the marked increases in serum and liver cholesterol levels and liver lipids of the rat obtained with the casein-sucrose basal diet; although these elevations were much less, guar gum still demonstrated greater hypocholesterolemic activity than pectin N. F. Similar results had been previously observed in our experiments with chickens(1) fed either the casein-sucrose basal diet or a commercial-type diet prepared from a variety of natural foodstuffs from vegetable or animal sources.

Summary. The oral administration of guar gum and pectin N. F. to rats in a casein-sucrose basal diet greatly reduced the elevations in liver sterol and total liver lipids produced by the feeding of 1% cholesterol. Similar results were also obtained in rats when a powdered Purina Lab Chow diet was employed. Guar gum was considerably more active than pectin N. F., which confirms the results of similar experiments previously carried out with chickens.

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Received October 3, 1966. P.S.E.B.M., 1967, v124.

Effect of Advancing Age on Thyroid Hormone Secretion Rate of Male and Female Rats.* (31845)

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A number of reports have been presented concerning the depression of thyroid function with advancing age in domestic and laboratory animals(1-14). Recently, a study was reported on the effect of advancing age (from 25 to 115 days) on the thyroid hormone secretion rate (TSR) of female rats(15). It was observed that the TSR of the same rats at 25 days was 1.52 μg L-thyroxine (L-T_4)/100 g bw and gradually declined to a level of 0.88 μg/100 g bw at 115 days.

Levey determined the TSH concentration in the pituitary of rats by a bio-assay from birth to 56 days of age and noted a progressive increase from 13 mμ/mg to over 100 mμ/mg(16). It has been observed that the pituitary and plasma levels of TSH were low at weaning time and gradually increased until 80 or 95 days of age, then showed a slight decline(17). The present investigations were undertaken to study the effect of age on the TSR of male rats from weaning time until they were about 4 months of age, at 30-day intervals since no data were available on the TSR of the male rats of increasing age. The effects of aging upon TSR in female rats were studied from weaning time up to 8 months of age.

Materials and methods. The TSR determination of 36 male and 29 female rats of the Sprague-Dawley-Rolfsmeyer strain, bred in this laboratory and maintained at a temperature of 78 $\pm$ 1°F, with 14 hours of light and 10 hours of darkness, was started when they were 30 days of age. The mean body weight of the males was 151 g and of the females was 117 g. In addition to these 2 groups, the TSR was estimated in a total of 118 male rats at 30 days of age. Carrier-free I^{131} was diluted in distilled water to contain 3 μc/ml for the first month and later 10 μc/ml was administered to each rat intraperitoneally.

The determination of TSR of the growing rats was based on a slight modification of the technique described by Grosvenor and

* Contribution from the Missouri Agr. Exp. Sta. Journal Series No. 4036. Approved by the Director.

† Aided in part by a grant from U. S. Atomic Energy Commission, Contract No. AT(11-1)-301-130.

TABLE I. Effect of Advancing Age on TSR in Male and Female Rats.

Sex	Age (days)	No. of rats	Mean body wt (g)	Mean TSR/100 g bw ± S.E. (μg L-T_4)	Change in TSR from previous month (%)	Frequency distribution of TSR, μg/100 g bw						
						.50	.75	1.00	1.25	1.50	1.75	2.00
♂	30	36	151	1.40 ± .04			1	7	7	14	5	2
"	60	36	284	1.22 ± .04	—14.75		5	7	13	10	1	
"	90	36	381	1.15 ± .05	— 6.08	2	6	6	12	10		
"	120	36	430	1.03 ± .06	—11.65	5	9	5	11	6		
♀	30	29	117	1.47 ± .07				10	2	1	14	2
"	60	29	193	1.55 ± .06	+ 7.74			1	13	1	7	7
"	90	29	223	1.24 ± .05	—25.00		3	8	7	9	2	
"	120	29	242	1.12 ± .06	— 9.68	1	6	8	6	8		
"	150	29	258	1.12 ± .05	.00	1	4	12	4	8		
"	180	29	258	1.16 ± .05	+ 3.44	1	2	10	10	6		
"	210	29	269	.92 ± .04	—26.09	1	11	13	4			
"	240	29	271	.87 ± .03	— 5.75	2	11	16				

S.E. = Standard error of mean. TSR = Thyroid hormone secretion rate.

Turner(18). In this study L-thyroxine (L-T_4) was administered subcutaneously daily in increments of 0.25 μg/100 g bw/day. The minimal dose of L-T_4 which blocked thyroidal I^{131} release was estimated as the TSR of the animals. Correction was made for radioactive decay and background. The same male and female rats were estimated at 30-day intervals starting at the ages of 60, 90 and 120 for both sexes and further continued in female rats up to 240 days at intervals of 30 days.

Results. The mean TSR of the 36 male rats as determined at the ages of 30, 60, 90 and 120 days were respectively 1.40 ± 0.04 μg L-T_4/100 g bw; 1.22 μg L-T_4/100 g bw, 1.15 μg L-T_4/100 g bw and 1.03 μg L-T_4/100 g bw, thus showing a gradual reduction in TSR of 14.75% at 60 days; 6.08% at 90 days and 11.65% at 120 days from that of the respective previous month (Table I). The total reduction during the period of active growth from 30 to 120 days was 26%. A total of 118 male rats 30 days of age and weighing a mean of 145 g had a mean TSR of 1.34 ± 0.03 μg/100 g bw. These data were used to draw a normal frequency distribution curve (Fig. 1).

The mean TSR of 29 female rats was determined at 30-day intervals. The mean TSR at 30 days of age was 1.47 ± 0.07 μg/100 g bw. The TSR declined gradually with advancing age and at 240 days of age the mean TSR was 0.87 ± 0.03 μg/100 g bw (Table I). The total reduction during the period of active growth and maturity from 30 to 240 days was 41%.

Discussion. In a previous report, the decline in TSR of female rats of the Sprague-Dawley-Rolfsmeyer strain from 25 to 115 days was reported(15). During this period a total decline of 42% was observed. In the present study with male rats of the same strain, the initial TSR was slightly lower (1.40 *vs* 1.52 μg/100 g bw) and the total decline was only 26%. A group of 118 male rats at 30 days of age had a mean TSR of 1.34 μg/100 g bw. The normal frequency distribution showed a variation from 0.75 to 2 μg/100 g bw.

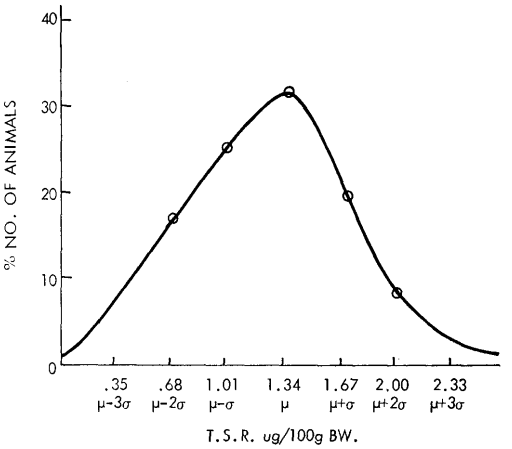

FIG. 1. Frequency distribution of normal thyroid hormone secretion rate (T.S.R.) of Sprague-Dawley-Rolfsmeyer male rats about 1 month of age. Mean daily T.S.R. value was 1.34 μg/100 g BW with ± one standard deviation(6) equal to 0.33 μg. Number of rats represented is 118, mean BW was 145 g.

In the female group, the initial mean TSR was only slightly lower than previously reported. However, the rate of decrease in TSR was somewhat slower. On the 120th day the mean TSR was 1.12 μg/100 g bw, compared to 0.88 μg in the previous study. Only by the 240th day had the present group reduced to 0.87 μg or 41% below the initial estimation of TSR.

While these two studies are similar in respect to the decline in TSR with age, they indicate that the rate of decline with age may vary in individuals and in groups of rats of the same strain.

Summary. The thyroid hormone secretion rate (TSR) of the same group of 36 male rats was estimated at 30 days and at 30-day intervals to 120 days. They declined from a mean of 1.40 μg/100 g bw to 1.03 μg at 120 days or 26%. A group of 118 male rats at 30 days of age had a mean TSR of 1.34 μg/100 g bw with a range from 0.75 μg to 2 μg/100 g bw. The TSR of a group of 29 females at 30 days of age was 1.47 μg/100 g bw and gradually declined to 0.87 μg at 240 days of age or 41%. It was shown that the TSR of both male and female rats decline with age but the rate of decline may vary in different groups of animals.

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Received October 10, 1966. P.S.E.B.M., 1967, v124.

Role of 2-Amino-4-Hydroxypteridine-6-Carboxaldehyde in Folic Acid Biosynthesis.* (31846)

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Recent studies on folic acid biosynthesis have focused attention on the role of P-6-CH_2OH‡ as an immediate pteridine precursor of the vitamin. This report describes studies which demonstrate the inhibition of growth of *E. coli* ATCC 9723 (Roepke Strain) by P-6-CH_2OH. This inhibition is reversed by dihydrofolic acid and even more effectively by dihydro P-6-CHO.‡ The implications of these results for folic acid biosynthesis are discussed.

The current state of information regarding the biochemical sequence leading to folic acid

* Aided by grant T-67G from Am. Cancer Soc.

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‡ Abbreviations: 2 - amino-4-hydroxy-6-hydroxymethylpteridine, P-6-CH_2OH; 2-amino-4-hydroxypteridine-6-carboxaldehyde, P-6-CHO; the terms dihydro or DH will in all cases refer to the 7,8-dihydro compounds.