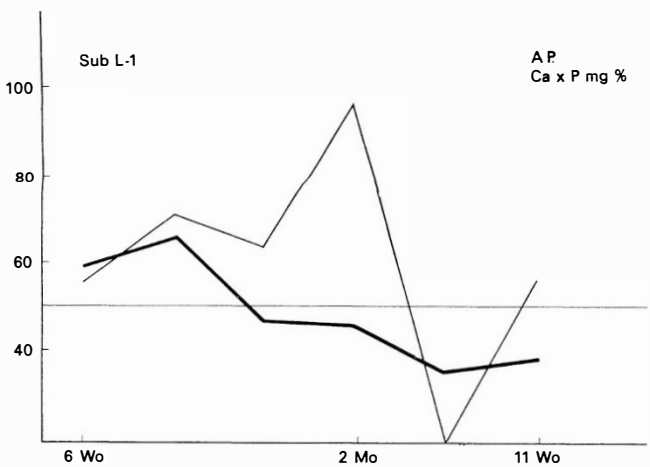


FIG. 1

Right hip-joint of a 40-year-old paraplegic male below T6 one year after injury and one year after severe renal insufficiency and acidosis. Clinical ankylosis of the hip and flexion contracture of 35 degrees.

FIG. 2

32-year-old paraplegic male below L1.Ap is insignificantly increased 7 weeks after the accident. After 6 weeks urea and creatinine have returned to normal, but the Ca-P-productisdistinctly increased. These values are even more elevated 12 hours after a nutritional load-testwith phosphates (blood samples were taken before breakfast). Latent hyperphosphataemia, probably a sensitive symptom of the already non-manifest renal in sufficiency.



determination of urea and creatinine represents a rather inaccurate test of renal function. Whereas the demonstration of hyperphosphataemia enables even the recognition of latent disturbances of renal function (fig. 2). Furthermore there consists a parallel between the seriousness of nephrogenic metabolic acidosis on admission of the injured and the heterotopic calcifications which appear later on.

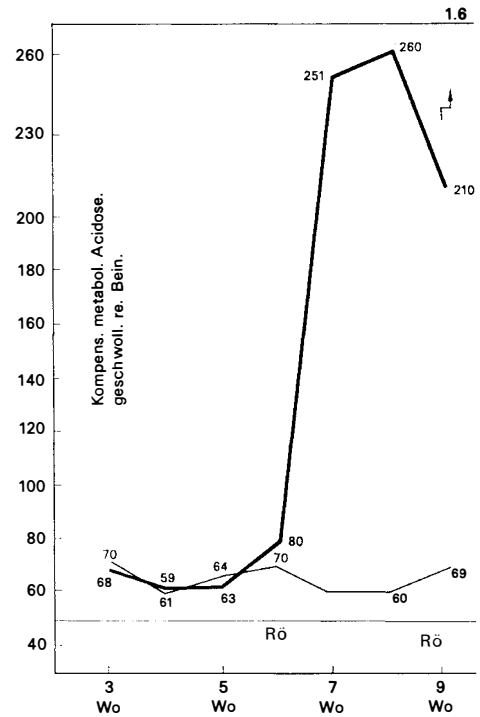


FIG. 3

33-year-old paraplegic female sub T6. On admission at the rehabilitation centre 3 weeks after injury, distinct signs of renal insufficiency with a compensated metabolic acidosis and with a 'critical' rise of the Ca-P-product could be seen. This was followed by periarticular ossifications of both hip- and knee-joints and a significant increase of ap in the 6th week after the accident.

In the time between October 1971 and May 1972 it was regularly found in enlarged examinations of electrolytes that the injured—having elevated values of urea and creatinine in their early phase—showed an increased phosphorus level too. From physiological aspects the product of calcium and inorganic phosphorus, calculated in mg. per cent., shall not exeed 35. In non-treated patients of the early stage values of between 60 and 90 were obtained, whereas such high values are already termed as 'critical' levels in chronic renal insufficiency (fig. 3). This rise of the product of calcium and phosphorus is caused by a significant elevation of inorganic phosphorus in the serum of 6-20 mg. per cent, while calcium is slightly

decreased, around 4·0-4·4 mval. In tests on healthy persons or in paraplegics in the late phase who had no renal impairment, there was never seen to be an elevation of the calcium-phosphorus-product of over 40. In paraplegics, however, an increase of creatinine can be seen related to a rise of phosphorus in serum.

From the 5th week after injury urea and creatinine in serum reached its normal levels in almost every case, while in non-treated patients the phosphorus remained elevated up to 11 mg. per cent. for weeks and months; this corresponds to a product of phosphorus of 90. It is noteworthy that phosphorus is also increased, when the

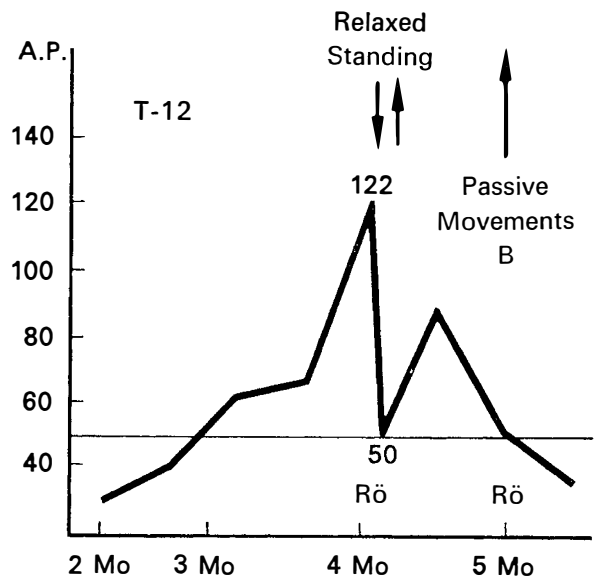


FIG. 4

25-year-old paraplegic male sub T12. Steep increase of ap during the phase of mobilisation in the 4th week after injury. Ap reaches its normal level after omission of passive mobilisation training, walking and standing: nevertheless, in the following 2 weeks we have noticed another increase up to 90 i.u., while standing training was continued.

ap gets to its critical raise. The azotaemia with both the metabolic acidosis and the hyperphosphataemia seems to be the forerunner for the heterotopic calcifications.

The alkaline phosphatase—the ap often accompanied with fever and swollen legs—is connected with an increased product of calcium and phosphorus. From the 4th week until the 4th month after injury it can increase immensely and come up to values of 280 m.U. resembling an increase of 5-6 times the normal value; usually assumed with 48 m.U. Attaining its highest level the limitation of a moderate degree can be stated in the involved joints. Finally the lasting contractures are completely developed only some weeks or months later, mainly during the decrease of the ap.

Subsequent controls of the ap serve as an early recognition of primary pathological calcifications in periarticular or paraosseus soft tissues. The ap in serum

being a measure for the activity of osteoblasts becomes, therefore, a parameter in paraplegic adults for the beginning of the calcification process. This symptom appears already 1-2 weeks before the calcification can be revealed by X-ray.

Excluding other osteoblastic or cholestatic processes, a steep increase of ap until the end of the 4th month proves the beginning of a pathological calcification in our patients. By experience the investigators know that a periarticular process of calcification is further more supported by a forced, non-regulated passive

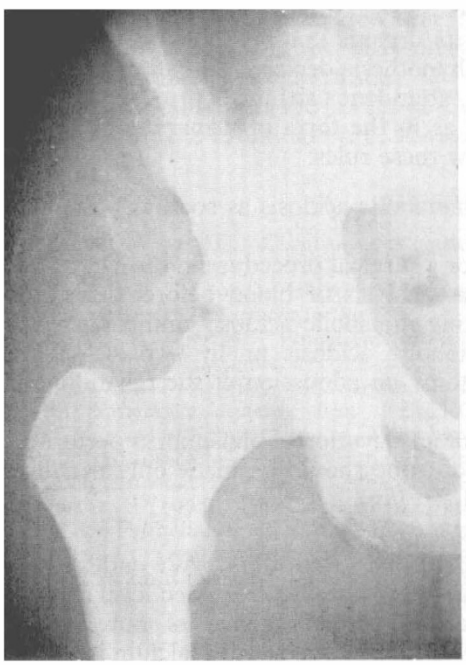


FIG. 5

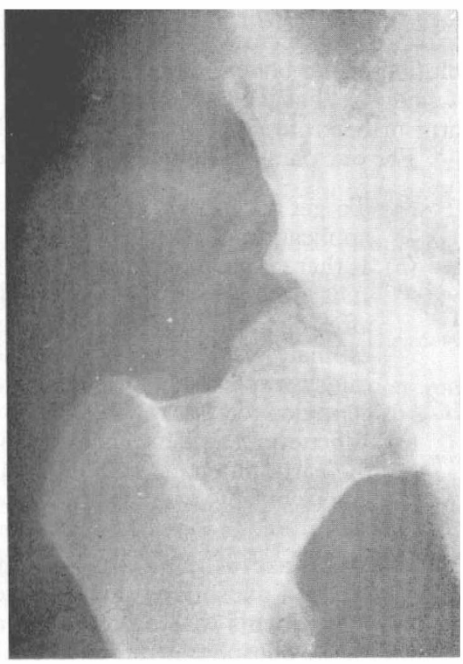


FIG. 6

Figs. 5 and 6.—Small traces of calcifications in peri-articular soft tissue of the right hip of the patient on Fig. 4. X-ray examination was made 4 and 5 months after injury. As neither clinical nor radiological signs of a deterioration of the condition had occurred and the ap attained its normal value, the passive mobilisation of the joints in the paralysed part of the body and walking training was resumed 5 months after injury.

mobilisation of the joints of the paralysed extremities. As a consequence the ap increases concomitant with fever. Resting physical reconvalescent treatment and avoiding passive mobilisation of the paralysed joints of the extremities the ap is definitely going to drop. This means at least a delay of the calcification respectively of the ossification process, which otherwise would continue to progress. The normal activity of osteoblasts and an ap of 50 or below indicates the stagnation or cessation of the process. Observing not any critical rise of ap in our patients during the first 3 weeks after injury we concluded that a paraplegic has to be controlled very closely between the 4th week and the end of the 4th month after injury (figs 4, 5, 6).

THERAPEUTIC CONSEQUENCES

The following chapter deals with the therapeutic consequences, resulting from an impaired metabolism like acidosis, renal insufficiency elevation of the calcium-phosphorus-product and increased ap. The treatment of renal shock is well known and shall not be discussed here, but it seems to be important to mention the acidosis, because there is a correlation between metabolic acidosis and calcium metabolism. In body fluids solubility of calcium is better in both acidified urine and in a low pH of the blood.

Some time ago Rossier (1964) drew attention to the fact that an acidified organism answers with osteoporosis; therefore the author wanted to point out the extraction of calcium in acidosis out of its organic compounds and a total dissolution of the bone mineral. Thus our hypothesis declares that after subsidence of acidosis, that is in the phase of repair, abundant calcium had to precipitate in form of heterotopic calcifications as well as in the form of urinary concrements.

For our paraplegics one should follow these rules:

(*a*) To get rid of the shock-caused metabolic acidosis as soon as possible by application of basic valencies.
(*b*) If there is an abolute indication for a surgical procedure in the early phase, it is necessary to control the gas analysis of blood before, during and after operation and to start treating metabolic acidosis immediately. We estimate the diagnosis of a metabolic acidosis finally two weeks after injury respectively after laminectomy on admission at the rehabilitation-centre as too late.
(*c*) Whenever a tendency of acidosis or an elevation of phosphorus performs in the early phase, an acidification of urine should be made only per instillation, but by avoiding the blood stream.

The Increase of the Calcium-phosphorus Products. We endeavour to lower the level of phosphorus and to increase the somethat decreased level of serum calcium. In patients with a product of calcium and phosphorus of more than 50, we omit highly phosphorated food like milk and eggs and supply calcium in form of effervescent powder. If the calcium-phosphorus product exceed 70, we additionally give aluminiumhydroxyde per os to stop the intestinal absorption of phosphorus.

The Elevation of ap. As already mentioned before, the critical time of the steep increase starts at the 4th week and lasts until 4 months after injury. During this time the ap should be examined at weekly intervals in order not to miss any elevation. Under these conditions we cancel the passive mobilising of the joints of the paralysed extremities completely from the therapy schedule. Even the walking training is omitted when the increase of ap occurs at the phase of mobilisation.

On the contrary we do allow sitting in the wheel chair and the training for the activities of daily life; the time course is dependent on the further rise of ap. Considering the level of ap or by revealing X-ray, it has to be decided individually, if the training of standing can be continued or not.

An increased ap during the so-called turning bed period of the patient implies that the joints of the paralysed extremities do not receive any passive movement-treatment too.

Particular attention is paid to the position of the legs, termed as 'relaxation positions'. According to a value of ap of 50 or below we allow walking exercises, passive mobilisation and physical strains. Even carefully performed mobilisation of the paralysed part of the body or the continuation of walking training cause activation of the process, and it would last months or years until it would stop as seen in X-rays or by estimation of ap-level. These results may strongly show that the mentioned prophylaxis has to start early enough.

SUMMARY

Our findings support the view that there is probably a correlation between the transitional renal shock in the early phase of paraplegia and the heterotopic periarticular or paraosseus calcifications.

For the evaluation, the levels of Ca, P and creatinine in serum have been combined with the examination of X-rays.

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