tinamide excretion produced by this feeding was in the same range as that which resulted from the intravenous administration. Differences between the two routes of administration are within the limits of the usual daily variations that occur in the excretion of this substance. We have noted that the daily N^1 methyl nicotinamide excretion may fluctuate as much as 1.7 mg even when the infant is maintained on a constant diet.

Discussion. The rise of urinary N^1methyl nicotinamide excretion produced by the intravenous administration of L-tryptophan leads to the conclusion that the conversion of tryptophan to nicotinic acid in man takes place in the tissues rather than in the gastrointestinal tract as a result of bacterial action. This premise is strengthened both by the fact that the N^1methyl nicotinamide values are the same regardless of the route of administration, and by the fact that this increase takes place so promptly. For this conversion to occur as a result of tryptophan excretion into the gastrointestinal tract and subsequent action by bacteria there, one would anticipate a considerable time lag which actually did not occur.

The differences in the rates of administration are sufficient to explain the variance of our results from those of Schweigert *et al.*[13-15] One can postulate that our slow rate of injection raised the blood tryptophan level for a prolonged period of time thereby giving the tissues more time to produce the conversion. The method of a single large injection may provide such a large excess of tryptophan that it may be disposed of in other ways. This may also account for the results obtained by Ellinger and Abdel-Kader[12] who do not give any details regarding the technic of their parenteral tryptophan.

Of interest in this connection are the recent communications of Schweigert *et al.*[17] and of Singal, Sydenstricker and Littlejohn.[18] The former, working with chick embryos observed an increase in the nicotinic acid content of the tissues after an injection of tryptophan. The latter authors reported that the administration of L-tryptophan to rats caused an increase above normal of the nicotinamide concentration of the liver, a phenomenon observed in this organ alone.

Summary. The intravenous administration of one gram of L-tryptophan to infants on constant diets gave a prompt and large rise in the urinary N^1methyl nicotinamide which was equal in magnitude to that provoked by oral administration of the tryptophan. In view of these findings, the conversion of tryptophan to N^1methyl nicotinamide in man seems to be mediated by the body tissues rather than by bacterial synthesis in the gastrointestinal tract.

[17] Schweigert, B. S., German, H. C., and Garber, M. J., *J. Biol. Chem.*, 1948, **174**, 383.

[18] Singal, S. A., Sydenstricker, V. P., and Littlejohn, J. M., *J. Biol. Chem.*, 1948, **176**, 1069.

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Effect of Iodide on Thyroid Glands of Rats Kept at Low Temperature.

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A number of workers have noted that the thyroid glands of rats kept in the cold develop hyperplasia, thickened acinar epithelium, and loss of colloid characteristic of a hyperactive thyroid gland. It was of interest to determine whether the administration of iodide to rats kept under cold-room conditions would cause involution of the thyroid gland as it does in toxic goiter.

Four groups of male albino rats of the

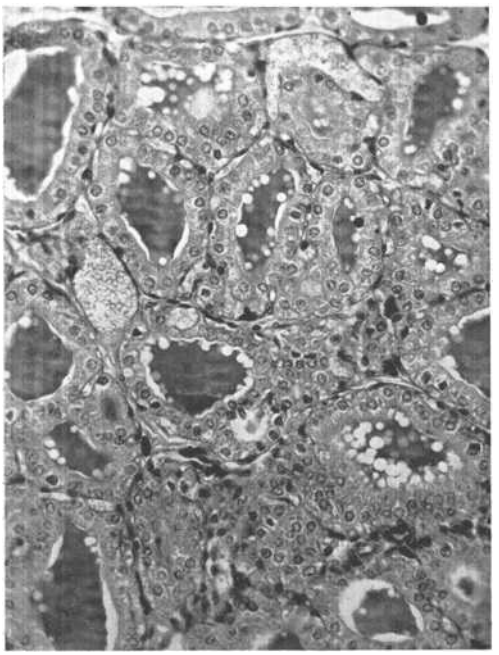

FIG. 1.

University of Southern California strain weighing between 200 and 350 g were used. Groups A and B were kept in single cages at room temperature (21 to 25°C) and groups C and D were kept in single cages with wire bottoms in a cold room maintained at 4°C. Groups A and C were on a stock diet consisting of ground oats 33%, cottonseed oil fortified with vitamins A and D 10%, wheat flour 38%, skimmed milk 14%, alfalfa 4%, yeast 2%, NaCl 0.5%, and $CaCO_3$ 0.5%. Groups B and D were maintained on this same diet to which had been added 50 mg KI per 100 g diet. The food intake and weight changes were determined at 3-day intervals.

At the end of 3 weeks, the animals were weighed, sacrificed, and the thyroid glands removed and weighed. The glands were fixed in formalin and stained with hematoxylin-eosin for histological examination. (In 6 cases animals were killed at the end of 2 weeks). The average epithelial heights and colloid diameters were determined on 100 different follicles from different parts of the thyroid glands.

Fig. I shows representative histological sections from thyroid glands of animals from the 4 groups. IA is typical of thyroid sections from Group A and shows a histological picture characteristic of a normal, moderately-active gland. 1B is a section from the thyroid gland of a rat from Group B receiving iodide at room temperature. It is seen that the gland is less active with thinner epithelium and more colloid. Exposure to low temperatures for 3 weeks brings about a marked hyperplasia with loss of colloid and thickened epithelium (1C). Administration of iodide prevented this hyperplasia and brought about a more normal-appearing thyroid gland in spite of the exposure to cold (1D).

Table I shows the data on the thyroid weights, epithelial heights, and colloid diameters of the 4 groups.

The data in Table I amplify the conclusions illustrated by Fig. 1 and show that iodide greatly reduces the thickness of the thyroid acinar epithelium and increases the colloid in the glands of animals made hyperactive by exposure to cold. These results are in accord with those obtained by Starr and Roskelley,[1] and stimulates the involuting effect of iodine in hyperthyroidism. It seems likely that iodine reduces the activity of the thyroid gland by a similar mechanism in both cases. It is of interest that the weight of the thyroid gland varied but little in the various groups—the amount of epithelium being inversely related to the amount of colloid.

Little can be said as to the mechanism of this involuting action of iodide at the present time. The work of Wolff and Chaikoff[2] clearly shows that increases in the blood iodide levels inhibit the formation of thyroxine by the thyroid gland of rats. Such an observation does not, however, explain the fact that iodide causes an accumulation of colloid in the thyroid follicles of cold-treated rats or of hyperthyroid individuals. It is possible that the effect of iodide on colloid accumulation may be brought about by a mechanism not related to hormone synthesis. The thyroid

[1] Starr, P., and Roskelley, R., *Am. J. Physiol.*, 1940, **130**, 549.

[2] Wolff, J., and Chaikoff, I. L., *J. Biol. Chem.*, 1948, **174**, 555.

TABLE I.
Effect of Iodide on the Thyroid Glands of Rats at Room Temperature or at 4°C.

Group	Treatment	No. of animals*	Wt gain	Thyroid weight, mg/100 g	Epithelial height, microns	Colloid diameter, microns§
A	Room temp. stock diet	5	10.8	10.4	9.1	41
B	Room temp. stock diet 0.05% KI	4	—26.3	12.7	3.5	60
C	4°C stock diet	11†	—18	12.8	12.9	34
D	4°C stock diet 0.05% KI	5‡	—43	13.4	8.3	47

* No. of experimental animals varies due to deaths during the course of the experiment. Figures represent animals surviving at end of 21 days.
† Including 4 animals killed at end of 2 weeks.
‡ Including 2 animals killed at end of 2 weeks.
§ Mean of long and short diameters.

develops like a salivary gland which later loses its excretory pathways, leaving the thyroglossal duct as a remnant. Colloid may, therefore, be considered as a secretory product of the thyroid gland trapped in the alveoli. Iodide is known to cause hypersecretion and hypersalivation and may therefore also be considered to induce secretion of colloid into the thyroid follicles. Such colloid would, from the results of Wolff and Chaikoff, be expected to be low in organic iodine.

Summary. The hyperplasia of the thyroid epithelium produced in rats by exposure to cold-room conditions for 3 weeks can be prevented by increasing the iodide level of the diet. The mechanism of this effect would appear to correspond to the involuting action of iodide in the thyroids of patients with hyperthyroidism. It is difficult to explain these effects on the basis of the inhibition of hormone synthesis, and it is submitted that iodide may stimulate the secretion of colloid into the lumen of thyroid follicles by a mechanism related to its stimulating influence on salivation.

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Tetanus Prophylaxis with Penicillin-Procaine G.

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Clostridium tetani is sensitive to penicillin *in vitro*[1] and *in vivo*.[2,3] The development of penicillin-procaine has resulted in prolonged therapeutic blood levels following a single injection.[4,5] Claims have been made for inhibitory levels which are maintained for as

1 Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, E. D., Heatley, N. G., Jennings, M. A., Florey, H. W., *Lancet*, 1941, **2**, 177.

2 Weinstein, L., and Wesselhoeft, C., *New England J. Med.*, 1946, **233**, 681.

3 Diaz-Rivera, R. S., Deliz, L. R., Berio-Suarez, J., *J.A.M.A.*, 1948, **138**, 191.

4 Herrell, W. E., Nichols, D. R., and Heilman, F. R., *Proc. Staff Meet., Mayo Clinic*, 1947, **22**, 567.

5 Sullivan, N. P., Symmes, A. T., Miller, H. C., Rhodehamel, H. W., Jr., *Science*, 1948, **107**, 169.