In nearly all the above mentioned characteristics Lag. obliquidens of the North Pacific corresponds with its southern relatives, but has a quite different geographic distribution so that we hesitate to incorporate these animals in the southern species until a good comparison between the different skeletons can be made.

It remains an open question whether within the limits of the new southern species Lagenorhynchus cruciger (Quoy et Gaim.) two or more of the old species may be regarded as subspecies, geographical races or not. The number of records about their distribution and colour variation is too small. With reference to this last information, however, some attention may in the future be paid to the statement of WILSON (1907; p. 9) that "the distribution of these two Dolphins (Lag. obscurus (Gray) and Lag. wilsoni Lillie) appears to overlap, and yet, though we had many schools of each from time to time around the ship, they never mingled".

(To be continued.)

Zoology. — On the position of the Golgi-apparatus in the thyroid-cell under normal and experimental conditions. (Preliminary note). By J. Lever. (Zoological Laboratory, Dept. of Endocrinology, University of Utrecht) 1). (Communicated by Prof. Chr. P. Raven.)

(Communicated at the meeting of November 29, 1947.)

It is generally accepted that the position of the Golgi-apparatus in a cell is related to its metabolic function. Consequently in secreting cells the Golgi-apparatus is mostly found between the nucleus and the pole of the cell where its secretion is discharged. Therefore one can easily understand that in cells in which the direction of secretion is always the same the position of the Golgi-apparatus is stable. It was also found by BEAMS and KING (1933) that the position of the Golgi-apparatus of the rat-ameloblast changes from the side of the cell, where the secretion takes place, to the other side when the inactive phase is initiated.

In case the direction of secretion changes, the position of the Golgiapparatus is not always necessarily constant, and may vary according to the physiological state of the cell.

An example of this mode of secretion is offered by the thyroid-epithe-liumcell. Many authors believe that the thyroidcell is not only able to pour its secretion into the follicular lumen, where it is stored in the so-called colloid, but also may resorb the hormone from the colloid in order to secrete it into the blood capillaries. According to COWDRY (1922) the differences in direction of secretion may be reflected by a reversal in the position of the Golgi-apparatus of the thyroidcell. In the latter the Golgi-apparatus is normally found at the apical side of the nucleus, which points to a secretion-activity towards the follicular lumen (fig. 1).

In some cases, however, COWDRY observed in the adult guinea-pig thyroid that the Golgi-apparatus had reversed to the other side of the nucleus, lying between the latter and the basal side of the thyroid cell. These observations seemed to prove that the Golgi-apparatus may migrate from one part of the cell to the other, according to the direction in which the hormone is secreted. On the other hand CRAMER and LUDFORD (1926) found that in thyroid glands, hyperactive under the influence of cold or of  $\beta$ -tetra-hydronaphthyl-amine, a reversed Golgi-apparatus is only very rarely observed. Moreover, these authors claim that COWDRY's observations relate to inactive thyroid cells. Reversals of the Golgi-apparatus were also found by LUDFORD and CRAMER (1928) in men and mice with exophthalmic goitre. Reversal of the Golgi-apparatus was stated by some other investigators too, e.g. by Shiro Ishimaru (1926) in the rabbit-

<sup>1) 24</sup>th Communication of the "Werkgemeenschap voor Endocrinologie", part of the "National Council for Agricultural Research T.N.O.".

thyroid, from which a large part had been resected; INGRAM (1930) and KROGH, LINDBERG and OKKELS (1932) induced in very rare cases reversal of the Golgi-apparatus after administering thyrotrophic hormone to guineapigs, but WAGSCHAL (1930), UHLENHUTH (1931), OKKELS (1932, 1934), SEVERINGHAUS (1933) and GILLMAN (1934) were not able to demonstrate it.

With regard to the functional state of the thyroid cell, GILLMAN (1934) distinguished 3 cellphases viz. 1. the resting stage, 2. the anabolic stage, in which secretion towards the lumen takes place, and 3. the katabolic stage, characterized by the secretion towards the interfollicular bloodsystem of the gland. After a detailed study of serial sections he concluded that the reversal of the Golgi-apparatus, observed by COWDRY and in rare cases by CRAMER and LUDFORD (1926), was only apparent, because in resting and in anabolic thyroid cells the Golgi-apparatus is often a perinuclear one. In katabolic cells, however, in which the nucleus is not so closely surrounded by the Golgi-apparatus, it is not possible to observe a basal fragment of the latter. Therefore a reversal of it has never been stated in katabolic cells. GILLMAN concludes that the phenomenon of reversal would be proved, if it could be observed in a katabolic cell stage, this being the only stage in which secretion towards the bloodvessels takes place.

Recent investigations with the aid of radioactive J<sup>131</sup> and of antithyroid substances have strongly enlarged our knowledge of the functional processes in the thyroid cell. It is now generally accepted that especially thiourea-derivatives prevent the normal production of the active thyroid hormone (LARSON c.s., 1945a, 1945b; RAWSON c.s., 1944, 1946). Moreover, it is known that as a result of the hormone synthesis being prevented in the thyroid, a decrease of the hormone concentration in the blood and of the basal metabolic rate in the peripheral bodycells takes place, when the colloid supply in the follicles begins to diminish, which results in an increased production of thyrotrophic hormone by the anterior lobe of the hypophysis. In addition BAUMANN c.s. (1942) showed that this hormone induces the resorption of the thyroid hormone by the follicle cell and its secretion towards the blood capillaries; moreover, ASTWOOD c.s. (1944), DEMPSEY (1944) and GRASSO (1946) found, after administering antithyroid substances that the thyroid is able to secrete an inactive product in which thyroxine is lacking.

Taking these facts into consideration we thought it interesting to trace the influence of 4-methyl-2-thiouracil (Brocapharm) on the position of the Golgi-apparatus in the follicle cells of the thyroid gland. We might expect that then the anterior lobe of the hypophysis would respond by a thyrotrophic hormone output, which likely would increase gradually and would cause a more physiological process in the thyroid than the injection of thyrotrophic hormone can accomplish.

J. LEVER: On the position of the Golgi-apparatus in the thyroid-cell under normal and experimental conditions.

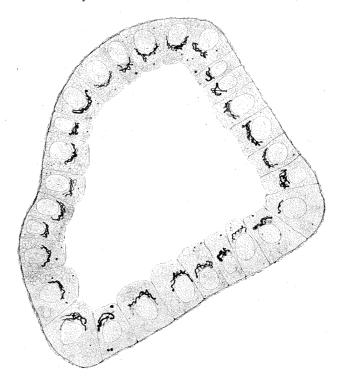


Fig. 1. Thyroid-follicle of a normal cockerel, Follicle cells more or less cubical; Golgi-apparatus exclusively at apical side of the nucleus.  $\times$  1200.

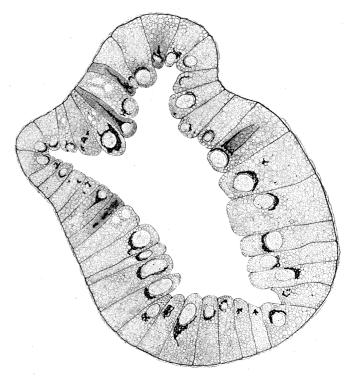


Fig. 2. Thyroid-follicle of a fattened cockerel, treated with 4-methyl-2 thiouracil. Follicle cells high columnar; in many cases reversal of the Golgi-apparatus to the basal side of the nucleus.  $\times$  1200.

As experimental animals cockerels, 10—14 weeks old, were used; they were kept in small cages in which their bodymovements were more or less hampered. Each cockerel received a daily dose of 50 mgr. 4-methyl-2-thiouracil pro 100 grams of food for 2 or 3 weeks; they were put on a diet, used normally in fattening, i.e. practically without proteins, but rich in carbohydrates. As controls birds on normal and fattening food were used.

The thyroid glands were fixed in Bouin's or Helly's fluid and stained with haematoxylin-eosin or azan, respectively. Moreover, Golgi-preparations were made after fixation in Champy's and Cajal's fluid.

It became evident that within 2 weeks the microscopical structure of the thyroids changed completely. In most of the follicles the colloid had disappeared totally. The epithelium cells which are cubical in normal animals, became high columnar in the experimentals, their height increasing from 5—10  $\mu$  to more than 20  $\mu$ . Their nuclei, lying normally at the basal pole of the cell, migrated towards the apical side.

In normal resting or anabolic thyroid cells the Golgi-apparatus was found lying as a small reticulum at the apical side of the nucleus (fig. 1). In methyl-thiouracil-treated birds it was found in about 60 % of the thyroid cells at the opposite side (fig. 2). As these cells have a high columnar shape and possess a migrated nucleus, they must be classified as katabolic cells.

In the thyroids of fattened birds, which had not been treated with methyl-thiouracil, the phenomena described above, i.e. increase in height of the epithelial cells, decrease of colloid content and reversal of the Golgi-apparatus, occurred in a less degree. In the food with which the cockerels had been fattened the iodine-content is much lower than normal, this obviously being the limiting factor for hormone synthesis, which finally results in an increase of the thyrotrophic hormone output.

From these observations it follows that under extreme conditions a reversal of the Golgi-apparatus can take place in the epithelium cells of the thyroid gland.

As in normal cockerels fed on a diet, containing iodine in sufficient quantities, this reversal does not take place and possibly the body's need of thyroid hormone is satisfied gradually, we presume that in this case a reversal of the Golgi-apparatus is not necessary. On the other hand a reversal in some cells may be thinkable under normal conditions as e.g. under the influence of severe cold, when the body needs much thyroid hormone. Also one can understand that an increased secretion of thyrotrophic hormone by the anterior lobe of the hypophysis may be the cause of reversal of the Golgi-apparatus after iodine deficiency. Therefore it is also comprehensible that under extreme pathological or pharmacological circumstances a general reversal will take place. Consequently it is understood that Shiro Ishimaru (1926) observed reversals in the thyroid of the rabbit after resection of a large part of it, as well as Ludford and

CRAMER (1928) in cases of exophthalmic goitre in men and mice. In such cases the thyroid cells must function as much as possible to provide the large quantity of thyroid hormone, needed by the body.

## Summary.

4-methyl-2-thiouracil in normal and in fattening diets was fed in a dose of 50 mgr. pro 100 grams of food during 2—3 weeks to cockerels, 10—14 weeks old.

In normal fattened cockerels and, in a higher degree, in fattened cockerels, treated with methylthiouracil, many reversals of the Golgiapparatus from the apical towards the basal side of the thyroid epitheliumcell were found.

As it is known that in the first case the iodine was deficient, in the second the antithyroid substance moreover acted on the thyroid by inhibiting the process of iodinization, resulting in hyperactivity of the thyroid gland, it is thought that both reactions are induced by thyrotrophic hormone, secreted in excess by the anterior lobe of the hypophysis.

Therefore all cases of reversal of the Golgi-apparatus, those found under pathological conditions [ISHIMARU (1926); LUDFORD and CRAMER (1928)] included, can be explained by an extreme activity of the thyroid epitheliumcell, being the result of an extreme output of thyrotrophic hormone.

Acknowledgements. I wish to thank Prof. G. J. VAN OORDT for his kind advice and encouragement during this investigation, Dr. I. I. DUYVENÉ DE WIT for suggesting histological studies on the influence of antithyroid substances on the fowl's thyroid and Ir. P. UBBELS for his valuable help in obtaining the experimental material. My thanks are also due to "Brocapharm" (Amsterdam) for the gift of methylthiouracil.

## REFERENCES.

- ASTWOOD, E. B. and A. BISSELL. Effect of thiouracil on the iodine content of the thyroid gland. Endocrinology, vol. 34, 282 (1944).
- BAUMANN, E. J., N. METZGER and D. MARINE. Total iodine and thyroxine of the thyroid after hypophysectomy. Endocrinology, vol. 31, 359 (1942).
- BEAMS, H. W. and R. L. King. The Golgi-apparatus in the developing tooth, with special reference to polarity, Anat. Rec., vol. 57, 29 (1933).
- COWDRY, E. V. The reticular material as an indicator of physiologic reversal in secretory polarity in the thyroid cells of the guinea-pig. Am. Journ. of Anat., vol. 30, 25 (1922).
- CRAMER, E. and R. J. LUDFORD. Cellular activity and cellular structure as studied in the thyroid gland. Journ. of Physiol., vol. 61, 398 (1926).
- DEMPSEY, E. W. Fluorescent and histochemical reactions in the rat thyroid gland at different states of physiological activity. Endocrinology, vol. 34, 27 (1944).
- GILLMAN, J. The cellular cycle, the Golgi-apparatus and the phenomenon of reversal in the human thyroidparenchyma. Anat. Rec., vol. 60, 209 (1934).
- GRASSO, R. The action of thiourea on the intracellular colloid of the thyroid gland-Anat. Rec., vol. 95, 365 (1946).

- INGRAM, W. R. Studies of amphibian neoteny. III. The Golgi-apparatus of thyroid cells of Rana clamitans in relation to the anterior pituitary. Anat. Rec., vol. 46, 233 (1930).
- ISHIMARU, SHIRO. Ueber den Golgi-Apparat in den Schilddrüsenzellen. Folia Anat. Japonica, vol. 4, 13 (1926).
- KROGH, M., A. L. LINDBERG and H. OKKELS. Studies on the thyroid gland. III. Experimental hyperactivity of the thyroid gland. Acta Pathol. et Microbiol. Scandinavica, vol. 9, 37 (1932).
- LARSON, R. A., F. R. KEATING JR., W. PEACOCK and R. W. RAWSON. A comparison of the effect of thiouracil and of injected thyrotropic hormone on the collection of radioactive iodine and the anatomic changes induced in the thyroid of the chick. Endocrinology, vol. 36, 149 (1945a).
- The effect of thiouracil on the collection of radio-active iodine by the thyroid of the chick. Endocrinology, vol. 36, 160 (1945b).
- LUDFORD, J. R. and W. CRAMER. The mechanism of secretion in the thyroid gland Proc. Roy. Soc., Series B, vol. 104, 28 (1928).
- OKKELS, H. Studies on the thyroid gland. I. On the histology and cytology of normal and abnormal thyroids in man. Acta Path. et Microbiol. Scandinavica, vol. 9,
- Cellular structure and cellular activity. Skand. Arch. für Physiol., vol. 69, 97 (1934).
- RAWSON, R. W., J. F. TANNHEIMER and W. PEACOCK. The uptake of radioactive iodine by the thyroids of rats made goiterous by potassium thiocyanate and by thiouracil. Endocrinology, vol. 34, 245 (1944).
- RAWSON, R. W., A. ALBERT, J. W. McARTHUR, P. MERRILL, B. LENNON and CH. RIDDELL. The reversible inactivation of thyrotropic hormone. Its inactivation by thyroid tissue and reactivation by thiouracil and other goitrogenic agents. Endocrinology, vol. 39, Abstracts (1946).
- SEVERINGHAUS, A. L. Cytological observations on secretion in normal and activated thyroids. Z. für Zellforsch. und mikr. Anat., vol. 19, 653 (1930).
- UHLENHUTH, E. The Golgi-apparatus in the secretion process of the thyroid gland, Anat. Rec., vol. 52, 40 (1932).
- WAGSCHAL, L. L'hyperactivité thyroïdienne. C. R. Soc. de Biol., vol. 107, 1015 (1931).