

Influence of Goitrogen (Tapazole) in Feed on Thyroxine Secretion Rate of Cockerels.*† (27016)

KENTARO HIMENO‡ AND C. W. TURNER

Department of Dairy Husbandry, University of Missouri, Columbia

In determination of thyroxine secretion rate (TSR) of mature birds, it has been found necessary to block recycling of I^{131} resulting from metabolism of thyroidal I^{131} (1). This is due to fact that apparent thyroidal- I^{131} release rate in many birds is so slow (flat curve) that the blocking action of increasing graded doses of L-thyroxine can not be observed clearly. For this reason, a goitrogen such as thiouracil (0.1-0.2%) or tapazole (0.05% of diet) has been used to prevent uptake of I^{131} by thyroid.

Reineke and Singh(2) reported that estimates of TSR in rats fed thiouracil to block recycling were about 10% higher than those in rats not receiving a goitrogen. Recently, Mellen(3) reported no significant difference in TSR between 0.1 and 0.2% thiouracil in feed of 10-week-old cockerels. Himeno *et al.*(4) suggested that the TSR of chicks fed 0.1% thiouracil increased significantly in comparison with birds fed control diet, and TSR also increased with the length of time that thiouracil was fed.

Baby chicks up to 3 or 4 weeks of age lose thyroidal- I^{131} so rapidly that their TSR can be determined without a goitrogen. On the other hand, use of goitrogen becomes increasingly necessary for older chicks and mature birds.

Since tapazole is routinely used in our laboratory in TSR determinations, TSR was determined in a group of young birds without tapazole, then repeated with graded levels of tapazole in order to determine its effect on TSR.

Materials and Methods. One hundred cockerels of a White Leghorn X New Hampshire cross were housed in room at 60° F. for 2

weeks, then TSR was determined individually starting at 7 weeks of age by method described by Pipes *et al.*(1) except that no goitrogen was used. Birds were then divided into 4 equal groups on basis of individual TSR when 9 weeks of age. TSR determination was then repeated with controls and groups fed 0.025, 0.0375, and 0.05% tapazole added to their ration. When birds were 19 weeks old TSR was determined again using 0.05% tapazole to prevent recycling.

Results. TSR of 100 cockerels without tapazole determined at 7 weeks ranged from 0.5 to 1.5 $\mu\text{g}/100$ g body weight with mean of 0.89 ± 0.02 μg . Upon repeating TSR at 9 weeks control group (no tapazole) showed a decreased mean of 0.74 ± 0.04 $\mu\text{g}/100$ g body weight. Groups on tapazole at levels of 0.025, 0.0375, and 0.05% of ration had TSR of 1.11 ± 0.08 , 1.18 ± 0.08 , and 1.27 ± 0.07 $\mu\text{g}/100$ g body weight, respectively. TSR of control group (without tapazole) was significantly lower than experimental groups ($P < 0.01$). However, mean TSR of birds on graded levels of tapazole were not significantly different although graded in response.

On basis of this comparison, it appeared that use of tapazole partially to completely blocking I^{131} recycling increased apparent TSR from 0.74 to 1.21 $\mu\text{g}/100$ g body weight or 63.5%. To determine whether such a percentage correction factor could be applied uniformly to birds with increasing TSR, data was reclassified on basis of TSR without tapazole in 7 week old cockerels. Birds with TSR of 0.5 μg without tapazole showed an increase to 1.05 μg or an increase of 110%, birds with TSR of 0.75 μg without tapazole an increase to 1.14 μg or an increase of 52%, birds with TSR of 1.00 μg without tapazole an increase to 1.23 μg or an increase of 23%, whereas birds with TSR of 1.25 μg without tapazole increased to 1.28 μg or 2.4%. Since effect of tapazole in birds with low TSR was very great, whereas birds with high TSR were

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‡ Research Fellow of Atomic Energy Commission of Japanese Government.

unaffected, question of tapazole truly increasing TSR may be raised.

When cockerels were 19 weeks of age, TSR was again repeated using 0.05% tapazole in ration. TSR ranged from .25 to .75 $\mu\text{g}/100\text{ g}$ body weight with mean of $.45 \pm .02$, a significant reduction from either 7 or 9 week determination.

Discussion. In determination of TSR in birds and mammals, goitrogens have been employed to block uptake of I^{131} resulting from metabolism of thyroxine- I^{131} . By its use, the true release rate of thyroidal- I^{131} is measured at successive intervals. When thyroxine is then administered at increasing levels to block thyrotropin discharge, the end-point in estimation of TSR is prevention of thyroidal- I^{131} release (at least 95% of previous reading). Goitrogens have been used exclusively in method to increase thyroidal- I^{131} release rate and thus make more obvious the point at which thyroxine level injected has stopped thyroidal- I^{131} release.

No evidence is available which indicates that goitrogens directly stimulate increased TSH secretion when thyroxine is present. Similarly, while goitrogens increase thyroidal- I^{131} release rate, the apparent increased release rate has been believed to be due to prevention of recycling of I^{131} . It is possible, however, it might have such action.

Present data might be interpreted as indicating that tapazole stimulated a 63.5% increase in TSR. However, analysis of data shows that greatest effect was upon birds with low TSR and a progressive reduced effect as TSR increased. If tapazole actually stimulated either increased TSH secretion or thyroidal- I^{131} release, one would expect a similar effect throughout range of TSR.

It is suggested that in 7-week-old birds, TSRs of birds in lower range were underestimated. That is, due to the flatness of thyroidal- I^{131} release curve, it was considered that blocking of release by thyroxine had occurred before it actually had been reached. On basis of present data, underestimation of TSR in birds showing $0.5\text{ }\mu\text{g}/100\text{ g}$ body weight without tapazole was about 100%, in those at 0.75

μg was about 50%, in those at 1.0 μg about 25%, whereas those at 1.25 μg were correctly estimated.

If this is correct explanation, need of a level of goitrogen to completely block recycling of I^{131} would be required in all studies of TSR even in young birds and other species with normal rapid release rates. In other words, the role of goitrogens is to increase accuracy of end-point of TSR determination.

Marked decline in mean TSR of these cockerels at 19 weeks with tapazole was quite unexpected since Stahl *et al.* (5) showed in a strain of New Hampshire cockerels only a slight decrease in TSR as sexual maturity was reached.

Summary. Thyroxine secretion rate (TSR) of 100 cross-bred cockerels was determined at 7 weeks of age without tapazole to block I^{131} uptake. At 9 weeks, 4 groups of equal TSR were separated. One group served as a control, whereas other groups were fed 0.025, 0.0375, and 0.05% tapazole in ration. TSR of groups were $.74 \pm .04$, $1.11 \pm .08$, $1.18 \pm .08$, and $1.27 \pm .07\text{ }\mu\text{g}/100\text{ g}$ body weight, respectively. Group not fed tapazole was significantly lower than where included, but differences between tapazole-fed birds were not significant. Tapazole appeared to increase TSR 63.5%. Analysis of these data showed that tapazole increased TSR to greatest extent in groups showing low TSR without tapazole. It is suggested that tapazole does not actually increase TSR but in its absence there is a tendency to underestimate the true TSR due to the slow release rate of thyroidal- I^{131} . It is recommended that in determination of TSR sufficient goitrogen be fed to completely block I^{131} recycling.

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