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HYPOPHOSPHATASIA

Alkaline phosphatase is a widely occurring tissue enzyme; its basic action appears to be the hydrolysis of organic phosphate-containing compounds with liberation of inorganic phosphorus. It is abundantly present in bone, but its exact function there remains disputed. The traditional concept that phosphatase precipitates calcium and phosphorus as calcium phosphate solely by the generation of a high local phosphate concentration, appears to have little foundation. The enzyme more probably affects osteoid directly, making it in some cases very more receptive to the seeding of calcium and phosphorus in normal concentrations.

A widespread deficiency of this enzyme—hypophosphatasia—occurs as a very rare genetically determined disorder. Fraser[1] has proposed 3 clinical groups based on age of presentation. All have 1 feature in common—a gross anomaly of skeletal calcification, most profound in the neonatal period, where the process may be so severe that an almost total absence of cranial membranous calcification may occur. In this group and in later childhood, rickets is closely simulated. Generalized undermineralization, soft deformed bones, fractures and pseudofractures, and radiological widening of the epiphyseal end of long bones with a frayed diaphyseal cup are usual. A coarse pattern is highly characteristic when present. In adulthood, the skeletal features mimic osteomalacia exactly, and spontaneous bone pain is prominent.

Clinical grouping has been defined for prognostic purposes—for not only is the severity of the bony disorder positively related to an early age of onset, but in the neonate a profound metabolic upset occurs. Hypercalcaemia and neurologic sequelae are common, while gastrointestinal and pulmonary complications are frequent causes of death. After six months of age prognosis improves and systemic disturbance is minimal. A unique feature is premature exfoliation of the anterior deciduous teeth, which may on occasion be the sole clinical manifestation of the disorder.[2] Less than a dozen case reports testify to the rarity of the disease in adulthood where the chief interest lies in the possible confusion with osteomalacia for reasons mentioned earlier.

In all age groups the presence of both a low blood and tissue alkaline phosphatase activity, and phosphoethanolamine[3] in the urine is the rule, although on isolated occasions either feature may be absent. The genetic transmission appears to follow a Mendelian recessive pattern,[4] though dominance has been reported in a single family.[5]

The bone pathology is very specific. There is loss of the very orderly cellular arrangement of hypertrophic cartilage with tongues of degenerating calcified cartilage and excessive accumulation of uncalcified osteoid in the metaphysis and subperiostial regions. There appears to be a gross reduction in the number of osteons, but those present remodel bone at a normal rate.[6] Electron microscopy shows an abnormality of the structure of osteoid collagen consisting of the presence of a very fine network of atypical interlacing fibrils without the characteristic banding.[6] In view of what has been mentioned earlier about the possible effects of alkaline phosphatase on osteoid tissue, the finding of a qualitatively abnormal osteoid in hypophosphatasia is of some interest.

The significance of phosphoethanolamine excretion in this disorder is likewise baffling. This amine is a degradation product of the phospholipid, phosphatidyl enthanolamine. Phospholipids are present along zones of active calcification and are probably important in this process[7,8] in relation to the formation of active osteoid. The potential link between phospholipids and calcification on the one hand, and phosphoethanolamine excretion in a disorder of calcification on the other, is fascinating and awaits urgent investigation.

In common with other inborn errors of metabolism, hypophosphatasia emphasizes a potential importance of rare diseases, where the study of the specific derangements of intermediary substances has greatly clarified the understanding of metabolic processes. The investigation of this puzzling condition may yet shed considerable light on the physiology of calcification.

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VAGINALE MONILIASE NA BEHANDELING MET TETRASIKLIEN

Vaginale pruritus is een van die lastigste, hoewel minder ernstige kwale, wat die ginekoloog en die algemene praktisyn se vindingrykheid van tyd tot tyd terg. Dit is dan ook opvallend hoe dikwels hierdie klagte volg op die behandeling van die pasiënt met tetrasiklien vir 'n onverwante siekte, bv. brongitis, sistitis en na 'n operasie. Die diagnose van vaginale moniliase is gewoonlik voor die hand liggend en maklik te onderskei van ander oorsake van jeukerigheid, soos servisitis met afskeiding en besmetting deur *Trichomonas vaginalis*.

Die vraag wat dan by die geneesheer opkom, indien dit nie reeds die pasiënt ook opgeval het nie, is of daar 'n werklike verband tussen die moniliase en die tetrasiklien is en of 'n ander antibiotikum verkieslik moes gegee gewees het. Ook word daar bespiegel oor die wenslikheid om 'n teenmiddel teen moniliase gelyktydig met die tetrasiklien toe te dien, en dan moet daar onthou word dat sommige universitêre leermeesters teen 'n dergelike gebruik gekant is. In die lig van genoemde oorweginge is 'n interessante proefneming nou uitgevoer.[1]

Tetrasiklienfosfaat in gelyke hoeveelhede is aan twee groepe (nie-swanger) vroue gegee in 'n dubbele gekontrolleerde toets. Die een preparaat het bestaan slegs uit 250 mg. tetrasiklien terwyl die ander kapsule dieselfde tetrasiklien bevat het plus 50 mg. amfoterisien B ('n swamdoder). Vier kapsules van elk is daagliks vir tydperke tot 3 weke toegedien. Vaginale ondersoeke en smere vir die kweking van organismes is voor die toets en

weekliks na die aanvang daarvan geneem.

Die voorkoms van *Candida albicans* in die vaginas van die vroue wat nie-aangevulde tetrasiklien ontvang het nie, was 12% voor behandeling en 28% daarna. By die ander groep het die voorkoms van *C. albicans* gedaal vanaf 13% voor behandeling tot 9% daarna. Die kliniese simptome van vulvovaginitis is ooreenstemmend by 9 en 1 pasiënt bespeur. Ander newe-gevolge van tetrasiklien-toediening (mislikheid, braking, epigastriese ongerief, ens.) het min of meer by gelyke getalle voorgekom.

Die gevolgtrekking wat uit hierdie toets gemaak kan word is dat die byvoeging van amfoterasien B by tetrasiklien 'n doeltreffende middel is teen die sekondêre infeksie deur *C. albicans*. Dit is jammer dat die waarnemers nie ook verslag gedoen het oor die moontlike voorkomende uitwerking van amfoterisien B in die ander swamoorgroeisels wat op die toediening van tetrasiklien kan volg nie, tw. in die mond en keel, die slukderm, die grootderm en anus, ens.

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DIE BEHANDELING VAN STUIPE BY BABAS

Stuipe kom algemeen by babas voor as gevolg van 'n groot verskeidenheid van oorsake, sommige ernstig, maar in die meeste gevalle onbenullig op sigself. Nietemin is daar min simptome wat 'n moeder by haar kind waarneem wat haar meer ontstel. Afgesien van emosionele oorwegings is dit die dokter se taak om die skadelike gevolge van herhaalde of uitgerekte gevalle van trekkings en bewusteloosheid te vermy. Watter stappe hy in hierdie verband doen, hang grootliks van die oorsaak van die stuipe af.

Kloraalhidraat behoort die eerste middel te wees om te probeer by pasgeborenes of baie jong babas, ongeag die feit òf die stuipe aan 'n besering, stimulasie van die sentrale senustelsel òf 'n idiopatiese oorsaak te wyte is.[1] Hierdie middel is vinnig en doeltreffend en hou geen nadelige gevolge in nie. Omdat daar in hierdie gevalle 'n onderdrukking van die asemhalingsentrum is, is dit beter om nie voorkeur aan fenobarbitoon te gee nie, dog dit word wel aangedui in die uitsonderlike gevalle waar kloraalhidraat nie die stuipe ten volle beheer nie. Stuipe wat herhaaldelik voorkom ten spyte van voldoende antikonwulsiewe behandeling sal moontlik reageer op 'n binnespierse toediening van 2 mg. piridoksien.

In gevalle van piëlonefritis, otitis, meningitis en dergelike ontstekings is dit beter om kalmeermiddels agterweë te hou totdat antibiotiese en pynverdowende middels, soos aspirien, die kans gekry het om hul uitwerking te toon. In die geval van stuipe as gevolg van 'n hoë koors is dit ook beter om nie kalmeermiddels te gee nie. Sulke gevalle reageer gewoonlik goed as die pasiëntjie met lou water afgespons word en as hy met klam lappe bedek word.

1. Craig, W. S. en MacKinnon, J. M. (1965): Brit. Med. J., **1**, 499.