

## *Effect of sexual maturity on the serum concentration of "hormonal" iodine in adolescence*

*Serum concentrations of protein precipitable iodine were determined both before and after elution from a Dowex-1 resin anion exchange column in 50 adolescent boys and 46 adolescent girls between the ages of 10 and 18 years. All subjects were well and in excellent nutritional status. Each subject received careful physical examination, during which sexual maturation was estimated, and each child was given a maturity rating of from 1 to 5. Attempted correlation of the peripheral concentration of hormonal iodine, done by two methods with individual maturity ratings, demonstrated a decrease in these values with increasing maturity in boys; the lowest iodine values were found during the period of the greatest rate of increase in sexual maturation.*

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ADVANCES in medical care for adolescents have paralleled efforts by investigators to relate physical findings and laboratory data to developmental age rather than to chronologic age. The changes in body composition occurring during adolescence and

the unpredictable timing of the growth spurt have led to the use of rating of secondary sexual characteristics rather than body weight and chronologic age as a basis for comparing physiologic and biologic data in this age group. Routine observations by the authors of poorly understood deviations in the concentration of serum hormonal iodine, as measured by protein-bound and butanol-extractable iodine, in adolescents have prompted this report.

### MATERIALS AND METHOD

Fifty boys and forty-six girls, 10 to 17 years of age, in apparent good health and with presumed normal intelligence formed

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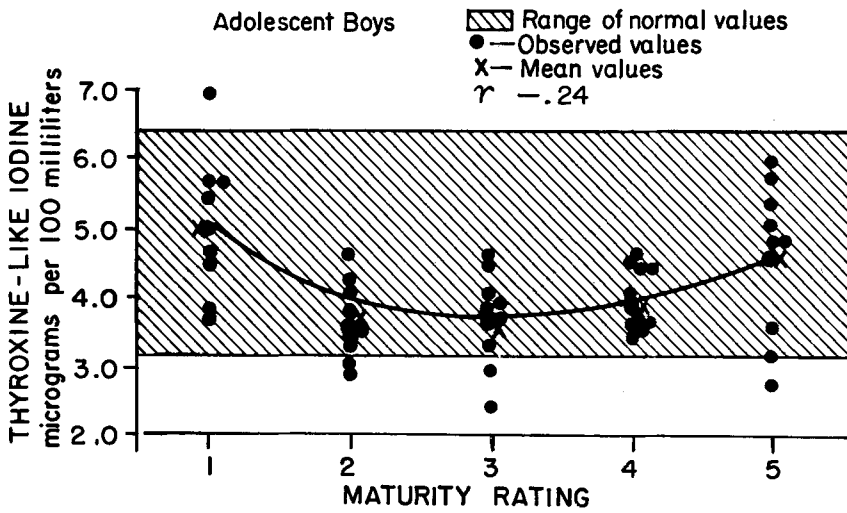


Fig. 1. Distribution of TLI values in males according to individual maturity ratings.

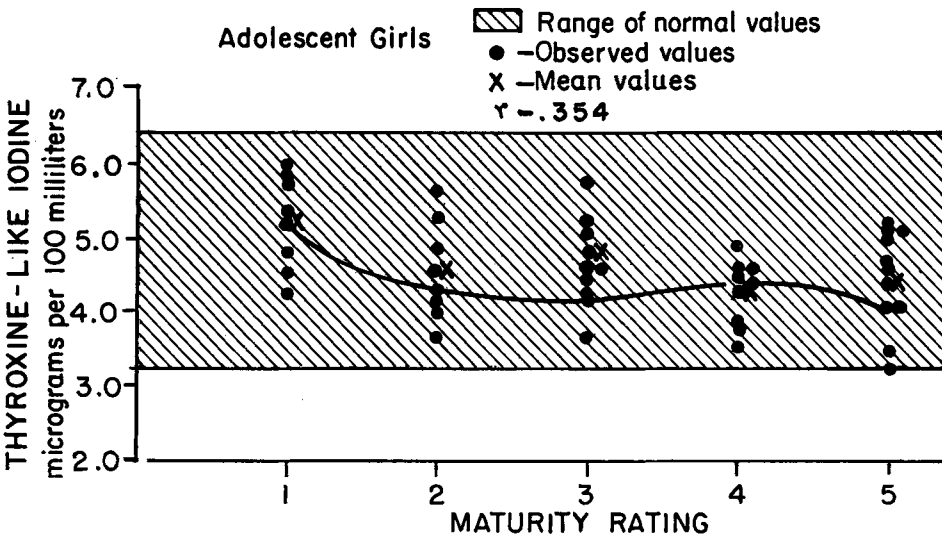


Fig. 2. Distribution of TLI values in females according to individual maturity ratings.

the nucleus of the subject material. None had any history of metabolic, and specifically of thyroid, abnormality. Each child was carefully examined without clothing at which time sexual development was estimated, each subject being given a rating from 1 to 5. In boys this rating was based on observations of pubic, axillary, and facial hair, and of genital development.<sup>1</sup> Girls were assessed according to distribution of pubic hair and breast development.<sup>2</sup> All serum was obtained from fasting subjects. Separation

of cells from serum was performed within a half hour after venipuncture. A minute quantity of thiouracil<sup>3</sup> was added to each aliquot of serum. These aliquots were then analyzed for "hormone" content as estimated by determinations of protein-bound (PBI) and thyroxine-like iodine (TLI) according to the methods of Barker, Humphrey, and Soley<sup>4</sup> for PBI and Pileggi and colleagues for TLI.<sup>5</sup> All statistical analyses were performed by the usual methods.<sup>6</sup>

## RESULTS

The results of the PBI and TLI determinations are given in Table I. The ranges for combined TLI values in this age group are similar to those of normal combined adult values (3.2 to 6.4  $\mu\text{g}$  per cent) reported elsewhere.<sup>7</sup> The mean TLI value and range in the boys are significantly lower than those for the girls ( $p = <0.04$ ); the 98 per cent confidence limits for the boys (3.8 to 4.4  $\mu\text{g}$  per cent) are in the lower half of this range. The same is true for the results of the PBI determinations. In fact, the associations to be noted were always the same for PBI and TLI analyses, and, for the sake of brevity, only the TLI results will be discussed.

The relationship between the serum TLI concentrations and increasing maturity in boys, with the subject population evenly dispersed among the 5 maturity divisions, is shown in Fig. 1. Whereas subjects with a maturity rating of 1 had a mean value of 5.0  $\mu\text{g}$  per cent, those demonstrating the next two ratings each had a mean TLI value of 3.6  $\mu\text{g}$  per cent, a value significantly lower than that for the girls with a similar maturity ratings, with  $p = <0.005$ . This value of 3.6  $\mu\text{g}$  per cent approaches the lower limits of normality for adults. While all the subjects were studied during a period of rapid growth, those assigned a rating of 3 were changing at the greatest rate. The means for the more mature, but less rapidly changing males rated 4 and 5, were 3.8 and 4.5  $\mu\text{g}$  per cent, respectively. This sequence demonstrates a tendency for the serum TLI concentration to rise as the rate of growth slows and sexual maturity is approached. A curvilinear line was fitted to these data for boys and showed a negative correlation ( $r = -0.235$ ).

The girls were also evenly distributed among the five maturity divisions. Those given a rating of 1 showed a mean TLI value of 5.2  $\mu\text{g}$  per cent; the mean values for girls with ratings of 2 and 3 exhibited a drop in serum TLI content inconsequential in comparison to the drop seen in males with the same ratings. Means for groups 2

**Table I.** Blood values for 96 normal adolescents (50 boys and 46 girls)

	Mean	Coefficient of variation (%)	Confidence limits (98%)
<i>Protein-bound iodine (<math>\mu\text{g}</math> %)</i>			
Males	4.9	15.95	4.7-5.2
Females	5.3	11.97	5.0-5.8
Combined	5.1	14.34	4.9-5.3
<i>Thyroxine-like iodine (<math>\mu\text{g}</math> %)</i>			
Males	4.1	21.38	3.8-4.4
Females	4.5	14.66	4.2-4.7
Combined	4.3	18.65	4.1-4.5

and 3 were 4.5 and 4.6  $\mu\text{g}$  per cent respectively. These data for girls describe a biphasic curvilinear line (Fig. 2) with an insignificant negative correlation between maturity and serum TLI concentration.

## DISCUSSION

Much evidence has accumulated in the literature to indicate that the concentration in the serum of thyroid hormone is highest in the newborn period in both sexes and falls continuously throughout childhood and during early adolescence.<sup>8-10</sup> Tanner<sup>11</sup> reviewed all these studies and questioned the existence both of a further fall during early adolescence and of any sex difference at the onset of adolescent maturation. The present data show the concentration of thyroid hormone in the serum, as determined in two different ways, to be lower in male than in female adolescents and to fall with increasing rate of maturation in males only to rise again as maturity is completed. Our results are consistent with those reported by Dreyer and Man<sup>12</sup> in a study of the concentrations of thyroxine-binding proteins and of butanol-extractable iodine in an adolescent male population. Their findings suggested some depressant effect exerted by the increased concentration of circulating androgenic hormones associated with the adolescent growth spurt on the concentration of thyroxine-binding proteins. In studies by Federman, Robbins, and Rall<sup>13</sup> and by Rosenberg, Ahn, and Mitchell,<sup>14</sup> a drop in the thyroxine-binding capacity of thyroxine-binding pro-

tein, and, consequently, in PBI concentration was found following the administration of androgenic gonadal steroids. Although the mechanism operating in adolescents is not clarified by the results, our results are consistent with the findings just referred to and appear to identify the period of greatest sexual maturation as the one where these phenomena are most obvious.

It is of interest that no increase of thyroid hormone concentration in the serum was observed concurrent with maturation in female adolescents, despite the known increase associated with pregnancy.<sup>15</sup> This may reflect a difference in the degree of estrogen effect.

One conclusion which is obvious from our results is that the measurement of the peripheral concentration of thyroxine, at least by the two methods herein reported, cannot be interpreted according to the same standards as are used for interpretation at other ages.

#### SUMMARY

Ninety-six normal adolescents were studied by clinical observation and by serum analysis for thyroid hormone content by two methods. For each determination the mean and ranges for the combined groups were similar to adult values. However, the mean for males was somewhat lower than that for females. In the adolescent males the mean values were observed to drop with early maturity and to be lowest during the period associated with the greatest adolescent growth spurt.

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