changes in this case have been progressive. On these grounds I think we should accept them as being of independent origin.

The low value for serum calcium is probably to be regarded as a normal finding in uraemia: it will be remembered that tetany due to hypocalcaemia is one of the causes of convulsive phenomena in this condition. Hence there is no real justification for postulating endocrine disorder (e.g., parathyroid deficiency) to explain the calcium deposit in the intervertebral disks.

Summary

A case is described of generalized calcification of the intervertebral disks.

This condition is diagnosed as the final phase of Schmorl's "spondylosis deformans"—itself considered to be a true osteoarthritis of the spine.

An attempt is made to evaluate other factors in a complex clinico-pathological picture.

I wish to thank Dr. J. H. Mather for the radiological reports, and Prof. T. P. McMurray and Mr. W. A. Thompson for a most valuable discussion of the case, publication of which is made possible by kind permission of the Director-General of Medical Services, Ministry of Pensions.

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SUBLINGUAL ADMINISTRATION OF METHYL TESTOSTERONE

BY

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The discovery of a preparation of testosterone that has a high degree of activity when given by mouth constitutes an advance in the treatment of those conditions for which male sex hormone therapy is indicated. Testosterone and testosterone propionate have little activity when given orally, and recourse therefore has been had to frequent intramuscular injections, periodic implantation of pellets, or the laborious daily inunction of these substances. Miescher and Tschopp (1938) first demonstrated that in castrated rats the oral administration of methyl testosterone was far more effective than that of free testosterone. Subsequent clinical observers have found that methyl testosterone by mouth produces all the effects of the injected propionate, and that to obtain equivalent results the dose required is from three to six times the dose of testosterone propionate given intramuscularly.

Sublingual therapy was first successfully applied by Anderson, Haymaker, and Henderson (1940) with desoxycorticosterone acetate in Addison's disease. The following case report shows that the effectiveness of methyl testosterone administered sublingually to a castrate is equal to, or even slightly greater than, its effectiveness when it is absorbed from the intestinal tract.

Case Report

The patient was a man aged 23 who had been castrated in childhood because of tuberculosis in both testes. His full history and previous treatment have already been reported (Spence, 1940, Case 1). During the last 2 years, except for a control period of 4 months, during which, unknown to him, he was receiving non-medicated tablets, he has been treated with methyl testosterone by mouth. At first he was given 50 mg. a day in 5 divided doses. This dose proved to be too high, and was subsequently reduced to 5 mg. thrice daily. On this dose

normal potency was maintained. After about 4 months' treatment with methyl testosterone he married, and intercourse proved to be satisfactory. During the first 2 months of the control period, when he was receiving no active substance, intercourse was occasionally possible, but the number of his erections greatly diminished. During the second half of this period he was impotent. A dose of 10 mg. a day was not quite enough to maintain normal potency.

It was established, therefore, that the minimum swallowed dose of methyl testosterone necessary was 15 mg. a day. He was then given 5-mg. tablets of methyl testosterone (perandren linguets, Ciba Ltd.) to suck under his tongue three times a day, with instructions to avoid swallowing his saliva in order to ensure maximum sublingual absorption. The tablets disappear in 5 to 10 minutes, and are not unpleasant to taste. With this daily dose of 15 mg. sublingually, erections increased in number from "not more than 4 a week" to 6 or 7 a week, and were rather stronger than when this dose of the hormone was swallowed. A sublingual dose of 10 mg. a day produced about the same effect as 15 mg. swallowed, and therefore constitutes his maintenance dose; 30 mg. daily caused "about twice as many erections" as 10 mg. daily.

Commentary

It should not be concluded that the maintenance dose in this patient is the same for all castrates. The dose varies in different patients, and is to be found by trial and error. Variations between 10 and 50 mg. a day are reported, but the majority of patients require a daily dose of 15 to 30 mg. when the substance is swallowed. In the treatment of eunuchism and eunuchoidism the doses of androgenic hormone during the first few months should be high—a total weekly dose of 150 to 200 mg. testosterone propionate intramuscularly—in order to bring about fairly rapid development of the secondary sexual characteristics. During this stage of treatment it would be inexpedient to rely on sublingual therapy alone, since the dose required is about 4 times the dose of the injected propionate. The most satisfactory method is to make use of intramuscular injections of the propionate or the implantation of pellets during the preliminary stages of treatment, and to reserve sublingual therapy for maintenance. In most cases the maintenance dose of methyl testosterone sublingually will probably vary from 10 to 20 mg. a day.

To explain the greater potency of methyl testosterone compared with other androgens absorbed from the intestinal tract two hypotheses have been advanced: (1) Miescher and Tschopp (1938) suggested that by virtue of the methyl group there is less destruction of methyl testosterone by intestinal ferments; (2) Biskind and Mark (1939) have shown that destruction by intestinal ferments is unlikely, and have suggested that, as androgens are probably destroyed by the liver, methyl testosterone escapes this immediate fate after absorption possibly through its being absorbed into the lymphatic rather than into the portal vessels. In the case reported sublingual administration of methyl testosterone appears to be slightly more effective than when the substance is absorbed from the intestinal tract. It is probable that when methyl testosterone is swallowed a certain proportion of it is absorbed into the portal system and destroyed in the liver before it can exert its specific effect, whereas this danger is avoided when it is administered sublingually and absorbed direct into the systemic circulation.

Summary

The case of a eunuch is reported in which it is shown that methyl testosterone is effective when administered sublingually. With two 5-mg. tablets a day normal potency was maintained, whereas when the substance was swallowed three 5-mg. tablets a day were required to produce the same effect.

As the sublingual dose of methyl testosterone is about 4 times the dose of testosterone propionate injected intramuscularly, and as large doses would thus be required in the early stages of the treatment of testicular deficiency, sublingual therapy should be reserved for maintenance.

I am indebted to Messrs. Ciba Ltd. for supplies of methyl testosterone (perandren linguets).

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