in contrast to the average value of 2% found in normal man(1). In any one animal there was no significant change in calculated shunt flow as ambient pressure was increased from 760 to 2000 mm Hg.

It remains to consider possible reasons for the low estimate of Pa_{O2} made by Lambertsen *et al.*(3) on the basis of analyses for arterial O_2 content in normal men breathing oxygen at 2650 mm Hg. If these estimates are correct they would imply a shunt flow of 25% of the cardiac output or alternatively an obscure physical limitation on diffusion of O_2 at 3.5 atm. which we could not detect at 2.5 atm. It seems more likely, on the basis of present results, that the discrepancy is due to a small systematic error in estimation of O_2 pressure by the indirect method. In the experiments of Lambertsen, *et al.*(3) O_2 pressure was calculated from the solubility of O_2 in whole blood and the difference between total and combined O_2 in arterial blood. Total O_2 was estimated manometrically at 1 atm. after anerobic transfer of samples from 3.5 atm.; O_2 capacity was estimated spectrophotometrically. A loss of 5% of the O_2 during transfer or an absolute error of 5% in comparing manometric with spectrophotometric analyses could account for the results. Dr. Lambertsen informs us, however, that in subsequent unpublished experiments using the same technics at 2 atm. he was unable to detect a significant increase in A-a O_2 difference. The possibility remains, therefore, that the original measurements were correct.

Summary. In supine, anesthetized dogs breathing 100% O_2 the alveolar-arterial O_2 difference is unaltered when ambient pressure is increased from 1 to 2.5 atm. The results can be explained in terms of constant admixture of systemic venous blood with fully oxygenated pulmonary capillary blood. It is likely, but not proven, that previous estimates of arterial O_2 pressure at high barometric pressures are too low.

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Effect of Lactation upon Thyroid Secretion Rate in the Rat.* (24404)

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The role of thyroid gland hormone in influencing lactation has been derived primarily from observing the effects of hypo- and hyperactivity of the gland upon milk production. Few data, however, have appeared in regard to whether thyroid function is altered at this time. There is some evidence thyroid hormone output may increase during lactation in the cow(1), ewe(2), goat(3) and mouse(4), but not in the rat(5). As the latter investigation was conducted during the last third of lactation it seemed of interest to reinvestigate, by use of modern radiobiological technics, thyroid hormone secretion in the rat during the period of intense lactation.

Materials and Methods. Adult primiparous female rats of the Sprague-Dawley-Rolfsmeyer strain weighing 260-300 g were kept under conditions of uniform temperature (78 ± 1°F) in a room artificially illuminated during normal daylight hours for 6 weeks prior to experiments. Some were bred with male rats of the same strain during this time. Each of 16 litters born within 36 hours of each other was reduced to 6 young shortly

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after birth and, on the 4th day postpartum, each mother was injected i.p. with 2 μc carrier-free I^{131}. Twenty nonlactating rats were similarly injected at the same time. Forty-eight hours were allowed for fixation of I^{131} by the thyroid and for urinary excretion of excess isotope. External thyroid counts were taken at this time and at 48-hour intervals thereafter by first anesthetizing each animal with ether, then placing it on a lead plate with its thyroid region over a scintillation probe. Preliminary experiments were conducted with 10 non-lactating rats to determine rate of thyroidal I^{131} release and to determine the position which resulted in maximal counts. Efforts were made to insure placement of animals in that position during each counting period. Measurements of thyroidal radioactivity were made with a scintillation counter, Nuclear-Chicago (N.C.) Model DS 5, connected to a pulse height analyzer (N.C. Model 1810) which, in turn, was connected to a rate meter (N.C. Model 1620A). Conventional corrections were made for radioactive decay and background. Eight lactating and 10 non-lactating rats were injected subc. with .5 μg/100 g, a similar number with 1 μg/100 g L-thyroxine, for 2 consecutive days commencing 4 days after injection of I^{131} (8th day postpartum for lactating animals). The thyroxine dose was increased twice at 1 μg/100 g increments so each rat received 3 different levels of L-thyroxine (.5-1.5-2.5 or 1-2-3 μg/100 g), each level for 2 consecutive days. A thyroid count was taken on the day of each increase and the last count was obtained 24 hours after last injection of thyroxine (14th day postpartum). Thyroid secretion rate (TSR) was determined by plotting percentage of the previous count with thyroxine dose. The dose which prevented further thyroidal I^{131} output in each rat (95-100% of previous count) was estimated as its TSR.

Results. In a preliminary experiment involving 10 non-lactating rats, the biological half-life of thyroidal I^{131} was 4 days indicating that thyroidal I^{131} release rate was rapid enough for accurate TSR determination.

Thyroidal I^{131} output of non-lactating rats was totally blocked in all cases with 2 or 2.5 μg/100 g L-thyroxine. The average TSR for those receiving .5-1.5-2.5 μg/100 g levels was 1.4 μg/100 g, for those receiving 1-2-3 μg/100 g, 1.3 μg/100 g. The aggregate average for 20 rats was 1.3 μg/100 g L-thyroxine. Thyroidal I^{131} output of all lactating rats injected with 1-2-3 μg/100 g was blocked. However, thyroidal I^{131} output of only 5 of 8 injected with .5-1.5-2.5 μg/100 g was inhibited. Extrapolation to 100% of previous count indicated 3 μg/100 g was necessary for total thyroidal blockade in the remaining 3 rats. Average TSR of 16 lactating rats of 2.2 μg/100 g L-thyroxine was significantly greater ($P > .001$) than for non-lactating rats of the same strain, age and weight range. Fig. 1

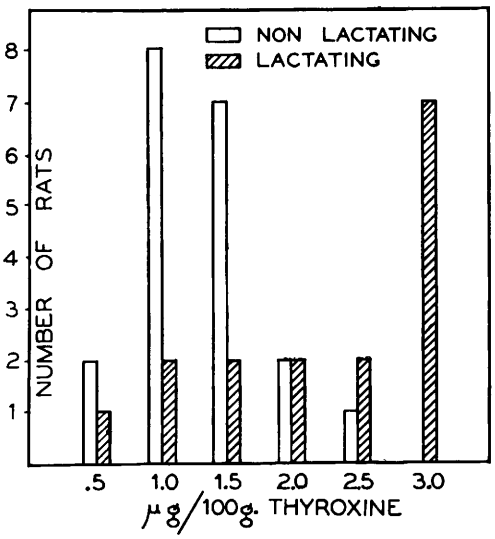

FIG. 1. Frequency distribution of thyroxine secretion rates for lactating and non-lactating rats.

indicates individual variance in TSR. A typical distribution pattern resulted for non-lactating rats. While a wider range in individual TSR is evident for lactating rats, a definite overall increase is apparent.

Discussion. Several investigators have estimated thyroid hormone output by administering varying doses of thyroxine to experimental animals and measuring by radioiodine technics, subsequent suppression of thyroidal I^{131} output(2,6-9). Inhibition of thyroid hormone output can be explained by the suppressing effect of thyroxine upon thyrotropic hormone release, high doses having the same effect as hypophysectomy(10). In employ-

ing these technics we were able totally to block thyroidal I^{131} output when thyroxine was administered in doses equivalent to their TSR. Unpublished observations indicate a small iodine turnover occurs in rats if thyroxine is injected daily for long periods of time at levels equal to their TSR. These observations are in accord with those of others(9). In the present study, the biological half-life of thyroidal I^{131} retention was 4 days, similar to that previously reported for normal rats and mice(11,12). The average TSR for non-lactating rats of 1.3 μg/100 g L-thyroxine obtained under our conditions is considerably lower than the estimates of 2.21-2.56 and 2.8 μg/100 g L-thyroxine reported by others(9, 13) with the use of similar technics. Our mean value, however, is very similar to the estimate of 1.4-1.75 μg/100 g L-thyroxine obtained by Monroe and Turner(5) using goitrogen technics and analyses of thyroid weights. It is possible, of course, strain differences and different laboratory conditions are reflected, to some extent, in thyroid secretion rates and thus account, in part, for these variations.

During mid-lactation we found the average TSR was increased 70% over non-lactating animals of the same strain and similar in age and body weight. A similar increase in thyroid hormone output has been found in the lactating ewe(2). These data are in accord with the general concept that a hyperthyroid state is generally desirable for optimal milk secretion(14). However, in a previous study (5), no difference was found by the use of goitrogenic techniques between lactating and non-lactating rats. As these data were obtained during the last third of lactation, at which time nursling young are eating solid food in addition to milk, the observed TSR may have been an indication of diminishing thyroid activity as lactation waned.

Summary. 1) Thyroid hormone secretion rate (TSR) was determined in lactating and non-lactating rats by administration of graded levels of L-thyroxine and measuring by radioiodine technics, subsequent suppression of thyroidal I^{131} output. 2) The average TSR of 2.2 μg/100 g L-thyroxine for lactating rats during the period of intense lactation (8-14 days postpartum) was significantly greater than the average of 1.3 μg/100 g for non-lactating rats of the same strain, age and weight range. These data are in accord with the concept that a hyperthyroid state is generally desirable for optimal milk secretion.

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