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Colloidophagy in the Human Thyroid Gland[1]

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Various investigators have observed invasion and ingestion of colloid by macrophages (colloidophagy) in the thyroids of animals. The first to describe this process were Leo Loeb and Gray (*1*). Thurston (*2*), after injection of pituitary extract, saw phagocytosis of colloid in the thyroid of guinea pigs, rats, and pigeons.

According to Eggert (*3*), phagocytes play an important role in the resorption of colloid. After giving large doses of thyrotropic hormone he saw, in the thyroids of lizards, wandering cells enter hypertrophic follicles, ingest colloid, and carry it into the interfollicular vessels. R. G. Williams (*4*) studied living thyroid follicles in transparent chambers inserted in rabbits' ears. He saw in the colloid of some activated follicles 1–20 wandering cells. Their number changed from day to day in the same follicles, eventually disappearing. Thyrotropic hormone increased the activity of these colloidophages; there was no evidence of degeneration of the epithelium in the invaded follicles.

In human thyroids, this process of colloidophagy has never been studied. Although cells have been described repeatedly in follicular lumens, they were regarded as desquamated, degenerated cells of the follicle wall.

During a study of microscopic slides from 435 goiters removed by operation and from 619 thyroids obtained by autopsy, I often found cells lying in colloid—i.e., in 63.9% of surgical goiters and in 16.2% of normal thyroids obtained by autopsy. Almost without exception we noticed groups of lymphocytes in the area surrounding the involved follicles.

These intrafollicular cells varied in number from 1 to 20 in one lumen; they were of large size, their cytoplasm was eosinophilic, and their nucleus was oval or kidney-shaped. They did not resemble thyroid cells at all, and there was no evidence of degeneration of the involved follicles. To discover the nature of these cells, small pieces of fresh surgical goiters were teased with dissecting needles on slides. They were stained supravitally with neutral-red (1:10,000 physiologic salt solution) and examined ½ hr later under the microscope. In 11 of the 23 cases typical macrophages

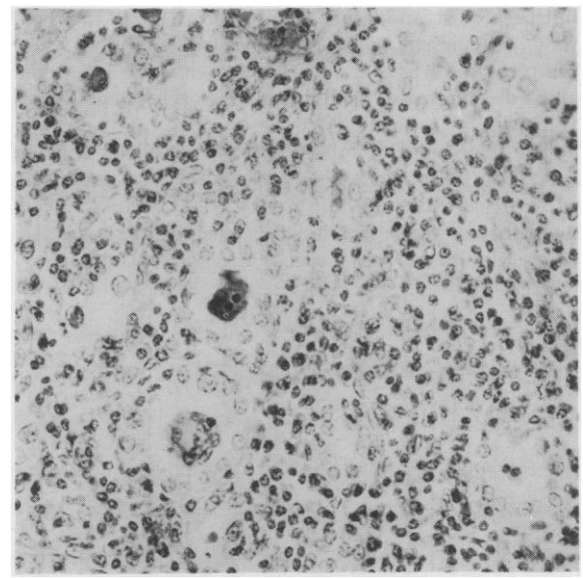

FIG. 1. Normal human thyroid with macrophages in follicles. (Colloidophages, × 400.)

filled with large salmon-red granules were seen within the lumen of thyroid follicles, and in 10 cases they were also present in the interfollicular tissue; the follicle epithelium remained unstained or showed only fine granules.

Although under normal conditions the macrophages, after ingestion of colloid, reenter the blood vessels, two pathological phenomena may result from colloidophagy in human goiter. First, in many exophthalmic and lymphadenoid goiters the macrophages within the follicular lumen fuse together, forming a large multinuclear syncytial mass (Fig. 1); second, macrophages loaded with colloid do not reenter the blood vessels

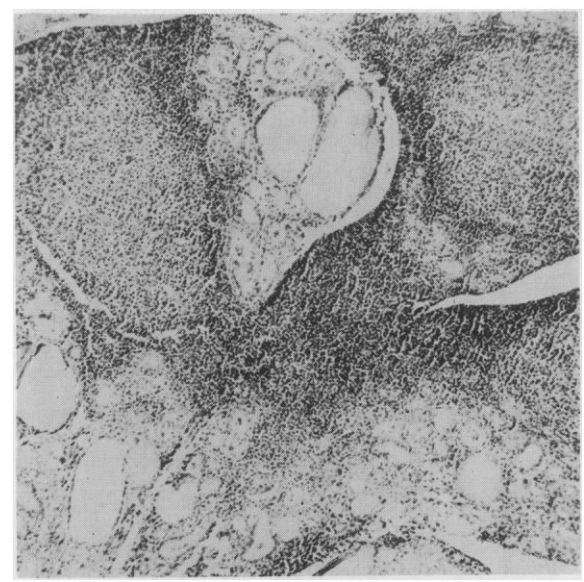

FIG. 2. Human thyroid with lymph follicles containing colloid; so-called chronic thyroiditis. (× 100.)

[1] The electron microscopic study of colloids was aided by a grant from the American Cancer Society.

but become stranded in the interfollicular tissue. Here they degenerate, and the liberated colloid attracts lymphocytes (Fig. 2). Then one can see large red-stained clumps of colloid in the center of lymph follicles.

The process of colloidophagy, followed by accumulation of lymphocytes, is apparently the underlying cause of so-called chronic thyroiditis, which is so common not only in normal-sized thyroids, but especially in exophthalmic goiter and lymphadenoid goiter (*5*).

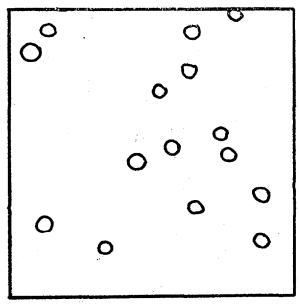

FIG. 3. Colloid of normal human thyroid, without colloidophagy. Camera lucida drawing, × 15 of original electronmicrograph × 5,000 m. (Total magnification × 75,000 m, reduced to × 37,500 in reproduction.)

The cause of chronic thyroiditis has never been satisfactorily explained, and chemical or bacterial agents responsible for this disease have never been found. What, then, causes this invasion of colloid by wandering cells? From animal experiments, we know that excess of thyrotropic hormone stimulates colloidophagy in the normal thyroid. Lymphadenoid goiter in which colloidophagy with aggregation of lymphocytes is always present has been related to an excess of thyrotropic hormone (*6*). We therefore feel justified in assuming that overstimulation of the thyroid by thyrotropic hormone changes the properties of the colloid in such a way that it attracts macrophages.

In the electron microscope the extract of human lymphadenoid goiters and of rabbit thyroids activated by thyrotropic hormone looks different from that of normal thyroids. The colloid of normal thyroids appears in the electron microscope to be composed of globules, about 25 mμ in diameter (Fig. 3), and the colloid of lymphadenoid goiter and of rabbit thyroids stimulated with thyrotropic hormone reveals bizarre, wedge-shaped, angular, and sharp-edged particles measuring about 160 mμ in length (Fig. 4). These structural changes of the colloid suggest chemical alterations that would explain the attraction of macrophages by chemotaxis.

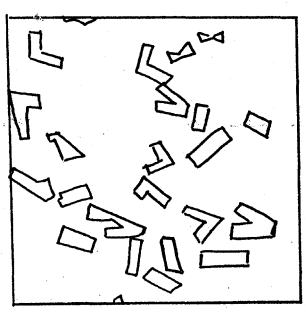

FIG. 4. Colloid of human lymphadenoid goiter with colloidophagy. Camera lucida drawing, × 15 of original electronmicrograph × 5,000 m. (Total magnification × 75,000 m, reduced to × 37,500 in reproduction.)

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Induction and Blossoming of *Xanthium*[1]

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Studies on the photoperiodic induction of *Xanthium* are particularly responsible for the widespread idea that the induction stimulus is the controlling factor that causes the blossoming of plants. A principal item contributing to this belief is the fact that the proper grafting of a flowering plant to a nonflowering one results in the blossoming of the latter. Other plants that blossom systematically (such as soybean) can be made to flower by grafting (*1*), but those that flower only terminally cannot be so "induced." Also, the latter "devernalize" readily with a change in the environment, such as temperature. Conspicuous examples are azalea (*2*), chrysanthemum (*3*) and onion (*4*). From this it is evident that induction does not necessitate flowering. So-called photoperiodic plants, such as pigweed and soybeans (not Biloxi), which become indeterminate with age, and also indeterminate forms, suggest a condition of either internal or self-induction or that flower formation may be independent of induction. At least "ripeness to flower" (*5*) occurs without any conspicuous or readily discernible induction condition having been detectable.

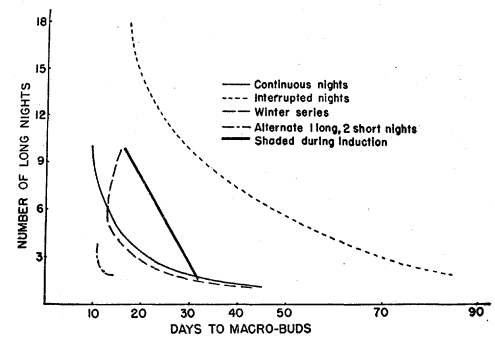

FIG. 1. Relation of inductions (long nights) to time of appearance of macro blossom buds in *Xanthium* (Wis. sp.) under various environmental conditions.

More recent studies with *Xanthium* sp. native to

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