

EDITORIAL

FLUORIDE AND THE THYROID GLAND

In 1854 Maumené (1) administered to a dog from 20 to 120 mg sodium fluoride daily for four months. He observed an enlargement of the neck which he interpreted as a goiter. Ever since then conflicting data concerning the action of fluoride on the thyroid gland have appeared in the medical literature. In the early part of this century several authors concurred that fluoride intake may contribute to the production of goiter. This concept led to the administration of sodium fluoride for the control of hyperthyroidism on a large scale, particularly in Germany, Switzerland and Argentina. Gorlitzer (2) even advocated baths in a dilute HF solution as a treatment for toxic goiter. Subsequently numerous papers favoring and denying a significant goitrogenic effect to fluoride have appeared.

The current issue of "Fluoride" contains two articles bearing on this subject. Both originated in countries where fluorosis is endemic. Siddiqui's observations were made in India and those of Fradà et al., in an area north of Rome.

Although Siddiqui's survey was carried out on a small population, it is well controlled and the results are noteworthy. In the group studied between the ages of 14 and 17 he established a direct relationship between the incidence of small, visible goiter and increasing concentration of fluoride in drinking water. Furthermore, his data suggests the possibility of an inverse relationship between the incidence of type b goiter and increasing concentration of iodine.

As pointed out by Baumann and Metzger (3), the affinity of the thyroid for halides leads to competition by the thyroid for fluoride and iodide ions. A level of fluoride which may produce physiological changes in the thyroid gland at one level of iodine intake, will not do so at a higher iodine intake.

Galletti et al. (4) observed that fluorine did not impair the capacity of the thyroid to synthesize the thyroid hormone when there was an abundance of iodine in the blood. However, when the total iodine pool was low, there was inhibition to the thyroidal concentration capacity. One of his patients was promptly cured of hyperthyroidism, with return of laboratory data to normal, following four months of fluoride therapy; but during this interval he developed a nodular goiter. Treatment with 100 to 120 μg of iodide resulted in a spectacular relapse with disappearance of the goiter. When the hyperthyroidism was subsequently controlled with fluorides, the goiter reappeared.

In Siddiqui's study, goiter occurred exclusively during the mid-teen years when growth and metabolic activity are high; furthermore, females were affected much more frequently than males.

The calcium content of the water supply in this study was randomly distributed except for the one high value of 7.99 mg/100 ml in one of the wells of Kamaguda. In any study attempting to correlate the fluoride level of water supplies with physiological changes the calcium level in water may be important because increasing calcium concentrations may decrease the effectiveness of fluorides (5).

Siddiqui observed that water containing approximately 5 mg of fluoride per liter will produce small goiters, a gross abnormality. The question arises as to how much more frequently such levels of fluoride produce subtle physiological changes. Such disturbances cannot be ruled out by the absence of macroscopic and microscopic changes in the thyroid in persons exposed to minute amounts of fluorides.

Fradà and co-workers studied the effect of fluoride ingestion on thyroid physiology in 52 patients chosen from 400 with signs of dental, skeletal or visceral fluorosis. The authors, employing radioisotope techniques, observed no significant differences in the experimental and control group. These findings contradict many reports and agree with others. Galetti's series in which he revealed a suppression of the initial and maximum radioactive iodine thyroid uptakes with 5 mg of fluoride, was composed wholly of patients with hyperthyroidism. Other parameters have been operative but not controlled in the studies.

The following points explain negative findings in the presence of possible subtle changes:

1. Whereas the radioactive uptake test is effective in differentiating between the hyperthyroid and the euthyroid patient, it is not reliable in distinguishing between hypothyroidism and euthyroidism. Since fluoride is expected to depress thyroid uptake, the radioactive iodine uptake test is not very discriminating. The wide range of normals (15-40%) for this test illustrates the difficulty encountered in its application for the detection of minor abnormalities. Obviously large control and test groups would be necessary to demonstrate any statistically significant depressing effect of fluorides unless such a defect were marked.

2. Most laboratories have abandoned the 24 hour conversion ratio in evaluating thyroid function. Instead, the serum radioactivity is determined 72 hours after ingestion of radioactive iodine. This time lapse permits the unbound ^{131}I to be excreted by the kidneys.

3. Thyroid scans correlated with careful palpation of the thyroid gland provide some impression as to the gland size. Yet this method is not very accurate. Some workers have injected air into the fascial planes in order to delineate the gland upon AP and lateral X-ray views of the neck. When a lateral scan of the thyroid is added to the anterior scan, the estimation of size can be made more accurately.

4. The average value of the 24 hour thyroid uptake appeared to be unusually high in the paper by Fradà et al. For comparison, I reviewed the 24 hour uptake in the last 50 cases performed in our laboratory. The possibility of bias for low values was eliminated by omitting all studies on patients with a suspected diagnosis of hypothyroidism and of cancer which is frequently associated with low values. Cases with suspected hyperthyroidism were not eliminated. The average uptake in the remaining 40 patients was 25.5%, compared with 39% for 48 subjects reported in the Italian study (four high readings in an obviously toxic range were eliminated). It is apparent that either our group of patients has a lower iodine uptake than Fradà's or the techniques of the tests in the two laboratories must be significantly different. Possibly the Italian technique includes a wider area of the neck and therefore more radioactivity is counted within the blood pool. This may also account for the differences in the short interval readings. All of their 8 hour readings were above 20% whereas the upper limits of normal for our 6 hour uptake is 10%. The differences in these two papers exemplify the conflicting literature during the past century. Although many agree with Hein et al, (6) who concluded on the basis of radioactive fluoride in rats that the thyroid selectivity concentrates fluoride from dilute solutions. Yet it is doubtful that such concentrations cause microscopic, macroscopic or physiological changes.

Nonetheless, the literature does permit some generalizations:

- 1) Fluoride enters the thyroid gland and under certain conditions suppresses the production of thyroxine.
- 2) The conflicting data suggest the operation of additional parameters which have not been controlled.
- 3) The more active the thyroid gland, the more sensitive it is to the effects of fluoride.

Bibliography

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