

## Hoe volg ik een patiënt(e) met SK lijden op?

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## Casus 1 struma, suppressieve therapie

- Vrouw, 63 jaar
- Matig struma sinds jeugd, waarvoor 100 µg Euthyrox sinds jaren



### doel

- TSH laag normaal (0,3-2,5 mU/l)  
DOCH NIET ONDERDRUKT!!!!  
FT4? Nuttig als TSH buiten range
- Cfr cave: hartrhythme, osteoporose
- pro/contra afwegen!
- BMD? Pols/EKG?
- Wat bij stoppen thyroxine?



## Casus 2 hypothyreose na thyroidectomie voor Graves

- Vrouw, 24 jaar
- Recidiverende Graves vanaf 16 j  
→ thyroidectomie 2014
- FU, kinderwens in nabije toekomst



### doel

- TSH normaal (0,3-4,0 mU/l)  
Kijk niet naar FT4, is vaak verhoogd!!!!  
FT4 enkel nuttig als buiten TSH range
- Kinderwens:
  - Thyroxine therapie
  - TSHrAb's



## Schildklier en zwangerschap: HYPO

ORIGINAL ARTICLE

Timing and Magnitude of Increases  
in Levothyroxine Requirements  
during Pregnancy in Women  
with Hypothyroidism

Erik K. Alexander, M.D., Ellen Marques, M.D., Jennifer Lawrence, M.D.,  
Petr Janáček, M.D., Ph.D., George A. Fischer, Ph.D., and P. Reed Larsen, M.D.

N Engl J Med 2004;351:241-9.

### CONCLUSIONS

Levothyroxine requirements increase as early as the fifth week of gestation. Given the importance of maternal euthyroidism for normal fetal cognitive development, we propose that women with hypothyroidism increase their levothyroxine dose by approximately 30 percent as soon as pregnancy is confirmed. Thereafter, serum thyrotropin levels should be monitored and the levothyroxine dose adjusted accordingly.



## Voorafbestaande hypothyreose

- Voor ZWSCHP: doel TSH < 2.5 (1.5?) IU/l
- 1<sup>ste</sup> trim: doel TSH < 2.5 IU/l at 4-6 wks  
→ dosis + 30-50%  
SK testen per maand tot 5<sup>de</sup> maand  
SK testen 26-32 wk
- Na bevalling: terug dosis van voor zwschp  
+ controle SK testen 4-6 wk na partus

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## TSHrecAb's

- afprikken: (in begin zwangerschap)  
rond 22 (20-26) weken

bij:

- actieve Graves
- voorgeschiedenis van Graves
- vroegere neonatus met Graves
- moeder met vroeger pos TSHrecAb's

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## TSHrecAb's

- als TSHrecAb's x 2-3: foetale SK dysfunctie?
  - SK vergroting?
  - Groei vertraging?
  - Tachycardie?
  - Hydrops?
  - Toegenomen botleeftijd?
  - Hartfalen?

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## Casus 3 papillair SK CA

- man, 43 jaar
- Papillair SK CA in 2012  
R/thyroidectomie, I-131

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## doel

- TSH naargelang risico
- pro/contra afwegen!
- BMD? Pols/EKG?

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## AJCC/TNM 7th edition

| T1  | ≤ 2cm (T1a <1 cm, T1b 1-2 cm)                    | N0       | no node involvement             |
|-----|--|----------|---------------------------------|
| T2  | > 2-4 cm   | N1a      | central (level VI)              |
| T3  | > 4 cm or minimal invasion                       | N1b      | other (level I-V or VII)        |
| T4a | gross invasion                                   |          |                                 |
| T4b | gross invasion<br>prevertebral fascia or vessels | M0<br>M1 | no distant mets<br>distant mets |

|           | Age < 45y    | Age ≥ 45y                  |
|-----------|--------------|----------------------------|
| Stage I   | anyT,anyN,M0 | T1N0M0                     |
| Stage II  | anyT,anyN,M1 | T2N0M0                     |
| Stage III |              | T3N0M0<br>T1-3,N1a,M0      |
| Stage IVa |              | T1-3,N1b,M0<br>T4a,anyN,M0 |
| Stage IVb |              | T4b,anyN,M0                |
| Stage IVc |              | anyT,anyN,M1               |

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### ATA risk classification for recurrence 2009

| Risk                   | pTNM   | "phrased"   |
|------------------------|--|---|
| Low (0 - 5%)           | pT1-T2 N0/Nx<br>+ no aggressive histology<br>+ no vascular invasion  | < 4 cm<br>+ intra-thyroid<br>+ R0<br>+ M0         |
| Intermediate (5 - 20%) | pT3 N0 Nx<br>or pT1-3, N1a-N1b<br>or aggressive histology<br>or vascular invasion<br>or RAI uptake outside thyroid bed | > 4 cm<br>or microsc ETE<br>or N1<br>+ R0<br>+ M0 |
| High (> 20%)           | pT4<br>or M1 or R1<br>or inappropriate post-op Tg  | persistent disease                                |

Cooper, ATA, 2009

| RESPONSE         | excellent                  | indeterminate               | incomplete biochemical      | incomplete structural          |
|------------------|----------------------------|-----------------------------|-----------------------------|--------------------------------|
| supressed Tg     | < 0.2 ng/ml                | 0.2-1 ng/ml                 | > 1 ng/ml                   |                                |
| stimulated Tg    | < 1 ng/ml                  | 1-10 ng/ml                  | > 10 ng/ml                  |                                |
| Tg trend         | absent                     | declining                   | stable rising               |                                |
| anti Tg Ab's     | absent                     | absent declining            | persistent rising           |                                |
| neck examination | normal                     | normal                      | normal                      | abnormal                       |
| imaging          | negative                   | nonspecific                 | normal nonspecific          | abnormal                       |
|                  | <b>Lower risk estimate</b> | <b>Stable risk estimate</b> | <b>Higher risk estimate</b> | <b>Very high risk estimate</b> |

### DRS → organisation FU

| RESPONSE      | excellent  | indeterminate | incomplete biochemical | incomplete structural |
|---------------|------------|---------------|------------------------|-----------------------|
| TSH target*   | 0.5-2 IU/l | 0.1-0.5 IU/l  | < 0.1 IU/l             | < 0.01 IU/l           |
| serum Tg      | yearly     | yearly        | 6-12 months            | 3-6 months            |
| neck US       | 5 years    | 1-3 years     | 6-12 months            | 3-6 months            |
| stimulated Tg | no         | maybe         | consider               | consider              |
| WBS           | no         | maybe         | consider               | consider              |
| other imaging | no         | no            | consider               | yes                   |

\*= for pts at low risk for T4 tt

Tuttle 2014

| Risk Factors        | Response to primary treatment |               |                        |                       |
|---------------------|-------------------------------|---------------|------------------------|-----------------------|
|                     | Excellent                     | Indeterminate | Biochemical incomplete | Structural incomplete |
| No risk factors     | None                          | Mild          | Mod/full               | Mod/full              |
| Menopause           | None                          | Mild          | Mild                   | Mod/full              |
| Tachycardia         | None                          | Mild          | Mild                   | Mod/full              |
| Osteopenia          | None                          | Mild          | Mild                   | Mod/full              |
| > 60 years of age   | None                          | None          | Mild                   | Mod/full              |
| Osteoporosis        | None                          | None          | Mild                   | Mild                  |
| Atrial fibrillation | None                          | None          | None                   | Mild                  |

Increasing risk of osteoporosis and/or cardiac complications

Degree of TSH Suppression:  
None: TSH 0.5-2.0 mU/L  
Mild: TSH 0.1-0.5 mU/L  
Mod/full: TSH <0.1 mU/L

Cabanillas Lancet 2016

### Casus 4 opstart hypothyreose

- vrouw, 63 jaar
- Nieuwe diagnose: Hashimoto, hypothyreose
- Vitiligo, RA

### doel

- TSH normaal (0,3-4,0 mU/l)
- Kijk bij opstart vooral naar FT4 cfr TSH normaliseert slechts traag!

### Casus 5 long term FU hypothyreose

- vrouw, 63 jaar
- Hashimoto, hypothyreose
- Vitiligo, RA

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### doel

- TSH normaal (0,3-4,0 mU/l)
- Kijk bij opstart vooral naar FT4  
cfr TSH normaliseert slechts traag!
- Kijk op termijn vooral naar TSH  
Kijk niet naar FT4, is vaak verhoogd als er weinig SK functie over is!!!!
- FT4 enkel nuttig als buiten TSH range

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### Casus 6 opstart hyperthyreose

- vrouw, 33 jaar
- Graves Basedow, hyperthyreose

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### doel

- FT4 (en FT3) normaal
- TSH loopt bij opstart achter
- Let op levertesten  
cave: keelpijn +++, koorts +++

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### Casus 7 long term opvolging hyperthyreose

- vrouw, 33 jaar
- Graves Basedow, hyperthyreose

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### doel

- FT4 (en FT3) normaal
- TSH normaal, of onderdrukt  
TSH zeker niet verhoogd  
→ indien nodig thyroxine titreren
- Let op levertesten  
cave: keelpijn +++, koorts +++

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### Casus 8 long term opvolging hyperthyreose patiënt "ontsnapt"

- vrouw, 33 jaar
- Graves Basedow, hyperthyreose

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### doel

- Compliance?
- Vergissing?
- Strumazol ophogen?  
Thyroxine verminderen?

Kijk naar dosissen, gewicht, TSHrAb,  
startwaarden, vorige evolutie, ...

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### Casus 9 long term opvolging hyperthyreose wanneer stoppen?

- vrouw, 33 jaar
- Graves Basedow, hyperthyreose

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### doel

- 18 maand?
- TSHrAb's liefst 6 maand laag nl  
→ vaak langere therapie als hoge TSI start
- Dit is bij Graves-Basedow!
- Bij toxisch adenoom of toxisch MNG:  
I-131 of chirurgie  
medic tt is geen definitieve oplossing!

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### Casus 9 long term opvolging hyperthyreose welke FU na stoppen?

- vrouw, 33 jaar
- Graves Basedow, hyperthyreose

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### doel

- TSH normaal
- In beginfase: cave recidief hyperthyreose  
Op lange termijn: cave AI hypothyreose
- Voorstel TSH controle:
  - 1<sup>ste</sup> jaar per 3 maand
  - 2<sup>de</sup> jaar per 6 maand
  - Daarna levenslang per jaar

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### Casus 10 zwanger, Hashimoto recidiverend miskraam

- vrouw, 29 jaar
- recidiverend miskraam
- Hashimoto, euthyreoot, nog geen T4 tt
- Nu 8 weken zwanger



### doel

- TSH 0,5-2,5 mU/l (0,5-4,0 mU/l?)
- Effect op foetale ontwikkeling?
- Effect op de zwangerschap?



### SKAb positief en miskraam

- x 2-5 (meta-analysis: x2.3, CI 1.80-2.95)
- universal screening? imperfect data
- R/thyroxine? Negro: 3.5 vs 13.8% miskraam but tt start at 10 wk, loss mostly < 11 wk
- Grotere studies nodig



Table 2 Meta-analysis of prospective studies analyzing abortion rates among women with thyroid autoantibodies (Ab +ve) versus women without antibodies (Ab -ve).

| Reference                  | Abortion rate in Ab +ve women | Abortion rate in Ab -ve women | Odds ratio | 95% CI     |
|----------------------------|-------------------------------|-------------------------------|------------|------------|
| Stagnaro-Green et al. (16) | 17/100 (17%)                  | 33/392 (8%)                   | 2.23       | 1.19-4.20  |
| Glinner et al. (17)        | 6/45 (13%)                    | 20/603 (3%)                   | 4.48       | 1.70-11.81 |
| Lejeune et al. (18)        | 5/23 (22%)                    | 16/340 (5%)                   | 5.63       | 1.82-17.1  |
| Pratt et al. (19)          | 8/13 (62%)                    | 12/42 (29%)                   | 10.0       | 2.20-46.5  |
| Singh et al. (20)          | 28/87 (32%)                   | 49/301 (16%)                  | 2.44       | 1.42-4.20  |
| Iijama et al. (21)         | 13/125 (10%)                  | 52/951 (5%)                   | 2.01       | 1.06-3.80  |
| Kim et al. (22)            | 4/10 (40%)                    | 4/35 (11%)                    | 5.17       | 2.72-26.54 |
| Muller et al. (23)         | 4/12 (33%)                    | 6/42 (14%)                    | 2.13       | 0.51-8.87  |
| Rushworth et al. (24)      | 10/24 (42%)                   | 30/77 (39%)                   | 1.12       | 0.44-2.84  |
| Poppe et al. (25)          | 9/17 (53%)                    | 20/87 (23%)                   | 3.77       | 1.34-10.63 |
| Total                      | 104/456 (23%)                 | 336/2957 (11%)                | 2.30       | 1.80-2.96  |

Prummel, Eur J Endocr 2004

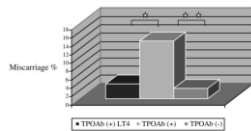
Table 3 Age difference (in years; mean ± s.d.) among women positive for thyroid autoantibodies as compared to antibody-negative women in studies on the association between thyroid antibodies and miscarriage where these data were available.

| Reference             | Age in TPO +ve women | Age in TPO -ve women | Difference | P       |
|-----------------------|----------------------|----------------------|------------|---------|
| Bussen & Steck (9)    | 31.0 ± 5.2           | 30.3 ± 4.5           | +0.7       | NS      |
| Baigs et al. (15)     | 27.7 ± 6.2           | 25.9 ± 5.2           | +1.8       | <0.0009 |
| Glinner et al. (17)   | 29.3 ± 1             | 27.3 ± 1             | +2.0       | <0.001  |
| Lejeune et al. (18)   | 28.2 ± 9.5           | 27.2 ± 6.8           | +1.0       | 0.06    |
| Pratt et al. (19)     | 33 ± 2.9             | 34 ± 3.4             | -1.0       | NS      |
| Iijama et al. (21)    | 30.2 ± 4.8           | 30.0 ± 4.3           | +0.2       | NS      |
| Muller et al. (23)    | 32.4 ± 3.3           | 32.4 ± 4.4           | 0          | NS      |
| Rushworth et al. (24) | 34 (20-41)*          | 34 (22-46)           | 0          | NS      |
| Poppe et al. (25)     | 33.2 ± 4.6           | 31.6 ± 5.4           | +1.6       | NS      |
| Average ± s.d.        | 31.0 ± 2.3           | 30.3 ± 3.0           | +0.7 ± 1.0 |         |

\*Median (range).



### SKAb positief en miskraam



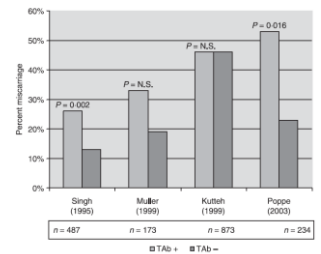
J. Clin. Endocrinol. Metab. 2006 91:2587-2591



Fig. 4. Percentage of miscarriages (top) and premature deliveries (bottom) in group A (TPOAb+ treated with LT4), group B (TPOAb+), and group C (TPOAb-). \*P < 0.05; \*\*P < 0.01.

### SKAb positief en miskraam na IVF

- Meta analysis: x 1.99, CI 1.42-2.79
- Universal screening?



Poppe, Clinical Endocrinology (2007) 66, 309-321



### SKAb positief en recidiverend miskraam

- = 2 consecutive losses or 3 total loss  
= 1% van vrouwen
- verband: contradictorisch!
- screening????
- R/thyroxine?  
R/iv Ig?  
R/selenium (maar meer DM2?)
- grotere studies nodig

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### doel

- TSH 0,5-2,5 mU/l (0,5-4,0 mU/l?)
- Effect op foetale ontwikkeling?
- Effect op de zwangerschap?
- Behandelen
- SK testen per maand tot 5<sup>de</sup> maand  
SK testen 26-32 wk
- Na bevalling: terug dosis van voor zwschp  
+ controle SK testen 4-6 wk na partus

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### Casus 11 subacute thyroiditis De Quervain opvolging behandeling?

- vrouw, 54 jaar
- pijn SK, Tc scan neg, inflammatie ++
- R/ NSAID → Medrol 40 mg

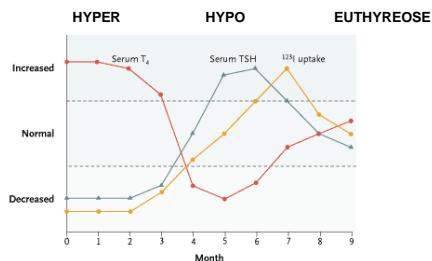
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### doel

- Inflammatie onder controle?  
→ dosis minderen met 25% per 7-10 d
- SK functie?

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### Subacute thyroiditis van De Quervain



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### Casus 12 Cordarone hyperthyrosis welke FU?

- man, 73 jaar
- Cordarone sinds 3 jaar
- T4 hyperthyrose +++
- AIT1 of AIT2?
- R/Na perchlooraat, Strumazol

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## Amio-induc thyreotoxicosis

- USA 3%, Europa 10%
- gemiddeld na 3 jaar
- soms vele maanden na stoppen inname
- baseline lage TSH = risk factor
- man/vrouw = 3/1
- ernstig!!!
  
- AIT type 1: verhoogde synthese T4 and T3  
vb autonoom MNG, Graves  
R/NaClO4 + antithyroidea; evt chirurgie
- AIT type 2: overmatige loslating T4 and T3  
normale thyroïed  
R/Medrol; evt chirurgie
- gemengde vormen



## doel

- Van dicht opvolgen!
- Klinische evaluatie: algemeen, hart

