to that of cortical bone but differs in degree of activity.[3] The 2 scarred teeth were split in such a way as to isolate the part containing the grooves and estimations were made both on this and the remainder of the tooth. There was no difference between the P* contents of the scarred and the unscarred parts. Within the 12-day experimental period, there was evidently no increase of phosphate turnover or deposition in response to the stimulus of scarring.

Several attempts were made to find evidence of the presence of P* in the enamel. In no case was a count obtained which was more than 0.2 or 0.3 counts per minute above the background count. This difference is either insignificant, showing no P* to be present, or indicates that the enamel contained less than 0.001% of the original P* dose. The disagreement with the findings of Hevesy and Armstrong may be due to the larger doses used by these workers. In a private communication, Armstrong indicated that with similar sized doses of P* he had found questionable evidence of P* in cat enamel.

Summary. The uptake of radioactive phosphorus was greater in spongy than in dense diaphyseal bone when salts of the element were administered orally to a dog. In dentine the amounts of radioactive phosphorus were constant for the various teeth and of the same order as that present in dense diaphyseal bone. No more than traces of P* were found in the enamel.

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Influence of Androgen Therapy on Growth Rate of Hypogonadal Adolescent Boys.*

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The fact that the sex hormones play a rôle in the control of linear growth of the adolescent human has been previously suggested.[1] The exact relationship of the androgen-estrogen levels or the balance

3 Manly, R. S., Hodge, H. C., and Manly, M. L., *J. Biol. Chem.*, 1940, **134**, 293.

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1 Webster, B., *J. Pediatrics*, 1939, **14**, 684.

which exists between them, to the growth processes has not been understood. Experiments which suggest that the administration of androgens to the immature rat closes the epiphyses and retards growth have been reported.[2, 3] We were unable to confirm these findings in the immature rat and rabbit. McCullagh and McGurl[4] have reported epiphyseal closure in 2 cases of eunuchoidism treated with moderately large doses of androgens over a period of several months. On the other hand, Moricard and Bize[5] have reported an acceleration of statural growth in 3 adolescent hypogonadal boys treated with testosterone propionate at weekly intervals for 3 to 6 months. No control periods were reported. A calculation of the growth rate reported by these authors shows it to be 2.0 to 2.6 cm per hundred days. Villaret[6] reported a growth of 4 cm in a 21-year-old hypogonadal man during 6 months' treatment with large doses of testosterone propionate. The rate of growth here was 2.2 cm per hundred days. This patient had shown no increase in height since his eighteenth year when he had grown 9 cm "sous l'influence de l'opotherapie thymique qui fait descendre les testicles a l'anneau." Although these reports are apparently in conflict, numerous authors have expressed caution in administering androgen therapy for fear of closing the epiphyses and arresting growth.

Webster[7] reported a series of cases of hypogonadism in the adolescent male treated with testosterone propionate. No special mention of linear growth was made at that time, although weight-height observations were made on all the patients. Many of these patients had been under observation for several years before treatment was begun. All of them have been followed since that time. Following the publication of the above report, other cases of adolescent hypogonadism were treated by the same method. As treatment progressed considerable attention was given to the question of linear growth and epiphyseal closure, since it was feared that epiphyses might be closed and growth stopped by the sudden production of the sexual changes associated with puberty. After a survey of the results, however, it became apparent that a reverse effect was taking place. The growth rate was markedly increased during

[2] Rubinstein, H. S., Kurland, A. A., and Goodwin, M., *Endocrinology*, 1939, **25**, 724.

[3] Levie, L. L., *Acta brev. Neerland*, 1938, **8**, 53.

[4] McCullagh, E. P., and McGurl, F. J., *Endocrinology*, 1940, **26**, 377.

[5] Moricard, M. P., and Bize, P. R., *Société de Pediatrié*, 1937, **35**, 26.

[6] Villaret, M., Justin Besancon, L., and Rubens-Duval, A., *Compt. rend. Soc. de biol.*, 1938, **127**, 599.

[7] Webster, B., *J. Pediatrics*, 1938, **13**, 847.

periods of androgen therapy and X-rays of the knees, ankles, and wrists, taken at the beginning and end of therapy, showed no evidence of epiphyseal closure.

Each of the 8 cases presented in this report was considered to have definite hypogonadism. The effect of the therapy on this condition has been reported elsewhere.[7] They ranged in age between 13 and 18 years. All were in good health except for the evidences of hypogonadism. One case, No. 3, exhibited marked undernutrition during the control periods but gained .6 kg during the first 4 weeks of therapy. All of the remaining cases were in a healthy nutritional state. The measurements were taken under standard conditions with outer clothing removed. The dosage of testosterone propionate ranged between 75 and 125 mg per week. Each individual dose consisted of 25 mg.

The accompanying table shows the growth rate of 8 cases, ranging in age between 9 and 18 years, before, during, and after testosterone propionate therapy. In 2 instances a second period of treatment has been included.

The average growth rate of this group of hypogonadal adolescent boys before treatment with testosterone propionate was 1.36 cm per 100 days. During the administration of from 75 to 125 mg of testosterone propionate weekly, the average growth rate increased to 3.6 cm per 100 days. Following the cessation of treatment this rate

TABLE I.
Growth Rate of Hypogonadal Adolescent Boys During Treatment with Testosterone Propionate.
(cm/100 days)

Case	Age range, years	Total change in height, cm	Growth rate before treatment. cm	days	Growth rate during treatment. cm	days	Growth rate after treatment. cm	days	Growth rate during 2nd period of treatment. cm	days
1	14⅓-16	142-154	3.0	288	4.5	105	1.5	91	3.0	111
			1.0		4.3		1.6		2.7	
2	13½-16	160-176	2.8	150	8.2	250	5.0	340		
			1.9		3.3		1.5			
3	12¼-15	144-172	12.5	703	10.5	316	5.5	364		
			1.8		3.3		1.5			
4	9¾-15½	130-162	16.7	1339	9.7	381	5.6	408		
			1.2		2.5		1.4			
5	13¾-15½	152-170	0.3	33	2.4	66	6.8	275		
			1.0		3.6		2.3			
6	13-14	140-150			5.7	123	3.8	270		
					4.6		1.4			
7	11-14	145-161	10.8	802	4.2	196	1.0	77		
			1.3		2.1		1.3			
8	16½-18	164-176			5.8	120	6.0	391	1.2	56
					4.8		1.5		2.1	

again fell to 1.56 cm per 100 days. In 2 cases a second period of therapy again increased the average growth rate to 2.4 cm per 100 days. As was stated above, there was no evidence of hastening of epiphyseal closure as demonstrated by X-ray before and after the periods of administration of the testosterone propionate.

The evidence in favor of the possibility of the increased androgen or estrogen level of the body at puberty playing a rôle in epiphyseal closure and body growth has been steadily increasing during recent years. The exact nature of that rôle is as yet not clear. Contrary to expectations, the administration of androgens to a series of hypogonadal boys apparently stimulated longitudinal growth. This is compatible with Kenyon's and associates'[8] observation that there is a reduction in the urinary excretion of inorganic phosphorus, potassium and creatine, as well as protein retention, during androgen therapy. The stimulation of growth by the administration of thyroid substance has long been recognized.[1] The mechanism is thought to act through the thyrotropic factor of the anterior lobe of the pituitary. It would seem that a similar mechanism has been involved in the growth stimulation by androgen therapy and that a disturbance of the gonadotropic factor in some way reacts upon the growth factor. Whether or not this mechanism will work in the case of normal adolescents is not known since it is not considered advisable to administer androgens to normal individuals.

Summary. The administration of testosterone propionate in doses of 75 to 125 mg weekly to 8 hypogonadal adolescent boys ranging in age between 9 and 18 years was accompanied by an increase in average growth rate from 1.36 cm per 100 days during the control period to 3.6 cm per 100 days during the period of therapy. Following the cessation of treatment the average growth rate again fell to 1.56 cm per 100 days. This apparent stimulation of growth rate was unaccompanied by X-ray evidence of epiphyseal closure. The exact mechanism of this growth stimulation is not clear. Since all of these individuals exhibited evidence of hypogonadism, it must be pointed out that, on the basis of these observations, there is no justification for the use of testosterone propionate as a growth stimulant in normal adolescence since such therapy might result in permanent damage to the individual.

[8] Kenyon, A. T., Knowlton, K., Sandiford, I., Koch, F. C., and Lotwin, G., *Endocrinology*, 1940, **26**, 26.