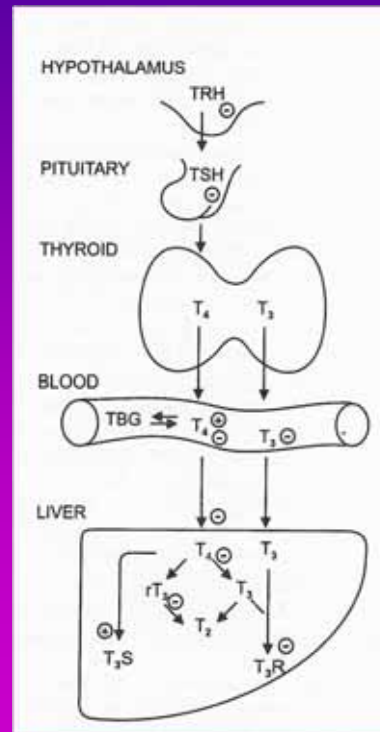


Thyroid Disease

Pierre-Marc Bouloux
Royal Free Campus UCL

Hypothalamic-Pituitary-Thyroid Axis



Thyroid Physiology

- Transport of iodide into thyroid cell
- Iodide is then oxidised to effect the iodination of thyroglobulin resulting in formation of mono- and di-iodotyrosines
- Iodotyrosines oxidised to form T_4 (100%) and T_3 (20%) - released into circulation
- 80% of T_3 is produced by peripheral monodeiodination of T_4 in liver – some circulating T_4 is converted into inactive reverse T_3 – alterations of activities of the deiodinases will change concs of T_4 , T_3 and reverse T_3

Case Study 1

- 68 year-old woman with 10-year history of anxiety - now has nocturnal palpitations and lethargy
- In sinus rhythm 100/min, no goitre
- TFTs performed to exclude thyrotoxicosis:
- TSH 3.6mU/l (0.5-5), FT4 40pmol/l (9-25)
- What should be done?

Normal/Raised TSH, Raised FT4 or FT3

- Interfering antibodies to thyroid hormones
- Intermittent T4 therapy or T4 overdose
- Resistance to thyroid hormone
- TSH secreting pituitary tumour
- Amiodarone
- Acute psychiatric illness
- Familial dysalbuminaemic hyperthyroxinaemia

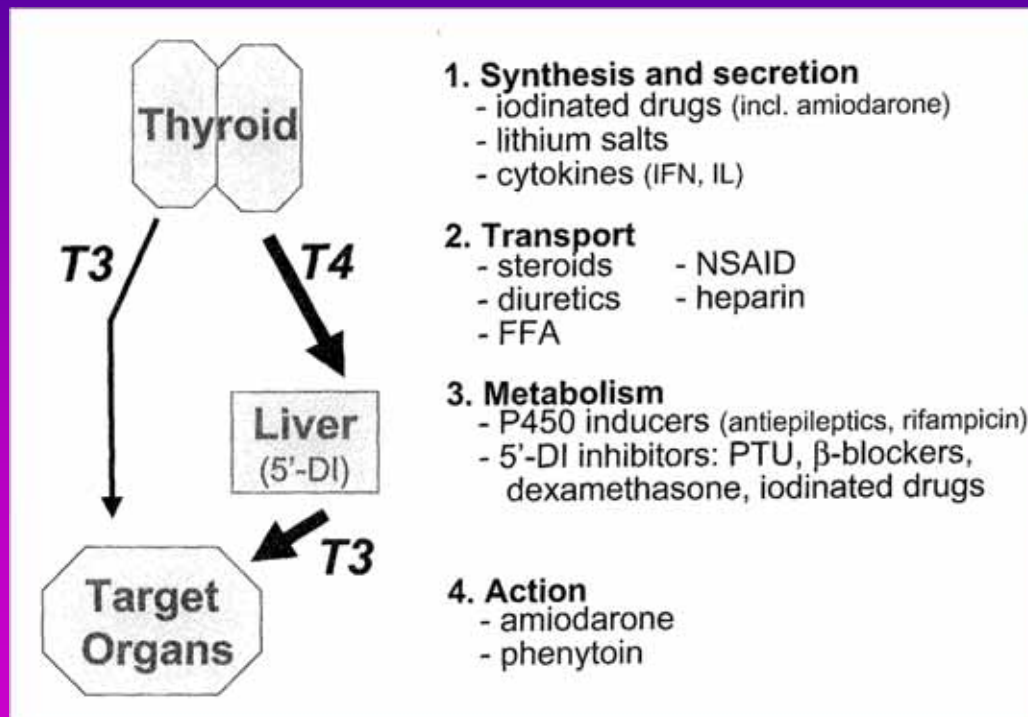
Anti-Thyroid Antibody Interference

- Suspect if FT4 and FT3 assays are widely discordant with each other
- Usually evidence of thyroid autoimmunity
- Anti-T4 and anti-T3 antibodies more common in free than total thyroid hormone assays
- Determine free thyroid hormone levels by equilibrium analysis where confounding antibody is excluded by dialysis membrane
- Thyroid function can be monitored by TSH once interference confirmed

Thyroid Hormone Resistance

- Syndrome of reduced responsiveness of target tissues to thyroid hormone
- Thyroid hormone receptor mutations
- Usually family history of thyroid hormone resistance or goitre (dominant)
- Absence of usual symptoms/consequences
- Absence of pituitary tumour on MRI
- Normal SHBG
- Normal/exaggerated response to TRH
- Normal alpha-subunit/TSH ratio
- Thyroablative treatment not indicated

Effects of Drugs on the Thyroid



Circumstances Associated with Altered T4 Requirements

- ↓requirements - ↑ age, androgen Rx
- ↑requirements – HRT, pregnancy, malabsorption
- Drugs which ↓absorption - high-fibre, sucralfate, aluminium hydroxide, ferrous sulphate, cholestyramine
- Drugs which ↑clearance - rifampicin, carbamazepine, phenytoin

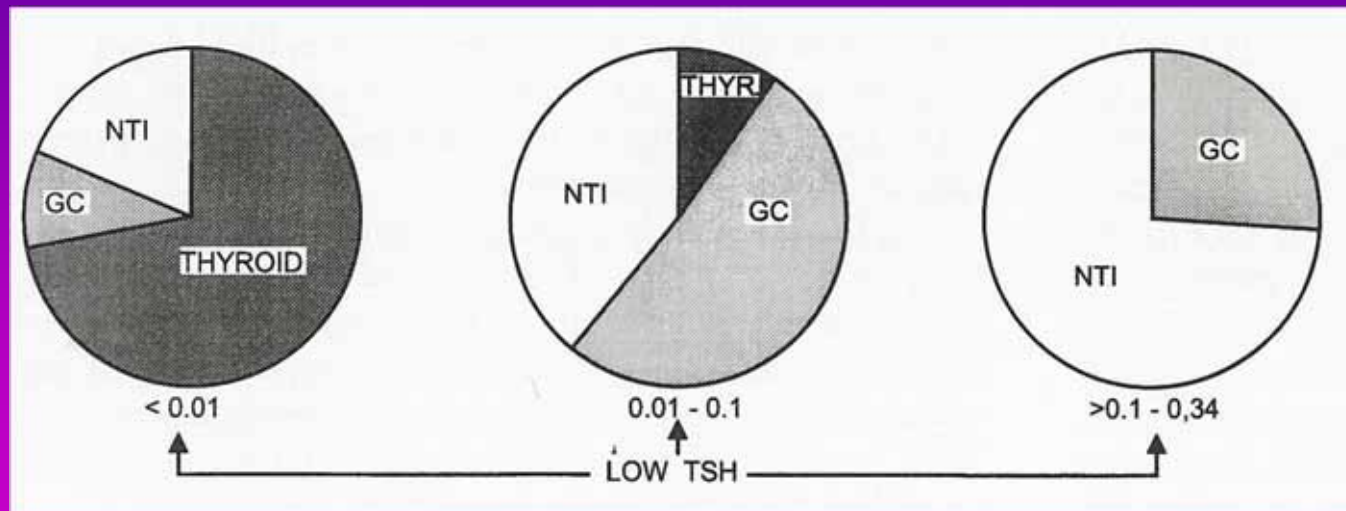
Case Study 2

- 74 year-old man with a diagnosis of CCF, presumed secondary to IHD, complains of having “no energy at all”
- TFTs:
TSH 7mU/l (0.5-5), FT4 12pmol/l (9-25)
- What should be done?

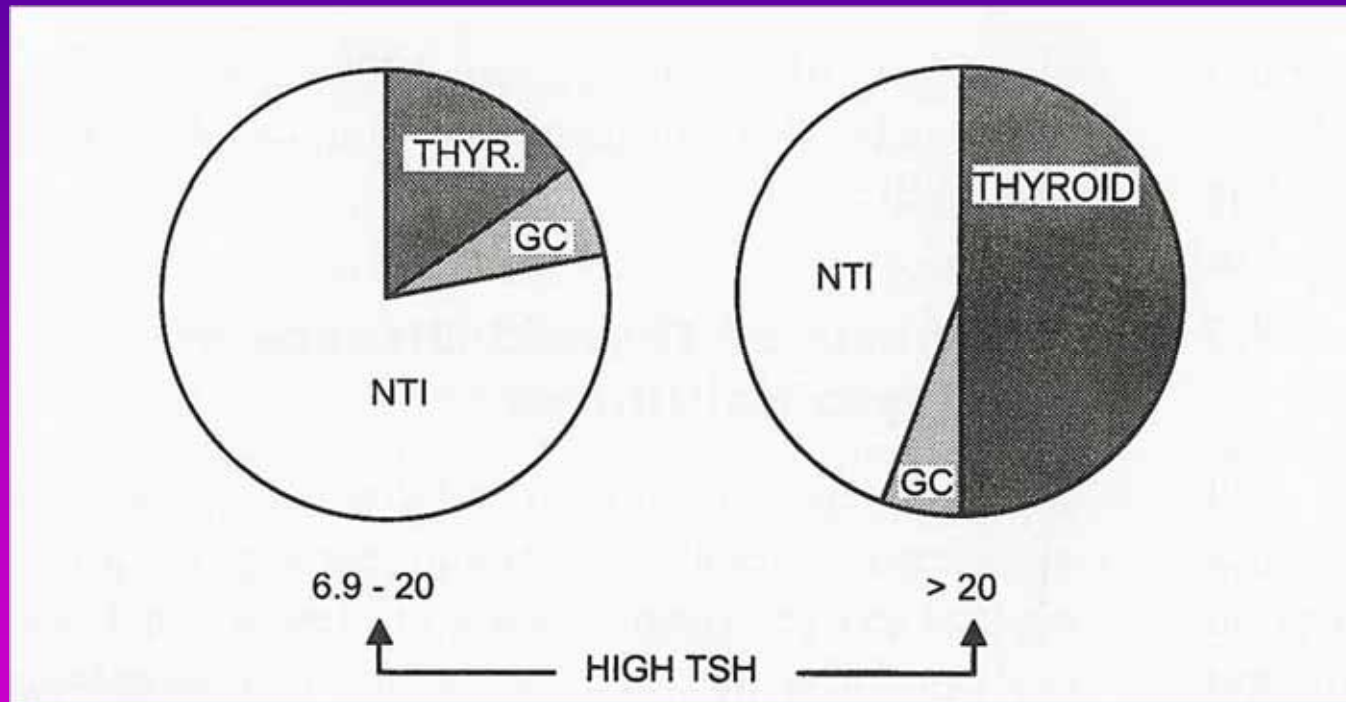
TFTs in Hospital In-Patients

- Isolated alterations in TSH concs (either low 0.1-0.3 or high 5-20mU/L) occur in 15% due to response to non-thyroidal illness or drugs
- 2-3% of hospitalised patients have suppressed TSH concs (<0.1 mU/L) or elevated (>20 mU/L)

Outcome - Low Serum TSH



Outcome – High Serum TSH



Prevalence of Overt Thyroid Disease

- **Hyperthyroidism**

Point prevalence rates 0.3-1%

Accurate diagnosis if clinical indications exist, accurate drug history, if abnormal TSH confirmed and reciprocal change in FT4

- **Hypothyroidism**

Point prevalence 2% even in elderly women

Subjects tend to be older and have more severe illnesses, but limiting to women >50 would have missed 40% of those with significant hypo

Case Study 2 continued

- TSH 7mU/l (0.5-5), FT4 12pmol/l (9-25)
- Diagnosis

Probably response to non-thyroidal illness

?evidence of mild thyroid failure

secondary to autoimmune thyroid disease

- Plan

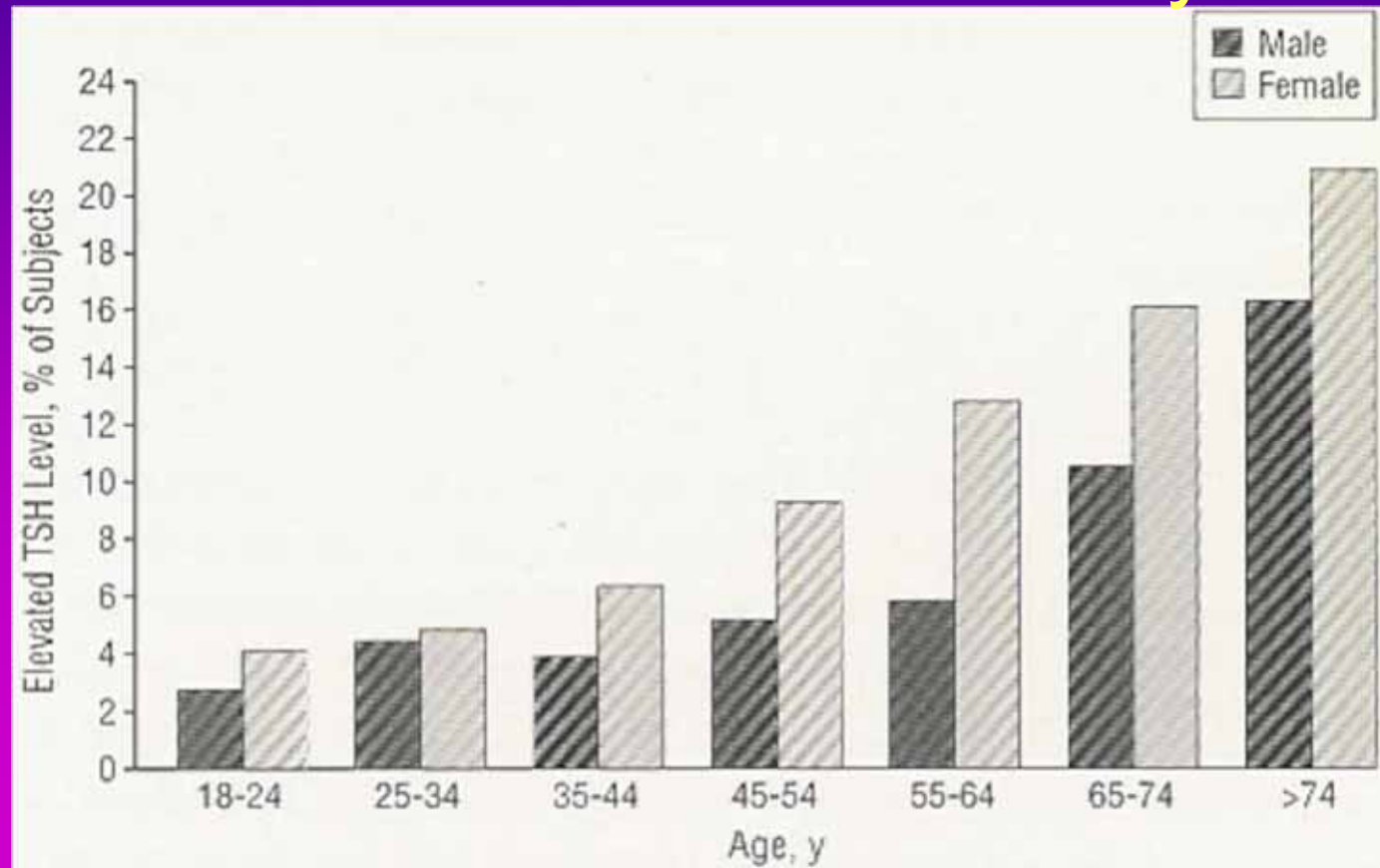
Do nothing and repeat TFTs in recovery in 2 months (plus thyroid antibodies)

Case Study 3

“Will thyroxine help me doctor?”

- 55 year-old woman (Teacher)
- C/o lethargy for many years to GP
- FT4 14pmol/L, TSH 5.6mU/L
- T-C 6.4mmol/L, LDL-C 4.2mmol/L, HDL 1.6mmol/L, Trig 1.5mmol/L
- Should this patient receive thyroxine?

The Percentage of Subjects with Elevated TSH by Age and Gender in Colorado Study



Mild Thyroid Failure

- Raised serum TSH $>4.5\text{mU/L}$ but normal FT4
- Absence of hypothalamic/pituitary disease, non-thyroidal illness or drugs
- Cause: Chronic autoimmune thyroiditis in iodine-replete communities
- 8% women (10% >55 yrs) and 3% men
- Most diagnosed in primary care after investigation of symptoms or screening
- 74-87% will have TSH 5-10mU/L

Hypothyroidism

Probability in 60 year-old Woman at Whickham 20-Year Follow-Up

TSH (mU/L)	Thy Ab	Probability
2	-	3%
2	+	17%
5	-	17%
5	+	55%
10	-	44%
10	+	83%

Mild Thyroid Failure Symptoms

- 5 double-blind randomised trials
- Follow-up periods 6 months to 1 year
- Sample sizes 20-63 in age 45-73 years
- 3 studies showed improvement in symptoms although 1 only if TSH >12
- 2 studies no benefit in symptom scores
- ?selection bias as patients with poor quality of life more likely to have TFTs

Dyslipidaemia

- Most studies show association with raised LDL-C, low HDL-C and raised lipoprotein(a)
- Total-C increased by 0.5mmol/L and intervention studies with T4 lower by 0.2-0.4mmol/L
- In the only RCT, improvement in lipid profile only seen if TSH >10mU/L

Subclinical Hypothyroidism

Quality of Evidence (JAMA 2004)

	Association?		Treatment?	
	4.5-10	>10	4.5-10	>10
Serum TSH	4.5-10	>10	4.5-10	>10
Hypothyroid	Good	Good	-	-
CVD	Insuf	Insuf	None	None
Lipids	Insuf	Fair	Insuf	Insuf
ECHO	?	Insuf	Insuf	Insuf
Symptoms	None	Insuf	Insuf	Insuf

Compliance

- Long-term consequences of inadequate treatment or over-treatment with T4
- In UK community studies 50% of treated hypothyroid patients have TSH levels above/below reference range
- Colorado survey – 1525 on T4 – subclin hypo in 18% and subclin hyper in 21%
- ?care with T4 in elderly with IHD

Subclinical Hypothyroidism Guidelines

- Raised TSH and low FT4 is overt hypothyroidism and requires T₄
- If FT4 normal and TSH >10mU/l, then T₄ is usually justified
- If TSH 5-10mU/L and thy ab+, then annual check - T₄ once TSH >10mU/L
- If TSH 5-10mU/L and thy ab-, then ensure check every 3-5 years only
- No evidence for T₄ if TSH 2.5-5mU/L

Case Study 4

“I don't feel right on thyroxine”

- 37 year old woman
- 12 months post I¹³¹ for Graves' disease and hypothyroid within 4 months
- On thyroxine 150mcg daily
- Still c/o lethargy
- FT4 23pmol/L, TSH 0.02mU/L
- Patient asks for a prescription for T3
- What would you do?

Treatment of Hypothyroidism

- Hypothyroid patients who continue to have symptoms despite T4 replacement
- Rat studies suggest that only the T4 and T3 ensures euthyroidism in all tissues except in brain where T4 alone
- Initial study showing benefit of T4 and T3 suggested benefit in thy ca patients
- 3 subsequent randomised crossover or parallel studies in 2003 failed to show benefit
- Significant improvement in symptom score in “control” group emphasises placebo effect

Case Study 5

“ I want you to prescribe armour”

- 55 year-old woman (Teacher)
- C/o lethargy, weight gain, scalp hair loss for six months
- FT4 14pmol/L, TSH 2.4mU/L
- Claims that she has the clinically syndrome of hypothyroidism and doesn't believe blood test
- Seen in Harley Street – begun on Armour
- Patient asks GP to continue prescription

What is “Armour”

- Natural desiccated thyroid hormone containing T4 and T3
- Extracted from pig thyroid glands
- Tablets contain approximately 38mcg of T4 and 9mcg of T3 – wide variety of strengths
- Authorised by the FDA but not by UK
- Can be imported if prescribed
- No evidence of benefit in those with normal TSH

Case Study 6

- 67 year-old woman
- Presented 30 years ago with myalgia and lethargy
- Told hypothyroid and begun on T3 40mcg daily
- Recent TFTs: FT3 10.3 (3-7), FT4 0.7 (10-20) and TSH 0.02 (0.4-4mU/l)
- What would you advise?

Treatment of Hypothyroidism

- Rat studies suggest that only the T4 and T3 ensures euthyroidism in all tissues except in brain where T4 alone
- Initial study showing benefit of T4 and T3 suggested benefit in thyroid cancer patients
- 3 subsequent randomised crossover or parallel studies in 2003 failed to show benefit
- Significant improvement in symptom score in “control” group emphasises placebo effect
- No evidence for benefit from desiccated thyroid hormone extracted from pig thyroid glands containing T4 and T3

Case Study 7

“Will treating my thyroid help my heart and bones?”

- 77 year-old lady
- Recent ward admission with AF – otherwise no symptoms
- TFTs returned after discharge: FT4 17.9pmol/l, FT3 6.8pmol/l, TSH 0.1mU/l
- Referral from cardiologists – should this abnormality be treated?

Prevalence of Subclinical Hyperthyroidism

Study	N	Age	Men	Women
Whickham	1704	38+		3%
Birmingham	1210	60+		6%
Colorado	25862	18+		1.0%
NHANES III	13344	12+		0.7%

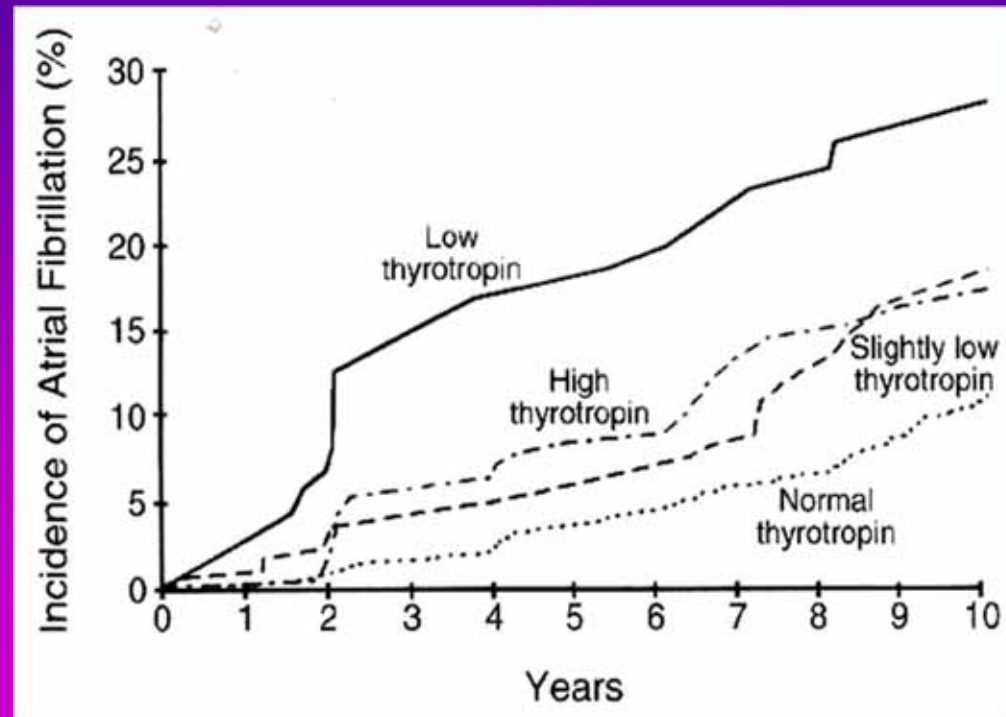
Subclinical Hyperthyroidism

- Low serum TSH but normal FT4
- Absence of hypothalamic/pituitary disease, non-thyroidal illness or drugs
- Cause: exogenous from T4 therapy or endogenous as in overt hyperthyroidism
- 2% of population have subnormal and 1% undetectable serum TSH
- Annual incidence of hyperthyroidism 5%

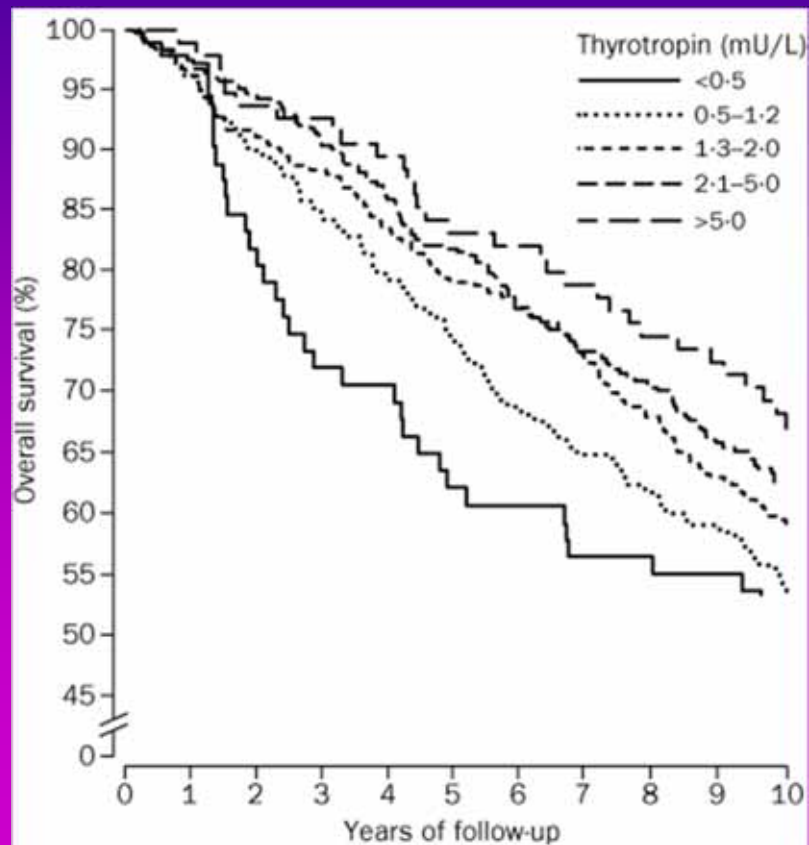
Subclinical Hyperthyroidism Symptoms

- Small case-control, cross-sectional, and cohort studies - more signs and symptoms but selected from hospital clinics and elderly in-patients
- Only large population study - no association between $TSH < 0.2 \text{ mU/l}$ and physical or psychological symptoms
- Subgroup of Rotterdam cohort - that $TSH < 0.4 \text{ mU/l}$ associated with x3 dementia risk

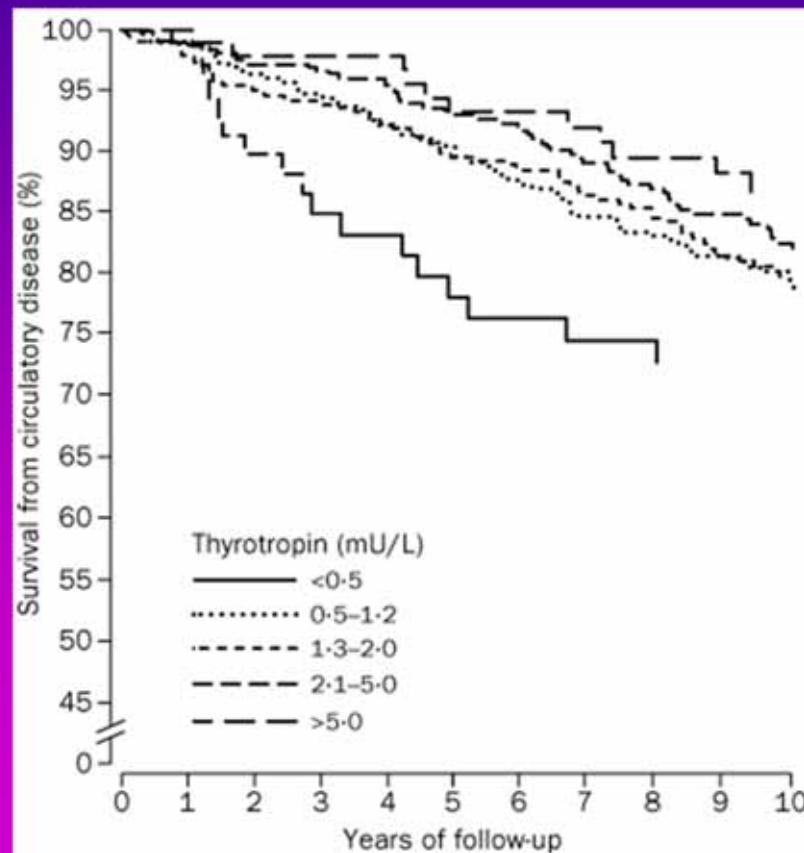
Subclinical Hyperthyroidism Atrial Fibrillation



Prediction of All-Cause Mortality from TSH: 10-year Cohort Study



Prediction of CVD Mortality from TSH 10-year Cohort Study



Subclinical Hyperthyroidism Bone Density

- Two meta-analyses report ↓BMD during prolonged subclinical hyperthyroidism - post-menopausal women only
- Prospective study reported increased hip/spine fracture in women >65 with TSH<0.1mU/l but not if 0.1-0.5mU/l
- Study of 1,100 patients on T4 in Scotland found no difference in fracture rates
- Population case-control study in 23,183 on T4 – independent fracture risk in men only

Subclinical Hyperthyroidism

Quality of Evidence (JAMA 2004)

	Association?		Treatment?	
	0.1-0.5	<0.1	0.1-0.5	>10
Hyperthyroid	Insuf	Good	None	None
Cardiac	Fair	Fair	None	None
AF	Insuf	Good	None	None
BMD	None	Fair	None	Fair
Symptoms	Insuf	Insuf	None	Insuf

Case Study 8

- 68 year-old woman with history of MI treated with amiodarone for 12 months for resistant PAF
- GP checks thyroid function at “well-woman screen” and result sent to cardiologist as due for routine review in 1 month
- FT4 14pmol/l, TSH 20mU/L
- How would you manage this patient?

Amiodarone and the Thyroid

- Amiodarone contains two iodine atoms
- 200mg Amiodarone contains 74.4mg iodine
- Metabolism in liver releases approx 3mg of inorganic iodine/100mg into the systemic circulation – diet average is 0.5mg/day
- Large iodine doses acutely (transiently in 2 weeks) inhibit binding of iodine to TG leading to reduced T4/T3 synthesis (Wolff-Chaikoff)
- Inhibits monodeiodination of T4 thus decreasing T3 production
- Blocks T3-receptor binding to nuclear receptors

Effects of Amiodarone on Thyroid Function

- Changes primarily due to impaired deiodination of T4 to T3
- TSH ↑ initially then ↓ to low/normal 2-3 months – occasional intervals of low TSH
- FT4 ↑ 20-40% in 1st month, then gradually fall to baseline but remains high/normal
- FT3 ↓ 30%, then remain low/normal
- rT3 ↑ 20% then remain high

Amiodarone-Induced Hypothyroidism 1

- Incidence of 13% in areas of high iodine intake to 6% where low iodine intake
- Risk is dose independent but enhanced in elderly and women – ATD
- Inability of thyroid to escape from the acute inhibitory effects of iodine on hormone synthesis and release
- May reflect underlying ATD –usually occurs early within 3-12 months

Amiodarone-Induced Hypothyroidism 2

- Clinical features not affected although most patients have few symptoms – lethargy
- Biochemical diagnosis – TSH > 20 mU/l and FT4 < 12 pmol/l
- Stop amiodarone? Rarely acceptable!
- Continue amiodarone and replace with T4 until TSH within reference range
- If TSH 5-20 mU/l, FT4 N – check thy ab
- If thy ab neg – watch for 3-6 months

Case Study 9

- 83 year old woman with recurrent VT begun on Amiodarone in November
- Presented with wt loss 5Kg and dysphagia
- Past history of nodular goitre Rx thyroidectomy
- FT4 40pmol/l, FT3 6pmol/l (3-7pmol/l), TSH <0.01mU/l
- How would you manage this patient?

Effects of Amiodarone on Thyroid Function

- Changes primarily due to impaired deiodination of T4 to T3
- TSH ↑ initially then ↓ to low/normal 2-3 months – occasional intervals of low TSH
- FT4 ↑ 20-40% in 1st month, then gradually fall to baseline but remains high/normal
- FT3 ↓ 30%, then remain low/normal
- rT3 ↑ 20% then remain high

Amiodarone-Induced Hyperthyroidism 1

- Less common in iodine-replete areas such as UK – 2% (cf 13% hypothyroidism)
- Occurs more frequently in men and ↓iodine
- No relation with daily or cumulative dose
- Onset often acute but may occur months after discontinuation. Remissions common.
- Clinical features often obscured but new/recurrent atrial arrhythmias, HF, wt loss
- ↑FT3 and undetectable TSH (↑SHBG)

Amiodarone-Induced Hyperthyroidism 2

	Type 1	Type 2
Prev thyroid abnormality	Yes	No
Pathogenesis	↑synthesis due to I excess	↑release of hormone
Goitre	MNG/diffuse	No occ tender
Isotope uptake	Normal/raised	Low/absent
Colour Doppler	Increased flow	Absent

When Amiodarone can be stopped

- Non-life threatening arrhythmia ?alternative
- Caution that amiodarone may paradoxically be protecting from effects of thyrotoxicosis
- Type 1 – rarely respond to amiodarone withdrawal alone – most still hyperthyroid 6-9 months later – use of Carbimazole in high doses often required and Potassium Perchlorate to block iodide uptake - ?I131 or thyroidectomy
- Type 2 – withdrawal may suffice – majority euthyroid in 3-5 months – steroids accelerate recovery – no use for carbimazole/I131

When Amiodarone cannot be stopped

- Cessation of amiodarone may exacerbate the thyrotoxic/cardiac status
- Alternative strategies such as ablation and implantable defibrillators inappropriate
- Further de novo assessment may be difficult to interpret if thyrotoxic/on amiodarone
- Consequences of new antiarrhythmic in thyrotoxic with tissues saturated with amiodarone cannot be predicted
- May be safer to persist with amiodarone and treat the thyrotoxicosis - ↓good outcome

Monitoring Thyroid Function in Patients on Amiodarone

- Baseline TFTs including FT4, TSH, thy ab
- If pre-treatment TSH ↑/N and thy ab+ then risk of hypothyroidism and need follow-up
- If TSH ↓/N, probable risk of thyrotoxicosis
- Check every 6 months routinely and low threshold for testing if any suspicion
- Equivocal results require repeat in 6 weeks
- Continue checking after withdrawing Rx

Case Study 10

- Philip presented in April 1998 aged 20
- Episode of chest tightness whilst training as professional rugby player
- FT4 77, TSH <0.03
- Visible large smooth goitre with bruit
- No eye signs
- How would you manage this patient?

Case Study 10

- Recommendation to commence CBZ therapy (60mg daily) with plan to consider thyroidectomy in 3 months
- At 3 months after extensive consultations (inc father who was former surgeon), opted for continuation of CBZ until rugby career over (Saracens/Eng U21s)
- Remained on high-dose CBZ
- Reported proximal myopathy and gynaecomastia and psych disturbance
- Signed off for rugby insurance Dec 1999

Case Study 10

- Lost to follow-up until April 2005
- Returned from Bristol after I131 2002
- Post I131 developed active thyroid eye disease – upset re info given
- Off and on low dose CBZ post I131
- Still toxic and recommenced CBZ 10mg daily
- Now offer thyroidectomy
- Begun on T4 therapy immediately post-op

Hyperthyroidism

- Affects approximately 2% women and 0.2% men
- 3 principle treatments – anti-thyroid drugs, radioiodine and surgery
- All effective
- Opinions differ about the indications because no single treatment regularly results in permanent euthyroidism

Investigation

- Confirm diagnosis biochemically
- Permanent or transient
- Aetiology – Graves', Nodular disease, Thyroiditis (viral, autoimmune), Drugs
- Select appropriate management

Initial Management

- Beta-blockers?
- Carbimazole therapy – titrate vrs block-replace
- Role of radioiodine therapy
- Role of surgery

Radioiodine

- Increasingly used as first line therapy for Graves hyperthyroidism
- Treatment of choice for recurrent hyperthyroidism after ATD Rx
- Dose
- Outcome
- Safety
- Eye Disease?

Surgery in Management of Overactive Thyroid

- Patient choice/Large goitres/Cosmetic
- Total thyroidectomy is usual
- Complication rate low
- Euthyroid prior to surgery
- Option for those with active eye disease
- All aetiologies but normally Graves'
- Good surgeon

Cost-Effectiveness of Treatment

- 135 patients with thyrotoxicosis referred in 12 months (13 transient)
- 62% Graves, 7% nodular, 5% thyroiditis, 27% unknown
- 74 received ATDs, 43 I131, 5 had Tx
- Cure defined as euthyroid 12 months after ATD or euthyroid or on T4 at 24 months post I131 or Tx
- Costs included OP attendances, lab tests and initial and subsequent treatments

Outcomes

Rx	N	Cured	Total Costs £	Costs /Cure £	Failed Rx	Lost F-U
ATD	74	54	2186	2995	12	15
Tx	5	5	6651	6551	0	0
¹³¹ I	43	41	1581	1618	1	1

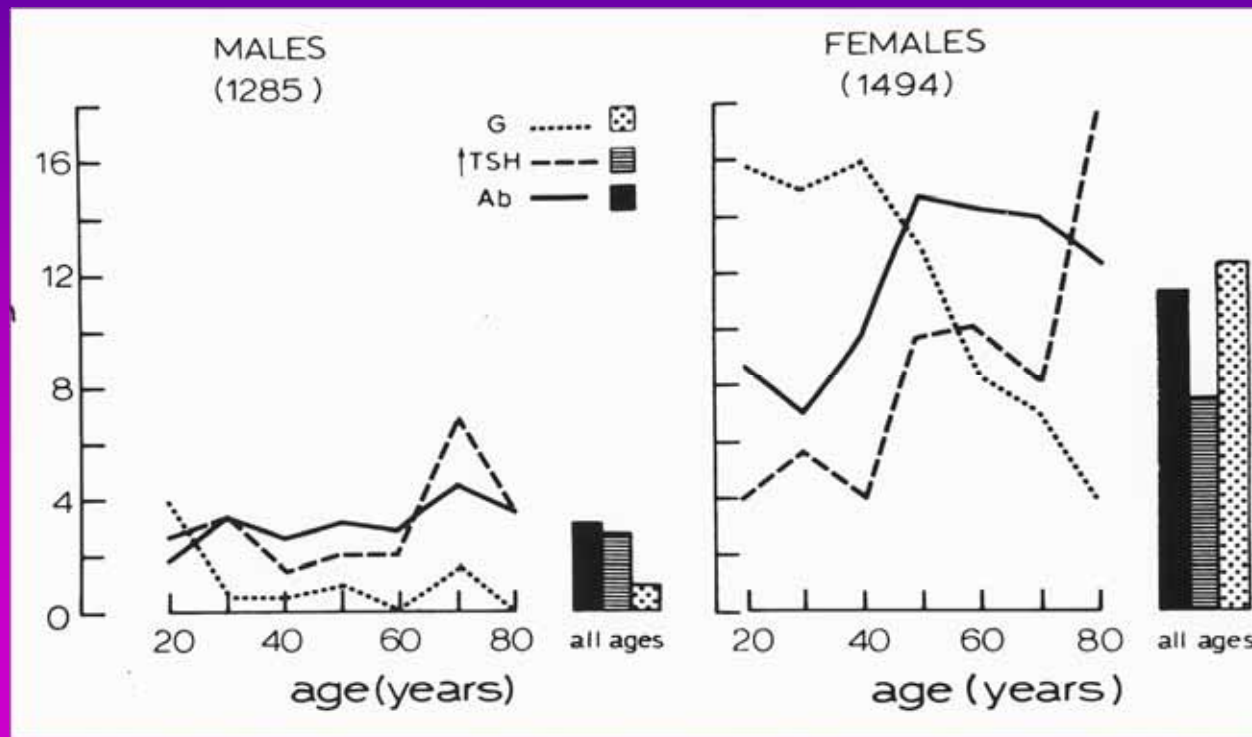
Hyperthyroidism - Summary

- Affects approximately 2% women and 0.2% men
- 3 principle treatments – anti-thyroid drugs, radioiodine and surgery
- Differential diagnosis of elevated thyroid hormone levels but normal TSH
- Management options in amiodarone-induced thyrotoxicosis

Thyroid Nodules Case Scenarios

1. 64-year-old woman with large multinodular goitre – presented with neck discomfort.
2. 33-year-old woman presented with neck swelling – clinically has 3cm on palpation.
3. 77-year-old man investigated for TIAs with carotid dopplers – told by radiologist that 1.2cm nodule seen which requires follow-up.

The Prevalence of Goitre, Raised Serum TSH and Thyroid Antibodies in Men and Women at first Whickham Survey



Nodular Goitre

Prevalence by Palpation

Study	Year	N	Age	Prevalence
Framingham	1968	5127	30-59	M 1.5%, W 6.4%
Whickham	1977	2779	18+	M 0.8%, W 5.3%
Denmark	1983	296	13-90	6.1%
Finland	1991	253	19-50	5.1%
Germany	1991	569	60+	17.6%
Jutland	1998	423	68	M 3.2%, W 12.2%
Iceland	1998	100	66-70	2%

Nodular Goitre

Incidence in Framingham Cohort

- 4909 subjects aged 30-60 years without nodules followed for 2-15 years
- Incidence 1.1/1000 women
 0.6/1000 men
- 74% of nodules unchanged at 15 years
- Prevalence much higher than incidence

Nodular Goitre

Prevalence by Ultrasound

Study	Year	N	Age	%
Belgium	1985	300	0-90	19
Finland	1991	253	19-50	27
Germany	1991	569	60+	18
France	1994	1000	18+	35
Italy	1999	992	15+	17

Nodular Goitre

Ultrasound Studies

- High resolution U/S can detect nodules as small as 1mm
- Prevalence of nodules higher in women than men and increase with age
- Comparison with palpation findings
- Significance of high prevalence (especially in older women) is unclear

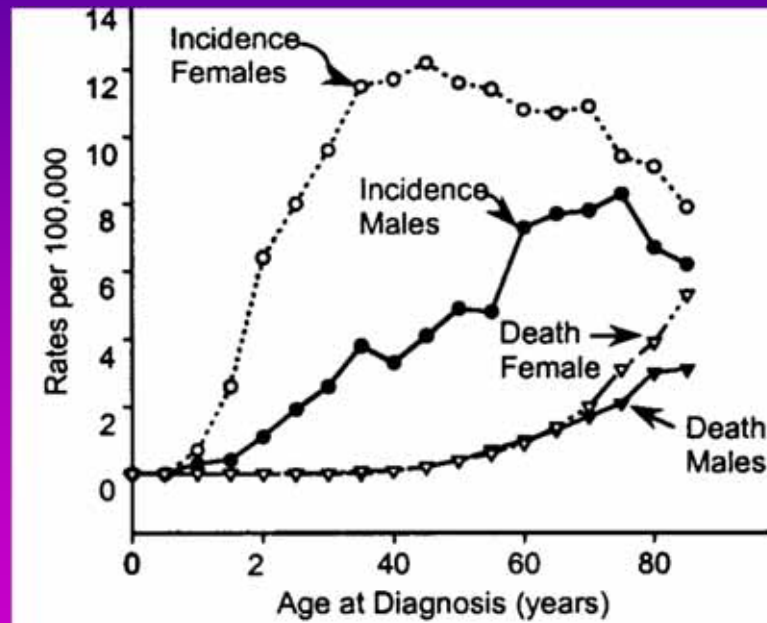
Nodular Goitre

Autopsy Studies

- Prevalence ranges from 8% to 65% in non-endemic and endemic regions
- Mayo Clinic autopsy series – 49.5% of 821 consecutive autopsies had macroscopic lesions seen in 2cm slices
- Boston Hospital Series – 8.2% had nodules >1cm
- High prevalence of occult thyroid cancer detected at autopsy 3-28% (median 6%)

Thyroid Cancer

Annual Incidence and Mortality Rates



*SEER cancer statistic review 1973
- 1992*

Nodular Goitres

- Clinically apparent nodules in 4-7% of the population
- More common in women and elderly
- When sought by U/S scan, unsuspected nodules found in 44% women/20% men
- Approx 90% of solitary nodules benign
- Thyroid cancer rare 2-4/100,000 per yr
- The challenge is to identify those few that are caused by thyroid cancer

Nodular Goitres

Factors Favoring Benign Disease

- Family history of ATD
- Family history of benign thyroid nodule
- Presence of hypo/hyperthyroidism
- Associated pain or tenderness
- Soft, smooth, mobile nodule
- Multinodular goitre without a dominant nodule

Nodular Goitres

Factors Increasing Suspicion

- Age <20 or >70 years
- Gender (Men x2 women)
- Associated dysphagia/hoarseness
- History of external neck DXT
- Family history of thyroid cancer
- Cervical lymphadenopathy
- Firm, hard, irregular, fixed nodule

Investigations

- Laboratory – serum TSH +/- TPO, Calcitonin if MTC or MEN 2 suspected
- Isotope scan – rarely needed unless thyroiditis suspected or TSH <0.1mU/L
- U/S – rarely required initially – can be used to guide FNA or determine dominant nodule within MNG – main other role is follow-up of thy ca

Fine Needle Aspiration Cytology

- Most effective method for distinguishing benign/malignant disease
- In large series: 57% benign, 24% indeterminant, 16% non-diagnostic and 3% malignant
- Sensitivity 68-93% (median 83%)
- Specificity 72-100% (median 92%)
- Surgical yield for thyroid cancer increased from 15% to 45% over past 2 decades

Thyroid Nodules

(Single >1cm or Dominant)

- Malignant – surgery (thyroidectomy)
- Benign – follow clinically (?repeat FNA in 3 months and if confirmed, discharge)
- Suspicious (ie follicular lesion) – recommend lobectomy and ?proceed
- Non-diagnostic – repeat in 3 months with U/S guidance

Fine Needle Aspiration Cytology - Problems

- Skill of person performing biopsy
- Experience of cytopathologist – importance of Multidisciplinary meetings
- Should it be U/S guided?
- Dominant nodules within MNG – same prevalence of malignancy as single nodules
- Thyroid incidentalomas? (1.0-1.5cm)

Thyroid Incidentalomas - Questions

- Is there a size criterion below which FNAC not required?
- Are there diagnostically reliable U/S criteria to determine selection for FNA? (solidity, hypoechogenicity, punctate calcification)
- If cytology non-diagnostic/inconclusive, is it useful/necessary to repeat FNAC?
- What does cytological diagnosis of malignancy mean biologically?

Management of Euthyroid Multinodular Goitre

- If symptomatic, investigate with flow-volume loop/CT scan ?tracheal compression
- Consider thyroidectomy or I131
- No role for thyroxine therapy
- Long-term risk of hyperthyroidism(?) – recommend follow-up TFTs

Clinical Scenarios - Answers

1. 64-year-old woman with large multinodular goitre – presented with neck discomfort.
2. 71-year-old man presented with neck swelling – clinically has 3cm on palpation.
3. 77-year-old man investigated for TIAs with carotid dopplers – told by radiologist that 1.2cm nodule seen which requires follow-up.

Conclusions

- Interpretation of thyroid function tests
- Subclinical thyroid disease
- Management of amiodarone induced thyroid dysfunction
- Controversy in hypothyroidism and thyroxine replacement
- Pitfalls in hyperthyroidism
- Management of thyroid nodules