

INTRODUCTION

- Paediatric thyrotoxicosis, usually caused by either Graves' disease (GD) and less commonly by Hashimoto's thyroiditis (HT), is less common and more severe than in adults.
- Management is often problematic with no agreed guidelines and no consistent strategy for when and how to stop antithyroid drug (ATD) therapy.
- In 2005, the Clinical Trials Unit of the British Society for Paediatric Endocrinology and Diabetes designed a prospective study of ATD (dose titration vs block and replace) which involved stopping treatment at 3 years to test for remission.
- In this study, we describe the outcome of thyrotoxicosis in the West of Scotland over 25 years, with focus on remission/relapse outcomes according to diagnosis (GD vs HT); and duration of treatment.

PATIENTS AND METHODS

- Clinical data were collected on all patients seen in West of Scotland between 1989-2013.
- We excluded patients with syndromes (e.g. Down) and neonatal thyrotoxicosis.
- In April 2015, a questionnaire was sent out to all family doctors, to establish current thyroid status.
- Treatment with ATD by dose titration (DT) or block and replace (B&R) therapy, surgery (partial and total thyroidectomy) and radioiodine (RI) was recorded.

Definitions:

Thyrotoxicosis: free T4>30 pmol/l or TT4>160 nmol/l, free T3>10 pmol/l or TT3>3 nmol/l) with TSH <0.1 mU/l in a patient with clinical symptoms of thyrotoxicosis

Graves' disease: thyrotoxicosis with either exophthalmos and/or elevated TSH receptor antibodies (either >10% displacement of TSH binding or <10 u/l) with or without positive TPO antibodies (≥ 30 iu/L)

Hashimoto's thyroiditis: thyrotoxicosis with +ve TPO antibodies but no exophthalmos and non-elevated TRAB

Remission: no recurrence of thyrotoxicosis or development of hypothyroidism

Relapse: recurrence of thyrotoxicosis after electively stopping treatment

RESULTS

- 76 patients were identified of whom 66 (88F:8M) were eligible/available for study (see Figure), with 52/66 and 14/66 satisfying the criteria for GD and HT.
- Recent thyroid status was confirmed by questionnaire (46); assumed from a) information available since 2014 (6); and b) known permanent hypothyroidism from previous RI/surgery (8), leaving current status unconfirmed in only 7.
- ATD treatment with DT (46) and B&R (20) resulted in no liver disease and no deaths; however 16 patients changed from Carbimazole to Propylthiouracil due to rash/neutropenia.
- In 35 patients in whom ATD was stopped for possible remission (Table 2), 11 patients had received ATD < 3 yrs (range 1.5-3 yrs) of whom 6 have stayed in remission (2 GD: 4 HT) while 23 had received ATD ≥ 3 years (range 3.2-11.5 yrs) of whom 13 (9 GD:4 HT) remain in remission.

SUMMARY OF FINDINGS

- The prognosis for remission with ATD alone was distinctly better for HT (10/14 patients remitting) compared with GD (10/52 patients remitting).
- There is no evidence to support an arbitrary interval (e.g. 3 years) before discontinuing ATD therapy.
- Over 2/3 (47/66) patients received second line treatment with surgery or radioiodine, 20 because of poor control/compliance.
- Radioiodine was given to 24 patients, median (range) dose 450 (250-500) MBq, resulting in hypothyroidism (22), persistent hyperthyroidism (2), euthyroidism (0).
- Surgery was carried out in 16 patients (subtotal 13, total 3). Only 2 are euthyroid, hypoparathyroidism in one.

Outcome flow diagram for paediatric thyrotoxicosis in West of Scotland 1989-2012.

NB All but two patients (*) receiving RI became hypothyroid

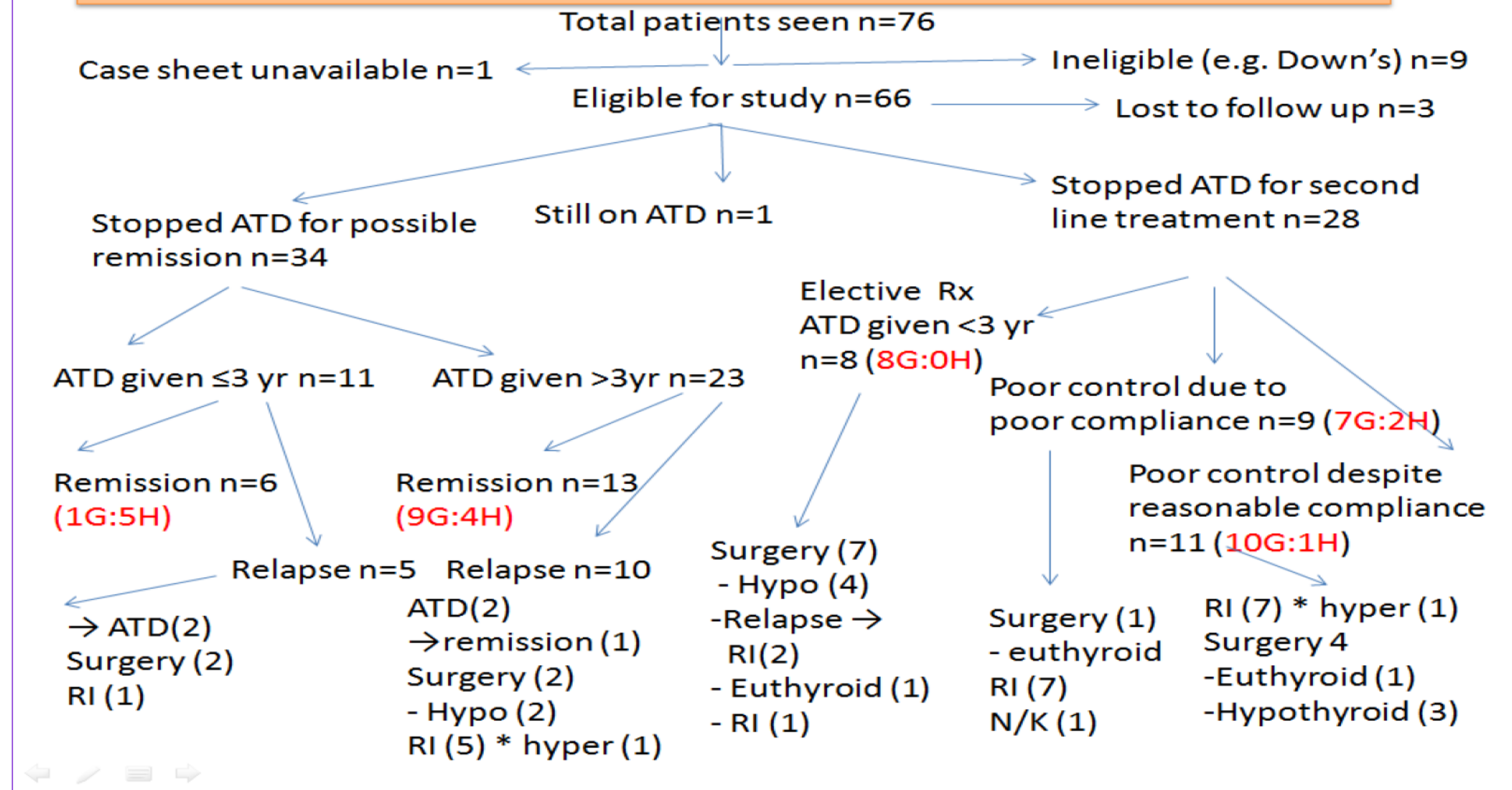


Table 1. Clinical and biochemical features at diagnosis of 67 patients with thyrotoxicosis in the West of Scotland between 1989 and 2013.

	Graves' disease	Hashimoto's thyroiditis
Number (F:M)	52 F:44 / M:8	14 F:14 / M:0
Median (range) age at time of diagnosis	10 (1.8-15.75)	13.45 (8.43-15.6)
TRAB +ve	39	-
TRAB -ve, Exophthalmos +ve	8	-
Exophthalmos	+ (15), ++ (25), +++ (6)	-
Goitre	- (3), + (2), ++ (8), +++ (1) N/R (43)	+ (3) ++ (1), N/R (9)
1° or 2° relative with thyroid disease	8	2
Median (range)[n=] FT4 (pmol/l)	61.5 (19-320) [n=34]	42.2 (31.7-78.4) [n=12]
Median (range)[n=] TT4 (nmol/l)	243 (45-324) [n=13]	173.5 (35-312) [n=2]
Median (range)[n=] TT3 (nmol/l)	8,9 (2,2-22,9) [n=35]	4,9 (3,07-10,8) [n= 13]
Median (range) TRAB - u/l	35.5 (3-94) [n=24]	3 (3-10) [n=11]
- %	45 (20-68) [n=15]	Not available
Mean/Median (range) TPO (mU/l)	1140/400 (7-7643) [n=16]	438.3/185.5 (10-2000) [n=14]
Mean/Median (range)[n=] microsomal	12,408/1600 (100-102 400) [n=13]	Not available

Table 2. Clinical and biochemical features relating to outcome in 45 patients with thyrotoxicosis in whom ATD treatment was electively stopped

	Graves' disease	Hashimoto's thyroiditis
Number (F:M)	22 (F19:M3)	13 (F12:M1)
Number (%) achieving sustained remission after stopping ATD	10 (45.5%)	10 (76.9%)
Median (range) age at time of stopping ATD (yrs)	16.0 (10.9-20.4)	15.795 (12.2-18)
Median (range) duration of ATD therapy	3,7 (0.32-16.2)	3,3 (1.5-9.2)
Median (range) duration of sustained remission (yrs)	6.9 (2.59-19.6)	6.54 (0.81-9)
Relapsed	12 (54.54%)	3 (23.07%)
< 6 months after d/c ATD	8	2
- ≥6 months after d/c ATD	4	1
Median (range) age at time of stopping ATD (yrs)	14.43 (7.4-20.4)	13.61 (4.3-16)
Number going on to receive --Radioiodine - Surgery	4 4 (2 partial)	2
Number (%) still on ATD	4	1

CONCLUSIONS AND RECOMMENDATIONS

- TRAB and TPO must be measured at diagnosis in thyrotoxicosis since a distinction between GD and HT affects prognosis and counselling.
- ATD treatment with dose titration is preferable to block and replace since thyroid status can be continuously assessed with DT.
- Remission may be anticipated with DT if ATD dose requirement is low (e.g. ≤ 5 mg Carbimazole daily). With B&R, treatment cannot be stopped abruptly since thyroid status is unknown; L-T4 should be phased out first in order to assess thyroid status.
- Second line treatment is indicated sooner rather than later if the family become weary of/non-compliant with ATD therapy and/or if control becomes unsatisfactory.
- However, RI and surgery almost always result in hypothyroidism so that pre-existing compliance difficulties with ATD may continue when L-T4 replacement rather than ATD is prescribed.
- An education package, similar to that offered to families with newly diagnosed diabetes, is recommended to fully counsel the families of children with GD. Families should understand that remission may take many years and that good compliance with ATD is needed to ensure good quality of life.

