**Summary**

**Background:** Although transient thyrotoxicosis occurring after ATD withdrawal in patients with hyperthyroidism due to Graves’ disease (GD) has been reported, the prevalence of transient thyrotoxicosis is as yet unknown.

**Objective:** To investigate the prevalence of transient thyrotoxicosis after ATD withdrawal.

**Design of study and Methods:** A group of 110 consecutive patients with GD was selected, in whom ATD therapy was stopped prospectively between December 2002 & September 2004. Patients were followed up for more than 1 year after ATD withdrawal (12 patients dropped out). Serum levels of free T4, TSH, and titers of TBII were measured at ATD withdrawal and 3, 6, and 12 months after withdrawal. When the patients showed mild thyrotoxicosis (i.e. serum free T4 above normal but below 3 ng/dl), they were followed for one month without reinstituting medication.

**Results:** The remission rate of the study group was 62% (68/110). Twenty eight patients became euthyroid after a phase of transient thyrotoxicosis, equivalent to 41% of the remission patients (28/68). Eight of 28 patients showed overt thyrotoxicosis and the rest subclinical thyrotoxicosis. Transient thyrotoxicosis occurred mostly 3-6 months after ATD withdrawal.

**Conclusions:** Transient thyrotoxicosis after ATD in patients with GD is not a rare phenomenon. Clinicians should be aware that the recurrence of GD after ATD withdrawal may be transient.

**Comment**

ATD therapy is the first-line treatment for hyperthyroidism due to Graves’ disease (GD) in Europe. After ATD withdrawal, when hyperthyroidism recurs rapidly (i.e. within the 1st year), clinicians usually embark on a 2nd ATD course or shift to radical treatment, mainly using radioiodine ablation (see Glinoer et al., in Acta Endocrinologica, 1987). In the present study, the authors tried to assess the fraction of patients with GD who recurred after ATD withdrawal, but in whom the recurrence was only transient. The study is interesting because it contains unusual features that make us ponder about some of the conclusions drawn by the authors.

First, the group of 110 patients was given ATD for a rather long period of time, with a mean treatment period reaching 43 months (± 30 months; S.D.). This extremely long treatment period is strikingly different from the classical attitude used by most clinicians, namely a treatment period of 12-18 months. Why was this? Mainly because the criteria used in the study to stop ATD therapy were: a) a euthyroid status for > 6 months with the lowest ATD dose used alone (2.5 mg MMI/d or 25 mg PTU/d); b) a small goiter
(not defined precisely); and c) a TBII value below 30% binding inhibition (normal value <15% in this assay). Our Japanese colleagues presumably used such criteria because of their well-known unwillingness to give radioiodine to patients with GD (see Solomon et al., JCEM 70:1518, 1990). Hence, they prefer maintaining ATD for long periods of time.

Second and despite the duration of ATD therapy, the overall remission rate was 62% (68/110 patients). The therapeutic fate in the other 42 patients – without remission – was not explained in the article. Among the patients who achieved remission, 40/68 remained euthyroid after a follow-up period up to 36 months, while 28/68 (41%) presented a phase of transient thyrotoxicosis, with a mean duration of 7 ± 8 (S.D.) months. It is not clear from the data presented whether these patients needed to receive a 2nd course of ATD therapy, except for those with a mild and short bout of transient thyrotoxicosis who were not retreated.

Thirdly concerning TBII determinations, TBII was lowest (13 ± 9%) among patients in remission who did not undergo transient thyrotoxicosis, while TBII was slightly higher among patients with transient thyrotoxicosis and those without remission (respectively, 16 ± 7% and 20 ± 10%). However, we were not shown the TBII data observed during the recurrence phase because the measurements presented (see figure below) were carried out at the time of ATD withdrawal.

The authors concluded that transient thyrotoxicosis after ATD withdrawal is not a rare event and that such patients should be identified in order not to receive unnecessary (ablative) therapy. One personal comment would be that it is quite plausible that after such a long period of ATD administration, the thyroid gland has been emptied of its iodine stores, thereby explaining euthyroidism despite the persistence of positive TBII values in many patients. The transient thyrotoxicosis phase could have been due to the progressive replenishment of intrathyroidal iodine stores after ATD withdrawal. Another comment is that the determination of TBII does not allow for discriminating between stimulatory-, neutral-, and blocking-type TSH-receptor antibodies. It would have been of great interest to compare present results with measurements of stimulatory TSHR-Ab (TSAb). Finally, nothing was said about the therapeutic attitude used by the authors for patients whose ‘transient’ thyrotoxicosis exceeded the 1st month of surveillance without therapy for a mild recurrence, given the fact that the average recurrence phase in some patients lasted for more than 1 year. Should this still be considered as a transient recurrence of thyrotoxicosis or were did these patients never achieve a true remission? (Daniel Glinoer, M.D.; Ph.D.)

See Figure

FIG. 1. Clinical data of patients with transient thyrotoxicosis. (A) Time elapsed from ATD withdrawal to thyrotoxicosis. Vertical lines indicate the normal range.