

## EFFECT OF IODIZED OIL TREATMENT ON THE DEVELOPMENT OF THYROID AUTOIMMUNITY IN ADOLESCENT FEMALES

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Thyroid enlargement due to iodine deficiency is widely prevalent worldwide. Iodized oil, either intramuscular or oral, has been used in a number of studies for goiter reduction and prophylaxis.<sup>1-4</sup> Both routes have been shown to be effective, however, iodine is known to cause thyroid dysfunction and change in thyroid immunology,<sup>5</sup> affecting both thyroid hormone secretion and autoantibody production.<sup>6</sup> These effects have been noticed more markedly among patients with underlying thyroid disease.<sup>7</sup> The prevalence of thyroid autoantibodies among the general population in Sudan is not known. However, the estimate for thyroid peroxidase (TPO) antibodies among the general population in other parts is said to be about 15%.<sup>8</sup> The prevalence has been found to rise with age.<sup>9,10</sup>

In this study, highly sensitive assays for measuring thyroid autoantibodies<sup>8-11</sup> were used to assess the immunological effects of a single moderate dose of oral iodized oil. This was compared with 0.1 mg of L. thyroxine daily for six months.

### Subjects and Methods

Eighty-seven female high school students (aged 15 to 18 years) with goiter (WHO grade Ib or above) were studied. All were students of the same high school in Khartoum, Sudan, and were divided at random into two groups. Group 1 (n=46) received 0.1 mg of L. thyroxine daily for six months, and group 2 (n=41) were given a single oral iodized oil capsule (400 mg iodine) (Lipiodol). All the subjects gave informed consent after consulting their parents.

Serum samples were taken immediately prior to the start of treatment, six months after the treatment, and 14 months later. The sera were stored at -20°C and at the end of the study, they were transported frozen to Cardiff (UK) for autoantibody assay. Autoantibodies to Tg and to TPO were measured using a highly sensitive direct assay<sup>6</sup> and

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### Results

Immediately prior to treatment, three subjects had detectable levels of both TgAb and TPOAb and one subject had detectable TgAb only (Tables 1 and 2). All the subjects were by chance allocated to group 1 (T<sub>4</sub> treatment) (Tables 1 and 2). After six months, one further group 1 subject developed low levels of TPOAb, but these were undetectable again at 14 months. An additional group 1 subject developed TgAb at 14 months. Overall, therefore, the prevalence of detectable TgAb and TPOAb in T<sub>4</sub>-treated females was 4/47 (8.5%) at the start of treatment and 3/46 (6.5%) after 14 months. One autoantibody-positive subject was not available for follow-up.

In the group treated with iodized oil (group 2, Table 2), none of the subjects was detectable for TgAb and/or TPOAb at the start of treatment, 2/41 (4.9%) were detectable at six months and 5/41 (12.2%) at 14 months. All five TgAb and/or TPOAb patients in this group were clinically euthyroid, and TSH and free T<sub>4</sub> levels were within normal range.

In terms of changes in levels of initially detectable TPOAb and TgAb over the 14-month period (group 1 patients only), TPOAb levels fell in the two subjects studied (Table 1, patients 1 and 3). Initially detectable TgAb levels fell in one of these subject (Table 1, patient 1) over 14 months and were essentially unchanged in two others (Table 1, patients 3 and 5). At the end of the 14-month period of the study, there was no statistically significant difference (Fisher's test,  $P < 0.19$ ) between the two groups.

In addition to TgAb and TPOAb measurements, serum TRAb levels were assessed and found negative in all sera. Both iodized oil treatment and thyroxine treatment resulted in a progressive reduction in goiter size in about 90% of subjects (Table 3).

### Discussion

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The biochemical changes in thyroid state following iodized oil have been well documented.<sup>3,4</sup> However, the effects on thyroid autoimmunity seem to vary with iodine

TABLE 1. Group 1 patients with detectable TPOAb and TgAb.

Patient	TPOAb (U/ mL)			TgAb (U/mL)		
	0	6 months	14 months	0	6 months	14 months
1	4	8	0	100	100	0
2	0	0	0	0	0	1.3
3	100	4	1.9	1.3	2.5	1.5
4	100	—*	—*	2	—*	—*
5	0	0.2	0	10	10	10

\* Patient unavailable for follow-up.

TABLE 2. Group 2 patients with detectable TPOAb and TgAb.

Patient	TPOAb (U/ mL)			TgAb (U/mL)		
	0	6 months	14 months	0	6 months	14 months
1	0	0	0	0	0.7	0.3
2	0	0	0	0	0	3.0
3	0	0	0	0	0	0.6
4	0	0	0	0	0	10.2
5	0	1.0	0.3	0	4.2	10.0

TABLE 3. Goiter size in T<sub>4</sub>-treated (Group 1) and iodized oil-treated (Group 2) subjects.

Time after Treatment	% of subjects showing					
	Smaller goiter		No change		Larger goiter	
	Iodized oil	T <sub>4</sub>	Iodized oil	T <sub>4</sub>	Iodized oil	T <sub>4</sub>
3 months	68%	71%	32%	27%	0%	2%
6 months	81%	73%	19%	27%	0%	0%
14 months	90%	88%	10%	12%	0%	0%

dose used and the age of the subjects.<sup>1,12</sup> Low doses of iodine were also found to cause transit dysfunction and autoimmunity in patients with endemic goiter.<sup>13</sup> The group was chosen because it was considered that if mass treatment of oral iodized oil were going to be given in Africa, it would be best to target schoolchildren. As our subjects were at the highest level of elementary schooling, they were the most likely to develop any autoimmune changes due to iodine, as the prevalence of thyroid autoantibodies increases with age.<sup>10</sup> Five out of 41 patients in group 2 (12.2%) developed either or both Tg and TPO antibodies. In group 1, only one patient out of the 42 who had no Tg and TPO antibodies developed anti-Tg antibodies (2.4%). There was no statistically significant difference (Fisher's test,  $P < 0.19$ ) between the two groups. This may indicate that iodized oil used in moderate doses early in life may not affect the thyroid immunology. In most of the studies where patients developed thyroid autoantibodies post-iodized oil, the patients were usually above the age of 25 years.<sup>1,14</sup> Supporting this suggestion, Eltom et al. found only two out of 128 schoolchildren with Tg antibodies one year after iodized oil therapy.<sup>3</sup>

As far as we know, thyroid receptor antibodies have not been assessed before in any study in iodized oil therapy subjects. We did not detect significant levels of TSH receptor antibodies (TRAb) in any of our patients before, during or after therapy in both groups. It was pure chance that all four patients with Tg or TPO antibodies were allocated to group 1. Thyroxine was noted to reduce TPO

and Tg antibody levels.<sup>15,16</sup> The number of patients with TPO and Tg antibodies at the start of treatment was too small to draw any conclusion of the effect of L. thyroxine in TPO and Tg antibodies in this group. However, the change from TgAb and/or TPOAb positivity from 0/40 to 5/40 over

14 months of iodized oil treatment presumably reflects an expected increase with age, not apparent in the thyroxine-treated group (3/46 to 3/46 over the 14 months). This suggests that thyroxine treatment might protect against the development of thyroid antibodies, possibly by shutting down synthesis and release of thyroid autoantibodies.<sup>16</sup>

In conclusion, moderate doses of oral iodized oil given during school age seem to have no major effects on the development of thyroid autoantibodies, but are effective in reducing goiter size in endemic areas.

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