Studies on the Effect of Hypothermia

II. The Active Role of the Thyroid Gland in Hypothermic States in the Rabbit*

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In rabbits subjected to lowered body temperature (28° to 10° C. rectal temperature) for various periods, an acute profound physical and histological change has been noted consistently in the thyroid gland. Believing that these changes have an important bearing on the ability of the animals, and perhaps of human beings, to withstand periods of reduced body temperature, we are describing them in some detail.

Extensive studies have been performed by numerous investigators (1, 3, 4, 5, 7, 8, 13, 23) on the effect of prolonged exposure to low temperature upon the thyroid gland of various animals, but the results do not always agree. Thyroidectomized animals have been said to suffer more severely in a cold environment than do normal ones (2, 11, 21, 22), yet the contrary is reported also (10). Dietrich and Schweigk (6) recorded an immediate increase of the blood flow through the thyroids of chilled dogs. In a series of extensive experiments, Cramer and Ludford (3) demonstrated that exposure to a cold environment for a short period was a powerful stimulus to the functional activity of the adrenals, but that low environmental temperatures of longer duration were necessary to induce hyperactivity of the thyroid. Ludford and Cramer (15) noted congestion of the thyroid capillaries and increased secretory activity of the follicular cells in epilated rats after 24 hours in an ice chest. Ring (20) observed that in rats exposed to cold for a short period of time the elevation of the basal metabolism was associated with a rise in body temperature. If they lived for 3 weeks or more in an environment of 8-5° C., there was an average elevation in metabolism of 16 to 21 per cent, and the increase in basal metabolic rate was brought about largely, if not entirely, by the thyroid gland since a smaller increase in basal metabolic rate was obtained in partially thyroidectomized animals.

Seasonal effects on the morphology of the thyroid in birds have been studied by several authors with conflicting results. Haecker (9) described maximal collections of colloid in the follicles in winter with a minimum of colloid in summer in crows and sparrows. Kuchler (14) reported that during the winter the thyroids of robins and sparrows are inactive. On the other hand, Riddle and Fisher (19) believed that the thyroid is most active in winter and Miller (17) agreed, having noted increased thyroid activity in sparrows on lowering the external temperature.

There are many reports indicating the role played by various other glands in heat production; i.e., the adrenal gland, the pancreas, and the brain. Thus many factors may control the reactions of the temperature-regulating mechanism of the body; yet in our studies the thyroid presented the most profound histological changes, and there was no obvious alteration in the adrenals except for the congestion seen in all the organs.

METHOD

Sixty-six normal, young adult, white male, rabbits of the New Zealand strain were used in these experiments over the period September, 1939–March, 1940. They weighed between 2 and 3 kg. each, and had been housed for at least 1 month previous to experimentation in a well lighted, ventilated room at a temperature of 20–26° C. They were fed a diet of alfalfa and oats. Their drinking water was the average city water, with an iodine content of 2 parts per billion. Forty-five of the animals had been inoculated intratesticularly with the Brown-Pearce rabbit epithelioma from 1 to 2 weeks previous to the reduced temperature experiments in order to study the effect of the lowered temperature upon this tumor. Since the general response of the tumor-bearing rabbits to the lowered

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The histological appearance of the thyroid gland suggests that parts of it were in a state of moderately increased activity. It will be shown later in this paper that it is in this period of the hypothermic state that the metabolic rate is notably increased. Apparently in this acute disturbance of the temperature-regulating mechanism the thyroid was stimulated to a considerable extent, yet because of the short duration of the experiment (2 to 5 hours) it was not able to get well under way (19). The appearance of the gland after this short period of reduced body temperature was similar to that reported by others (3, 25) after almost 2 weeks’ exposure of rats to a cold environment.

Occasionally death occurred in a very short period while the temperature was falling rapidly at a rate of 4–8°C per hour. The animal would become highly agitated and after a particularly violent episode, almost resembling a maniacal state, would suddenly become cyanotic, breathe stertorously, and the respirations and heart would stop. This might occur at any time during the induction period of 1 to 8 hours. Usually in these cases the thyroid would be 1½ to 2 times its normal size, highly congested, and soft. No other gross abnormalities were to be found except for a general congestion of the vessels. The colloid was usually absent and replaced by a small collection of vacuoles. The acini were nearly circular in cross section as if under pressure from inside, and there was often a clear space around the dense and slightly shrunken nucleus (Figs. 3 a and 3 b). This gave the impression that the gland had been acutely exhausted of its colloid after a period of extreme activity and had become edematous. A similar picture was occasionally seen in animals unable to recover spontaneously during the relatively short therapeutic experiments (8 to 10 hours at a low temperature), and in which violent movements aggravated the acute physical exhaustion with resultant death.

Whether edema in the thyroid cells (Fig. 3 c) was a primary or a secondary factor cannot be determined. Such a condition (rapid exhaustion of the colloid and
All the sections shown in this paper were photographed at the same magnification, X 300.

Fig. 1.—Thyroid glands of 2 normal rabbits showing various sizes and shapes of acini, amounts of colloid, and cell types. The acinar walls in (a) are lined with flattened cuboidal cells containing rather small, densely stained, oval or spindle-shaped nuclei. The epithelial cells in (a) are definitely cuboidal, and the nuclei are round and show some structure. In some fields there are numerous vacuoles and much less colloid. These variations represent the extremes that may be seen in a single gland as well as in glands from different normal stock rabbits during the winter season.

Fig. 2.—Acute changes due to rapid reduction of body temperature resulting in death. The rectal temperature in one rabbit was reduced to 18° C. in 2 hours, when death occurred suddenly and violently. The thyroid was normal in size. Section A shows almost no colloid, the acini being collapsed or containing vacuoles. The acini are small and made up of large, swollen, cuboidal or columnar-cuboidal cells that have a granular appearance. The nuclear detail is clear and there is no definite pyknosis. Another rabbit was reduced to 10° C. in 5 hours when death occurred imperceptibly. The thyroid gland was normal in size. The colloid in (a) is very darkly stained with eosin. The epithelial cells are swollen and columnar in shape. The nuclei are clear and paler than usual.
Fig. 3.—Extreme yet characteristic changes in the thyroid resulting from acute exhaustion. Glandular enlargement, cellular enlargement, and beginning cellular disintegration and congestion.

In rabbit 5 the temperature was lowered to 18°C in 8 hours, when death occurred suddenly. The thyroid gland was 1½ times normal size, congested, and soft. The illustration (A) is characteristic of the large cell size and the small acini almost devoid of colloid or filled with vacuoles. The capillaries, not shown well here, are dilated and engorged with blood. There seems to be considerable free fluid between the acini. The epithelium is swollen and columnar in type, the nuclei being dense and frequently isolated from the cytoplasm by a clear zone. The number of acini seem much greater than normal. The increase in cell size, the edema, and the congestion probably account for the increase in gland size.

Rabbits 6 and 7 were both reduced to a temperature of 18°C in 6 hours, when death occurred suddenly. The thyroid glands were each enlarged almost to twice normal size, and were soft and engorged with blood. The tremendous cellular enlargement and edema, shown in (B) and (C) are striking. The nuclei are dark and often in various stages of disintegration. This is most prominent in (C) where the cell boundaries are almost lost. Colloid is replaced almost entirely by vacuoles. Small capillaries gorged with red blood cells are seen everywhere. Section B seems to show more actual cell disintegration, while cytoplasmic swelling is more prominent in (C).
swelling of the cells from ingress of fluid) would certainly hinder the normal functioning of the thyroid gland and must have contributed in some respect to the distress and fatal incapacity of the animal to maintain itself.

Evidently some acute hypertrophy (functional) occurred in these glands in this short period since all the enlargement, both in gross and in the histological appearance of the epithelium, was probably not due to edema alone. Similar observations were made on 20 animals that were either sacrificed or that died during the induction period. Some could only partially compensate for the continued loss of heat for 4 to 6 hours. Others succumbed after 10 to 12 hours. In all these brief experiments the thyroid showed a definite abnormality, the degree of which was usually in keeping with either the rapidity of fall of the temperature, the low level reached and maintained for a few hours, or an exhausting violent episode just before death. The temperature at which death occurred varied between 28° and 10° C. The reason some rabbits succumbed when the body temperature was lowered only 8–10° C. while others were able to withstand a drop of 25° C. before death occurred is not known. There seemed to be no difference in the physical condition or in the reaction of the animals to the cold up to the time of death. The soporific effect of the falling body temperature came on rather promptly in most cases.

**Spontaneous Recovery Following Reduction of Temperature—Acute Hypertrophy of the Thyroid**

Eight animals were reduced to various low levels of hypothermia in order to observe the level from which they could warm themselves spontaneously when kept at room temperature, or from which they had to be aided artificially. Some of these were sacrificed at various stages at the end of the induction and during the periods of recovery, after 6 to 12 hours' low temperature, in order to study the morphology of the thyroid gland in these stages.

The rectal temperature of rabbit 28 at the beginning of the experiment was 38.0° C. It was placed in an ice bath for 6 hours, when the rectal temperature reached 23.0° C. The water was then removed and the cage partially surrounded by crushed ice. When the body temperature reached 17.0° C., 3 hours later, the animal was removed from the ice and placed on a table at room temperature (24.0° C.) It attempted to stand but its movements were slow and uncoordinated, partly because of the shivering that started immediately. This slow muscular activity continued for 3 hours, at the end of which the rectal temperature had reached 35.0° C. The rabbit appeared then to be normal except for a somewhat dull, listless appearance. The hair was dry. The animal was sacrificed at this point after a total of 6 hours at a reduced temperature, and the thyroid gland was studied.

It was approximately 3 times the normal size and its vessels were considerably engorged and dilated. It was bright red in color, greatly congested, and had a hyperplastic, fleshy appearance. Cut section revealed a red, roughened, nonhomogeneous, rather soft surface from which a great deal of blood could be scraped. Histological study (Fig. 4 A) showed that most of the follicles were devoid of colloid with the exception of a few scattered here and there that might contain a little, or even a large amount. Vacuoles were numerous. The cells were large cuboidal to low columnar in shape, their nuclei sharply defined, and the cytoplasmic details were readily seen. The blood vessels were dilated, engorged, and numerous throughout the entire section. There was no evidence of edema. Most of the enlargement of the gland must have been due to actual cellular hypertrophy (3 to 4 times) and blood vessel congestion.

There was evidently a definite thyroid hyperactivity in this stage of the animal's attempt to maintain body temperature. In 5 rabbits the temperature had been lowered to 17.0° C. with spontaneous recovery, and in 3 to 11.0° C., with artificial heating to aid in restoring the temperature to normal. Similar changes or evidences of hyperactivity of this degree were noted in the thyroid glands of all 8 animals. There were no signs of hyperplasia or mitotic activity, probably because of the short duration of the experiments.

As the rabbit starts to raise its temperature from the levels above 20.0° C., the basal metabolic rate has been found to be definitely increased (Table I). This is probably the period at which the thyroid gland is undergoing its greatest stimulus and activity. It is apparently able (8 rabbits) to change the size of its epithelial cells in this short time of 6 to 12 hours or less, and to compensate for the tremendous acute drain that has been thrust upon it. It is interesting to note that this morphological change can occur so quickly. The change is of much greater magnitude than, although similar to, the slower alteration brought about by exposure to low air temperature for weeks (3, 23).

**Prolonged Hypothermia or Pseudohibernation—Acute Hyperactivity of the Thyroid**

If the temperature of the rabbit was maintained in the vicinity of 28–25° C. or lower, the animal usually remained in a quiescent state resembling hibernation. Several animals were sacrificed at early periods during this state while others were kept in the quiescent,
pseudohibernating state for various periods up to 48 hours. They were then permitted to recover spontaneously at room temperature of 20–26°C, or were aided by artificial means to establish their normal temperature (Fig. 4 A). Some were sacrificed at various periods following recovery and their thyroids studied. Still others were subjected to lower body temperature (21–11°C) at which point they appeared to be in a state of deep coma or even suspended animation. Spontaneous recovery was possible if this lowered temperature was not prolonged beyond an hour or so (resembled Fig. 4 A). A longer period required artificial

Fig. 4.—Hypertrophy due to stimulus of low body temperature. Spontaneous recovery is possible.

(a) Rabbit 28 was sacrificed after 6 hours at temperatures between 17° and 35° C. (including a 6 hour reduction period). The thyroid gland was 3 times normal size, firm, and engorged with blood. The colloid varies in amount, in some cases being almost absent or replaced by vacuoles. The epithelial cells are sharply defined and large cuboidal or low columnar in type. Blood vessels are numerous and congested.

(b) Rabbit 32 was reduced to 13° C. in 6 hours with spontaneous recovery to 31° C. in 17 hours at room temperature. Additional mild heating for 6 hours more restored the rabbit to normal temperature (36.5° C.), at which time it was sacrificed. The thyroid gland was not enlarged. Some epithelial cells appear swollen and are paler and less sharply defined than others, suggesting the beginning of focal edema and possible disintegration. Some acini have cells on one side that are low cuboidal or flat and contain darkly stained, small nuclei, with large cuboidal or columnar cells almost opposite them.

<table>
<thead>
<tr>
<th>State</th>
<th>Rabbit No.</th>
<th>Average rectal ( \text{temperature, } ^\circ \text{C.} )</th>
<th>Cal. per m.² per hr.</th>
<th>Change from basal, ( ^\circ \text{C.} ) per cent</th>
<th>R. Q.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st induction</td>
<td>1</td>
<td>20.0</td>
<td>109</td>
<td>185</td>
<td>0.750</td>
</tr>
<tr>
<td>1st hour</td>
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<td>25.0</td>
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<td>130</td>
<td>0.752</td>
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<tr>
<td>2nd hour</td>
<td>3</td>
<td>19.0</td>
<td>45</td>
<td>27</td>
<td>0.765</td>
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<tr>
<td>Pseudohibernating</td>
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<td>0.68</td>
<td>-97</td>
<td>0.735</td>
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<tr>
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<td>5</td>
<td>25.5</td>
<td>13</td>
<td>-65</td>
<td>0.784</td>
</tr>
<tr>
<td>2nd hour</td>
<td>6</td>
<td>25.0</td>
<td>15</td>
<td>-57</td>
<td>0.850</td>
</tr>
<tr>
<td>Normal control</td>
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<td>37.0±0.5</td>
<td>35±2 cal.</td>
<td>0.0</td>
<td>0.800±0.050</td>
</tr>
</tbody>
</table>

by artificial means to establish their normal temperature (Fig. 4 A). Some were sacrificed at various periods following recovery and their thyroids studied. Still others were subjected to lower body temperature (21–11°C) at which point they appeared to be in a state of deep coma or even suspended animation. Spontaneous recovery was possible if this lowered temperature was not prolonged beyond an hour or so (resembled Fig. 4 A). A longer period required artificial heating and a still longer period was usually fatal (Fig. 4 B). The following experiment is typical.

The thyroid was of normal size and the larger vessels were engorged. Cut section revealed a grayish red, homogeneous surface. In the histological section the follicles were small and almost devoid of colloid.
There were remnants of colloid present as small islands or streaks in a few follicles; otherwise the small follicular space was filled with vacuoles. The large epithelial cells of the follicles were of uniform cuboidal shape (resembled Fig. 4 b, except for more uniformity of cell size). The capillaries were hard to find and were not engorged or dilated. The presence of large cuboidal epithelial cells and follicles almost devoid of colloid suggested an acutely hyperactive gland. Since at this low body temperature (16–21 °C.) there is little circulation of the blood and apparently little metabolic activity, most of the hyperplasia and removal of colloid must have occurred in the earlier period at higher levels above 21 °C., and the gland had little opportunity to reimburse its deficits while at the lower level.

Several animals suddenly succumbed: 1 at the end of 1 day, and 2 after 3 days, after making an apparently uneventful recovery following the prolonged hypothermic state. The thyroid gland in each instance appeared normal upon gross examination and nearly normal histologically, enough time apparently having elapsed for it to recover. The cause of death remained undetermined.

**The Effect of Repeated or Greatly Prolonged Temperature Reductions—Slow Exhaustion**

Nine animals were cooled and then were permitted to heat themselves to normal or almost normal temperature. Their body temperatures then were lowered again and they were allowed to recover spontaneously. In a few it was done 3 times. This is the severest strain that can be put upon the heat-regulating mechanism, and probably resembles in many respects those conditions to which the wild rabbit may be subject in its natural surroundings.

Rabbit 29 had its temperature reduced 3 times to between 26° and 29° C. over a period of 48 hours, when it succumbed.

Gross examination revealed an apparently normal thyroid gland of average size. Histological study showed many moderately dilated vessels. There was abundant colloid in most of the follicles, and in many vacuoles were present. The epithelial cells of the follicles were low cuboidal in shape. This was similar to the appearance of a normal, although rather active, thyroid.

When the animal has partially heated itself spontaneously after the first temperature reduction, each additional reduction can be obtained more rapidly and with a relatively smaller decrease in the temperature of the environment. Following each reduction, it takes the animal longer to recover. While still giving the appearance of activity, the thyroid gland in this animal was not in a hyperactive state, yet showed signs of being active, or perhaps the end results of exhaustion of a hyperactive state coincident with the final inability of the animal to increase its temperature. Thyroids of 4 animals after the second reduction showed a picture similar to that described above. Two others demonstrated a small amount of hyperactivity, and 3 definite hyperactivity without colloid, showing that variations in the state of hyperactivity occur and bear some relationship to the ability of the animals to regain their normal temperature and status. From the appearance of notable and rapidly developing hyperactivity of the thyroid following the first reduction, and similar changes in animals capable of recovering subsequent to the first hypothermic state (Fig. 4 a), one may assume that the hypertrophy could have been brought about at first and that then, as the gland or its resources became less able to supply the demands made upon it, the epithelial hypertrophy diminished (Fig. 5 a). Some of the abnormality may have been due to a decrease in chemical exchange or reduction of blood flow at the low temperature.

Animal 36 illustrates prolonged (62 hours), unsuccessful effort to recover with the thyroid gland in a hypoplectic state. The period of the experiment was long enough to allow considerable change to occur. The rabbit had remained at a temperature slightly below 30 °C. for 62 hours, at the end of which time it succumbed.

Postmortem examination revealed a fleshy thyroid gland approximately 1½ times the normal size, of a dull, grayish red color and rubbery consistency. Microscopic study showed an abundance of colloid. All follicles were enlarged to twice the normal size. Practically no vacuoles were present in the colloid. The epithelial cells were flattened and the nuclei large and densely stained, resembling Fig. 5 a. The gland seemed to be definitely hypoactive, and its appearance was not unlike that brought about by prolonged fasting (Fig. 5 b). Stephens (24) has noted that when rats are maintained on a subminimal diet for a period of 3 to 4 weeks, the thyroid gland assumes a notably hypoplastic state. Three control rabbits, therefore, were fasted for 3 days and then sacrificed. Their thyroid glands likewise presented a picture of hypoplasia (Fig. 5 h), which closely resembled Fig. 5 a.

In 4 animals that could not regain their body temperature after a second reduction to the hypothermic state, the blood sugar was found to be between 20 and 40 mgm. per 100 cc. compared to a normal of 80 to 100 mgm. per 100 cc. This suggests that during attempts to regain its normal body temperature while being reduced to a hypothermic state, the animal apparently had depleted its stores of body sugar, a situation analogous to fasting for several days or a
subminimal diet for several weeks (23). Similar changes of the thyroid gland, which develop slowly and are characterized by atrophy and involution, have been described by Jackson (12), Meyers (16), and Rabinovitch (18).

**Basal metabolism in hypothermia.**—Basal metabolism studies were performed by Mr. Robert Ryer, III, in an attempt to correlate the morphological appearance of the thyroid gland to the oxygen consumption during various states of hypothermia. In each instance the animal was fasted for 24 hours before the metabolic studies were performed. This did not seem to change the clinical reactions to the short period of reduced body temperature in any way. The histological appearance of the thyroid glands from animals that had been fasted 1 day was essentially normal. Normal rabbits were placed in the indirect respiration apparatus, and their metabolism was calculated from the gaseous interchanges for control values. In a series of 50 New Zealand white rabbits, the average value for the normal rabbit was 35 calories per square meter per hour.

**Experiment 1.**—Two rabbits were cooled until their rectal temperatures were in the vicinity of 25.0°C. They were sluggishly active and yet not in the pseudohibernating state. They were placed in the respiration apparatus at room temperature, at which time they commenced to regain normal body temperature promptly. During the first hour, 1 animal with an average temperature of 25.0°C. produced 84 cal. per m² per hour, an increase of 130 per cent (Table I). During the second hour, it raised its rectal temperature to 28.0°C. and produced 45 cal. per m² per hour, an increase of 27 per cent. The other rabbit produced 109 cal. per m² per hour, an increase of 185 per cent, at an average rectal temperature of 20.0°C. Both animals recovered spontaneously.

**Experiment 2.**—Two rabbits were cooled to a rectal temperature of 19.0°C. at which point they were quiescent and inactive (pseudohibernating state). The...
calories produced per square meter of body surface per hour at an average temperature of 19.0°C were 0.67 and 0.57 respectively, or the rather fantastic figure of 97 per cent below the basal metabolic rate (Table I). Both recovered spontaneously in the usual manner.

Experiment 3.—Two animals were reduced to 20.0°C rectal temperature, and allowed to recover, following which their temperatures were lowered immediately a second time to 25.0°C. Their calory productions at this time were 13 cal. per m² per hour and 15 cal. per m² per hour, respectively, with a percentage change from the basal rate of 65 per cent and 57 per cent below the basal metabolic rate. This seems to indicate a definite depletion of reserves, yet both animals recovered spontaneously, although slowly.

SUMMARY

Profound changes in the size of the follicular epithelium and changes in the follicular contents of the thyroid gland may occur rapidly, even within one-half hour, in the various stages of artificial hypothermia. These may be extensive enough when combined with vascular engorgement to enlarge the thyroid in the gross from 1½ to 3 times its normal size. A certain amount of correlation between these histological changes and the sequence of events is possible. There is apparently at first a tremendous increase in the circulation, indicated by the increased heart rate and the engorged blood vessels in the gland. There is a progressive increase in the size of the follicular epithelium, an increase in the number of vacuoles, and a rapid diminution of colloid. Recovery from low temperatures, with histological evidence of cellular hypertrophy and decrease in the amount of colloid, may be accompanied by metabolic rates of 150 per cent above the normal. Continued low body temperatures tend to restrict the circulation and to reduce the chemical activity and exchange. Excessive demand tends to deplete the gland of its colloid, and since it is slow in being replaced the acini may be made up of large cuboidal cells and vacuoles, and yet have no ability to stimulate metabolic activity because either the supply of colloid is lacking or other mechanisms such as glucose stores may be inoperative. In a prolonged quiescent state at very low temperatures the metabolic activities may be almost abolished. If the thyroid can continue to function, even at a very slow rate, it may eventually return to normal or assume the histological appearance of slight activity, as the animal slowly recovers. If the low temperature is prolonged too much a hypotrophic status may develop, not unlike that resulting from starvation.

The mechanism for maintaining life in an artificial state of hypothermia, and the ability to recover normal body temperature following either a short or a prolonged state of hypothermia thus involve a number of complicated mechanisms calling into play several of the endocrine glands and a vast number of complex chemical reactions. The thyroid gland evidently plays an important role in this complex picture.

CONCLUSIONS

1. There is a gross enlargement of from 1 to 3 times normal size, and an engorgement of the thyroid gland, together with microscopic evidence of hyperactivity of the follicular epithelium in a large proportion of rabbits whose body temperatures have been reduced to 27-10°C. within a period of 2 to 5 hours.

2. The metabolism is greatly increased, particularly during the stage of recovery from temperatures near 25.0°C., but as the temperature falls the metabolism diminishes rapidly. It was nearly zero at the lowest temperature measured (19.0°C.).

3. If the temperature is reduced too rapidly, death occurs. An increase in circulation and follicular cell size takes place but the gland is devoid of colloid. In particularly severe reactions diffuse edema is also present in the gland.

4. Most rabbits lapse into a state of artificial hibernation at a body temperature below 28.0°C. The thyroid gland appears hyperactive, shows a loss of colloid, large cuboidal follicular cells, and a considerable increase in circulation during the early phases of this state. Yet after prolonged periods of 6 to 24 hours at this level or lower a hypoplastic status develops, usually in keeping with the length of the hibernation status, from which the animal may not be able to recover spontaneously. Recovery can be brought about in some cases by the application of heat.

5. Prolonged maintenance of hypothermia (30 to 48 hours) at higher levels of 25–28°C. may result in a thyroid picture of hypoactivity, showing excessive colloid and flattened epithelium and resembling the picture of starvation.

6. Following either partial or complete recovery from a state of hypothermia, each consecutive additional hypothermic state can be produced more rapidly and easily and with less ability on the part of the rabbit to recover. In such cases the thyroid shows an abundance of colloid, suggesting an ability of the gland to manufacture and store this material, but an inability to utilize it—probably due to the failure of other mechanisms such as glucose stores, etc.

7. The ability of the rabbit to withstand hypothermic states thus depends in part upon the state of activity of the thyroid, as well as upon its capacity to function over a prolonged period at low temperature.
basal metabolism equipment and facilities used by Mr. Robert Ryer, III.

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