갑상샘 기능 이상과 생식 기능

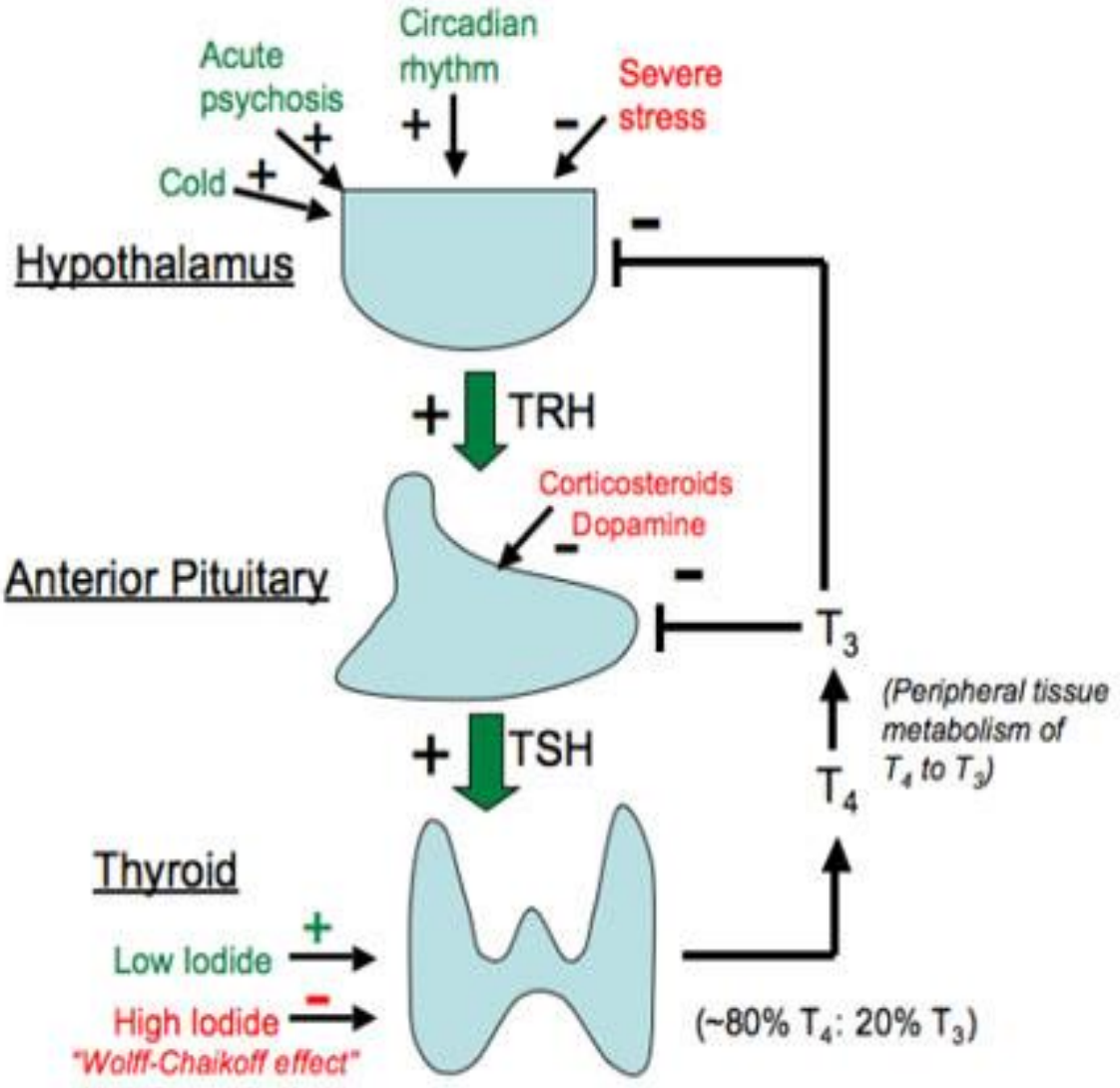
분당서울대학교병원
김슬기

Clinical Practice Guidelines

- 대한갑상선학회
- American Association of Clinical Endocrinologists (AACE) and the American Thyroid Association (ATA)
- The American College of Obstetrics and Gynecologists (ACOG)
- American Society for Reproductive Medicine (ASRM)
- Endocrine Society

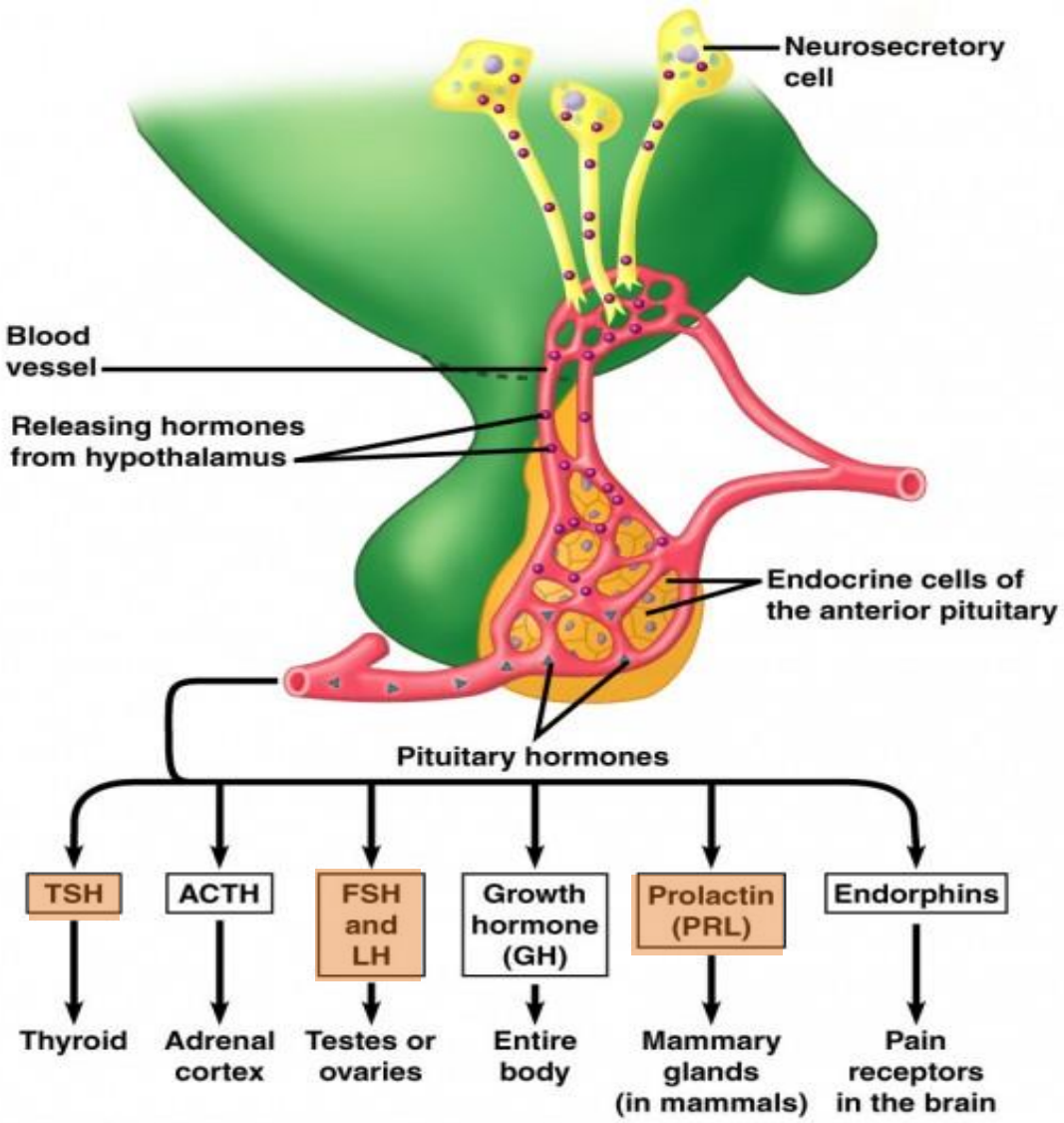
Garber et al. Thyroid 2012
Groot et al. J Clin Endocrinol Metab 2012
Practice Committee of the ASRM. Fertil Steril 2015

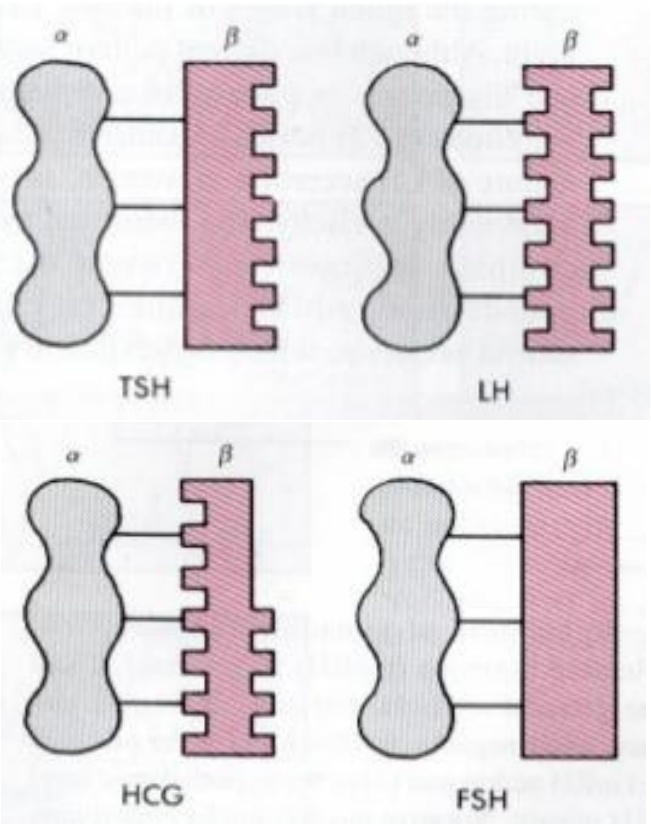
Thyroid hormone



SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Thyroid hormone





SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Thyroid hormone - Pregnancy

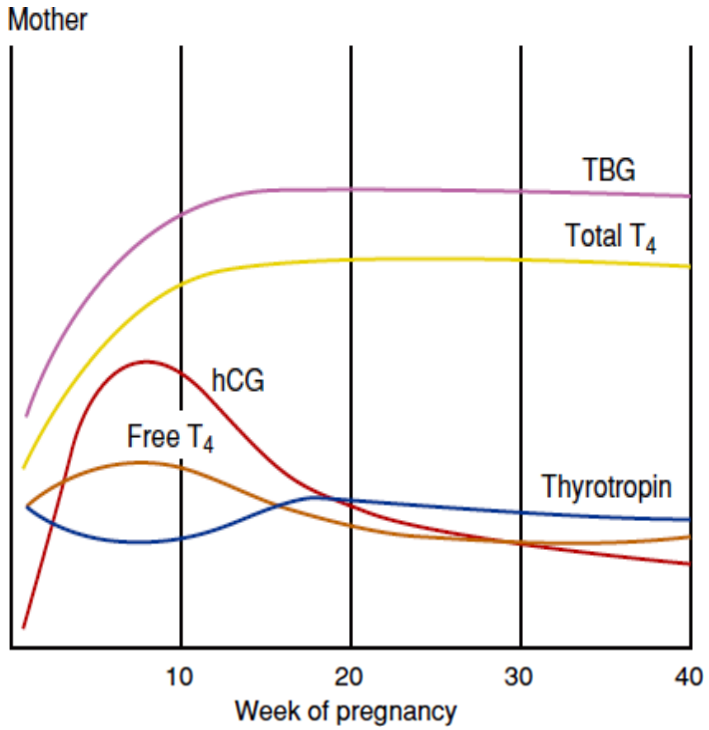
- 임신 중 모체 및 태아의 갑상선 호르몬 요구량의 증가
  - 크기 10–30% 증가
- 태아 갑상선 : 임신 12주 이후부터 합성
- 모체 갑상선 호르몬은 태아의 정상 뇌 발달에 중요

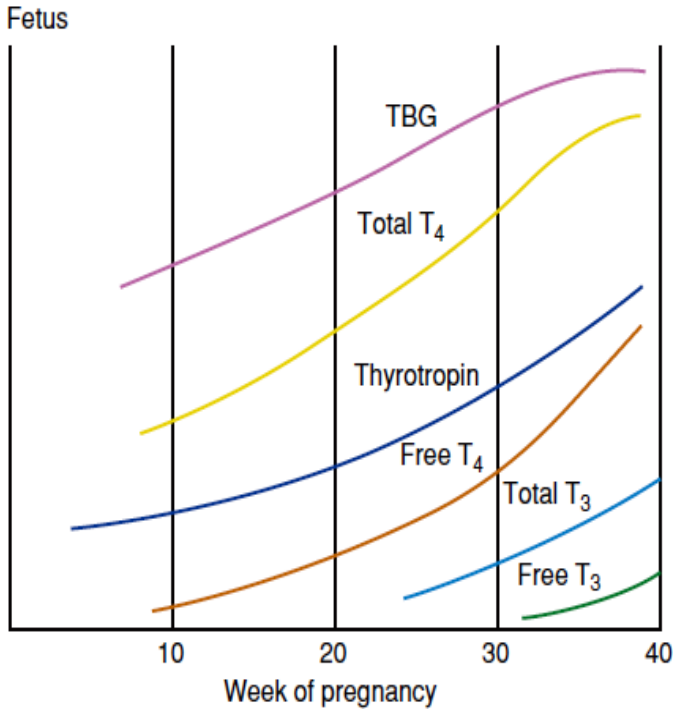
Williams Obstetrics 24th ed

Thyroid hormone - Pregnancy

- 임신 초기 hCG 의 작용으로 TSH 는 비임신 상태에 비해 낮아짐

  (hCG 최대 농도 도달 : 임신 7-11주)





Williams Obstetrics 24th ed

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

Reference range

4.0 – 5.0 mIU/L

Group, study, society	*TSH upper normal*	*Comments*
NACB	2.5	When there is no evidence of thyroid disease
NHANES III, disease free	4.5	No self-reported thyroid disease Not on thyroid medications
NHANES III, reference population	4.12	No self-reported thyroid disease Not on thyroid medications Negative anti-thyroid antibodies Not pregnant Not on estrogens, androgens, lithium
Hanford Thyroid Disease Study	4.10	No evidence of thyroid disease Negative anti-thyroid antibodies Not on thyroid medications Normal ultrasound (no nodules or thyroiditis)
Pregnancy, first trimester	2.0–2.5	See sections *L-thyroxine treatment of hypothyroidism* and *Hypothyroidism during pregnancy*
Pregnancy, second trimester	3.0	See sections *L-thyroxine treatment of hypothyroidism* and *Hypothyroidism during pregnancy*
Pregnancy, third trimester	3.5	See sections *L-thyroxine treatment of hypothyroidism* and *Hypothyroidism during pregnancy*

Garber et al. Thyroid 2012

Reference range

Group, study, society	*TSH upper normal*	*Comments*
NACB	2.5	When there is no evidence of thyroid disease
NHANES III, disease free	4.5	No self-reported thyroid disease Not on thyroid medications
NHANES III, reference population	4.12	No self-reported thyroid disease Not on thyroid medications Negative anti-thyroid antibodies Not pregnant Not on estrogens, androgens, lithium
Hanford Thyroid Disease Study	4.10	No evidence of thyroid disease Negative anti-thyroid antibodies Not on thyroid medications Normal ultrasound (no nodules or thyroiditis)
Pregnancy, first trimester	2.0–2.5	See sections *L-thyroxine treatment of hypothyroidism* and *Hypothyroidism during pregnancy*
Pregnancy, second trimester	3.0	See sections *L-thyroxine treatment of hypothyroidism* and *Hypothyroidism during pregnancy*
Pregnancy, third trimester	3.5	See sections *L-thyroxine treatment of hypothyroidism* and *Hypothyroidism during pregnancy*

Garber et al. Thyroid 2012

Thyroid dysfunction in Male

Hormonal changes in male

	Thyrotoxicosis		Hypothyroidism	
	Males	Females	Males	Females
SHBG	↑	↑	↓ or N	↓
E_2	N or ↑	↑	N	↓
Estrone		↑		↓
Production rate of estrogens		→		→ or ↓
Metabolic clearance rate of estrogens or androgens	↓	↓	↓	↓
Free E_2	↑	→		N
Testosterone	↑	↑	↓	↓
Δ4-Androstenedione		↑	↓	↓
DHEA	↑	↑	↓	
Free testosterone	→		↓	N
Bioavailable testosterone	↑			
Conversion of testosterone to Δ4-androstenedione	↑	→ or ↑	↓	↑
Androgen conversion to estrone	↑	↑		
Progesterone	↑	↓ or →		↓ or →
LH	↑ or →	↑ or →	N	N
FSH	↑ or →	↑ or →	N	N
After GnRH				
LH	↑	↑	↓	↓
FSH	↑	↑	↓	↓

↑, Increase; ↓, decrease; →, no change; N, normal; —, not available.

Krassas et al. Endocrine Reviews 2010

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Hormonal changes in male

	Thyrotoxicosis		Hypothyroidism	
	Males	Females	Males	Females
SHBG	↑	↑	↓ or N	↓
E_2	N or ↑	↑	N	↓
Estrone		↑		↓
Progesterone	↑	↓ or →		↓ or →
LH	↑ or →	↑ or →	N	N
FSH	↑ or →	↑ or →	N	N
After GnRH				
LH	↑	↑	↓	↓
FSH	↑	↑	↓	↓

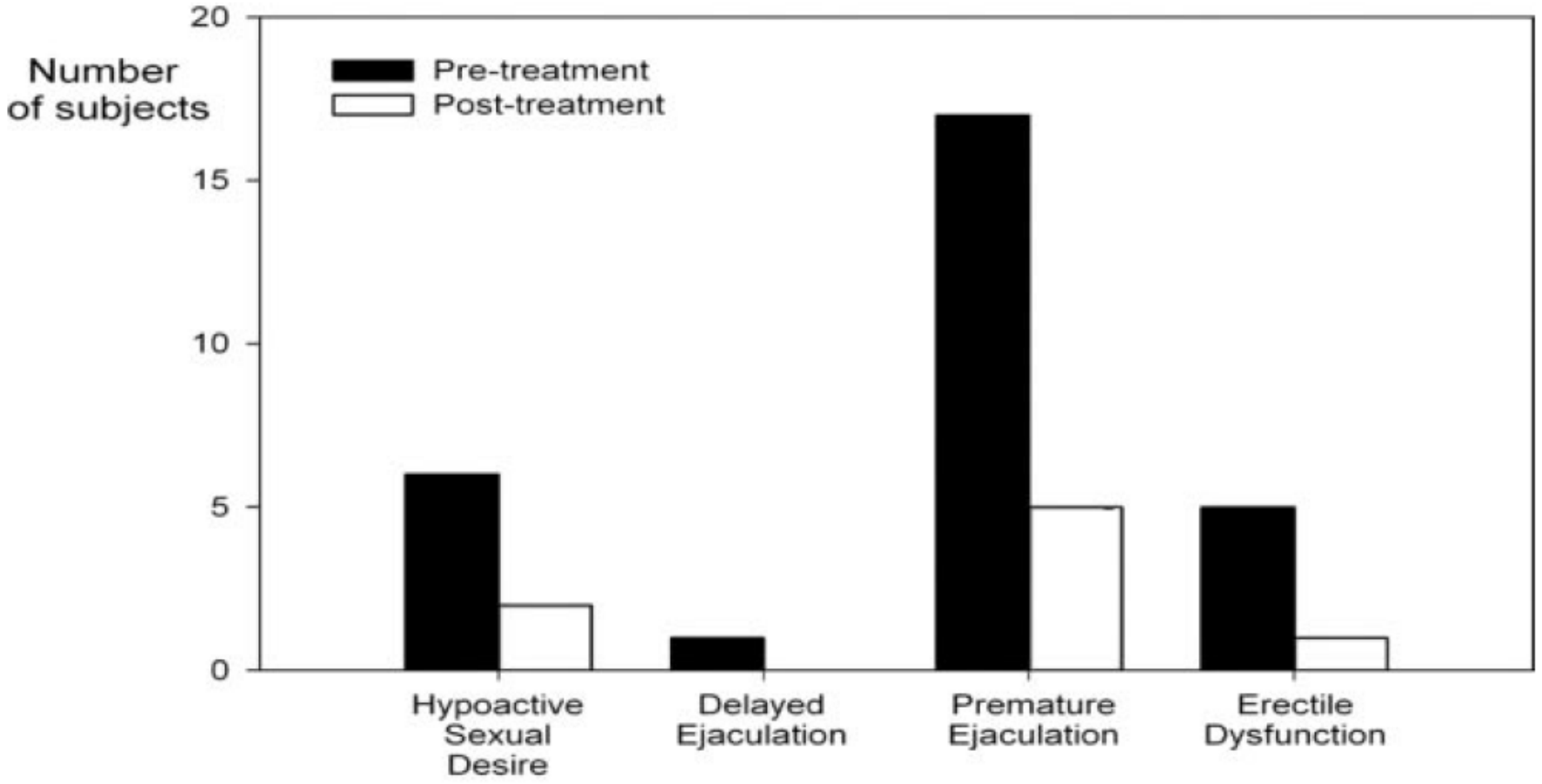
↑, Increase; ↓, decrease; →, no change; N, normal; —, not available.

Changes in SHBG and sex steroids

Krassas et al. Endocrine Reviews 2010

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

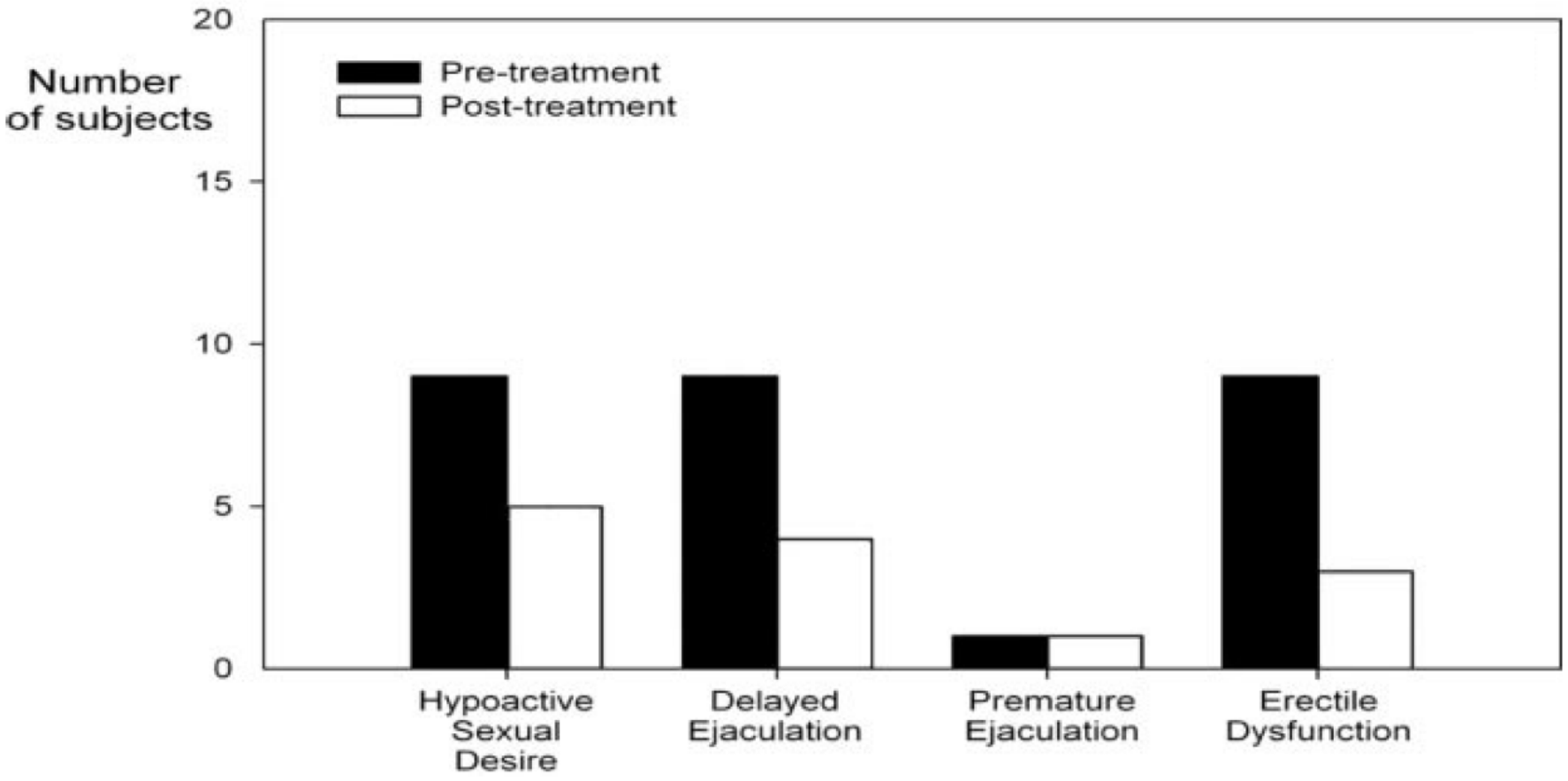
Hyperthyroidism in male



Carani et al. J Clin Endocrinol Metab 2005

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Hypothyroidism in male



Carani et al. J Clin Endocrinol Metab 2005

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

in Male

- Many patients with erectile dysfunction display thyroid dysfunction

- Hyperthyroidism
  - ➢ abnormalities in sperm motility
- Hypothyroidism
  - ➢ abnormalities in sperm morphology

❖ These abnormalities improve or normalize when euthyroidism is restored

Krassas et al. Endocrine Reviews 2010

in Male

human reproduction

ORIGINAL ARTICLE *Andrology*

Is thyroid hormones evaluation of clinical value in the work-up of males of infertile couples?

F. Lotti[1], E. Maseroli[1], N. Fralassi[1], S. Degl'Innocenti[1], L. Boni[2], E. Baldi[1], and M. Maggi[1,*]

Lotti et al. Hum Reprod 2016

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

in Male

human reproduction

ORIGINAL ARTICLE *Andrology*

Is thyroid hormones evaluation of clinical value in the work-up of males of infertile couples?

F. Lotti[1], E. Maseroli[1], N. Fralassi[1], S. Degl'Innocenti[1], L. Boni[2], E. Baldi[1], and M. Maggi[1,*]

- cross-sectional analysis
- consecutive series of 172 subjects
- 2010.09 ~ 2014.11

Lotti et al. Hum Reprod 2016

in Male

Table III Associations among TSH, fT3, fT4 levels and seminal parameters or significant ultrasound features of the organs of the male genital tract in the whole sample.

	TSH (mU/l)		fT3 (pmol/l)		fT4 (pmol/l)	
	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis
Seminal parameters						
Semen volume (ml)	$r = 0.070$, $P = 0.377$	—	**$r = 0.163$, $P = 0.028$**	**Adj. $r = 0.167$, $P = 0.041$**	**$r = 0.178$, $P = 0.024$**	$r = 0.081$, $P = 0.319$
pH	$r = -0.001$, $P = 0.991$	—	$r = -0.001$, $P = 0.991$	—	$r = -0.012$, $P = 0.875$	—
Seminal fructose levels (mg/ejaculate)	**$r = 0.201$, $P = 0.034$**	$r = 0.167$, $P = 0.189$	**$r = 0.215$, $P = 0.023$**	**Adj. $r = 0.241$, $P = 0.021$**	**$r = 0.198$, $P = 0.036$**	$r = 0.181$, $P = 0.093$
Sperm concentration, $\times 10^6$/ml	$r = 0.017$, $P = 0.830$	—	$r = -0.079$, $P = 0.316$	—	$r = -0.099$, $P = 0.208$	—
Sperm total count, $\times 10^6$/ejaculate	$r = 0.031$, $P = 0.699$	—	$r = -0.037$, $P = 0.641$	—	$r = -0.028$, $P = 0.722$	—
Sperm progressive motility, %	$r = -0.005$, $P = 0.954$	—	$r = -0.034$, $P = 0.694$	—	$r = -0.080$, $P = 0.356$	—
Sperm morphology, % normal forms	$r = 0.097$, $P = 0.260$	—	$r = -0.113$, $P = 0.186$	—	$r = -0.181$, $P = 0.063$	—
sIL-8 (ng/ml)	$r = 0.083$, $P = 0.308$	—	$r = -0.005$, $P = 0.952$	—	$r = 0.010$, $P = 0.905$	—
Ultrasound parameters						
SV total volume before ejaculation (ml)	**$r = 0.174$, $P = 0.027$**	**Adj. $r = 0.187$, $P = 0.046$**	**$r = 0.327$, $P < 0.0001$**	**Adj. $r = 0.354$, $P < 0.0001$**	$r = 0.046$, $P = 0.560$	—
SV total volume after ejaculation (ml)	**$r = 0.155$, $P = 0.05$**	**Adj. $r = 0.175$, $P = 0.049$**	**$r = 0.301$, $P < 0.0001$**	**Adj. $r = 0.318$, $P < 0.0001$**	$r = 0.069$, $P = 0.387$	—
ΔSV volume (ml)	**$r = 0.208$, $P = 0.009$**	**Adj. $r = 0.225$, $P = 0.018$**	**$r = 0.304$, $P < 0.0001$**	**Adj. $r = 0.346$, $P < 0.0001$**	$r = 0.056$, $P = 0.485$	—
SV inhomogeneity before ejaculation	**RR = 3.60 [1.21–10.71], $P = 0.021$**	**RR = 6.34 [1.48–22.34], $P = 0.013$**	**RR = 2.60 [1.47–4.62], $P = 0.001$**	**OR = 3.18 [1.66–6.07], $P < 0.0001$**	RR = 091 [0.80–1.03], $P = 0.146$	—
SV inhomogeneity after ejaculation	RR = 2.23 [0.82–6.07], $P = 0.118$	—	**RR = 2.33 [1.31–4.15], $P = 0.004$**	**OR = 2.79 [1.48–5.27], $P = 0.002$**	RR = 0.96 [0.84–1.08], $P = 0.498$	—
Epididymal body diameter (mm)	$r = 0.094$, $P = 0.237$	—	$r = -0.031$, $P = 0.698$	—	**$r = -0.213$, $P = 0.007$**	**Adj. $r = -0.191$, $P = 0.028$**
Epididymal tail diameter (mm)	$r = 0.100$, $P = 0.210$	—	$r = 0.003$, $P = 0.967$	—	**$r = -0.217$, $P = 0.006$**	**Adj. $r = -0.208$, $P = 0.018$**
Proximal vas deferens diameter (mm)	$r = -0.077$, $P = 0.335$	—	$r = -0.150$, $P = 0.067$	—	**$r = -0.172$, $P = 0.029$**	Adj. $r = -0.121$, $P = 0.176$

Multivariate analysis has been adjusted for age, body mass index, smoking habit (pack-years), sexual abstinence (days), calculated free testosterone, prolactin and seminal interleukin 8 (sIL-8) levels. RR and OR values are reported for each fT3 unit increment. Significant associations are reported in bold.
TSH, thyroid-stimulating hormone; fT3, free triiodothyronine; fT4, free thyroxine; SV, seminal vesicles; RR, relative risk; OR, odds ratio.

Lotti et al. Hum Reprod 2016

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

in Male

Table III Associations among TSH, fT3, fT4 levels and seminal parameters or significant ultrasound features of the organs of the male genital tract in the whole sample.

	TSH (mU/l)		fT3 (pmol/l)		fT4 (pmol/l)	
	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis
Seminal parameters						
					$P = 0.007$	**$P = 0.028$**
Epididymal tail diameter (mm)	$r = 0.100$, $P = 0.210$	—	$r = 0.003$, $P = 0.967$	—	**$r = -0.217$, $P = 0.006$**	**Adj. $r = -0.208$, $P = 0.018$**
Proximal vas deferens diameter (mm)	$r = -0.077$, $P = 0.335$	—	$r = -0.150$, $P = 0.067$	—	**$r = -0.172$, $P = 0.029$**	Adj. $r = -0.121$, $P = 0.176$

Multivariate analysis has been adjusted for age, body mass index, smoking habit (pack-years), sexual abstinence (days), calculated free testosterone, prolactin and seminal interleukin 8 (sIL-8) levels. RR and OR values are reported for each fT3 unit increment. Significant associations are reported in bold.
TSH, thyroid-stimulating hormone; fT3, free triiodothyronine; fT4, free thyroxine; SV, seminal vesicles; RR, relative risk; OR, odds ratio.

No associations between TH and sperm parameters

Positive effect of TH on seminal vesicle size

Lotti et al. Hum Reprod 2016

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

in Male

Table III Associations among TSH, fT3, fT4 levels and seminal parameters or significant ultrasound features of the organs of the male genital tract in the whole sample.

	TSH (mU/l)		fT3 (pmol/l)		fT4 (pmol/l)	
	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis	Univariate analysis	Multivariate analysis
Seminal parameters						

No associations between TH and sperm parameters

Positive effect of TH on seminal vesicle size

STUDY ANSWER:

Our results suggest that TH evaluation is not mandatory in the work-up of male infertility.

Lotti et al. Hum Reprod 2016

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

Thyroid dysfunction in Female

in Female

	Prevalence (%)
Thyrotoxicosis	
Early studies	
Oligomenorrhea	58
Menstrual irregularities	65
Recent study	
Abnormal menses	22
Control subjects	8
Hypothyroidism	
Early studies	
Menstrual disturbances	80
Menstrual irregularities	56
Menstrual irregularities	68
Recent study	
Irregular cycles	23
Control subjects	8

Krassas et al. Endocrine Reviews 2010

in Female

- Hyperthyroidism
  - Hypomenorrhea, polymenorrhea
- Hypothyroidism
  - Oligomenorrhea, amenorrhea

- Hyper- and hypothyroidism has been linked with reduced fertility

Krassas et al. Endocrine Reviews 2010

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

임신 중 갑상선 기능 검사 – 모두에서 필요한가?

- Universal screening group 에서 약물 치료를 받을 확률이 3.15 배 증가
- no differences

  between universal screening group VS. no screening group

  - Miscarriage, fetal and neonatal death, preeclmpsia
  - PTL, Placenta abruption, C/S, maternal GDM, CHF
  - Fetal malformation, LBW, ICU admission rate, fetal neurosensory disability (IQ)

Spencer L et al. Cochrane Database Systemic review 2015

임신 중 갑상선 기능의 선별검사

1) 모든 임신부를 대상으로 TSH 선별검사 적용 하는 것은 근거 부족

2) 일상적인 fT4 선별검사는 권고되지 않음

3) Hyperemesis gravida 환자에서도 일시적인 생리적 변화이므로 routine 한 screening 을 권고하지 않음

임신 중 갑상선 기능 선별검사 대상

- 갑상선 기능 이상 및 갑상선 수술 병력
- 두경부 방사선 조사 병력
- 아미오다론, 리튬 복용, 6주 이내의 방사선 조영제 노출
- 요오드 결핍지역 거주
- 갑상선 기능이상의 증상 또는 갑상선종
- TPO Ab(+)
- 갑상선 기능 이상의 가족력
- 제 1형 당뇨병 또는 다른 자가 면역 질환
- BMI ≥ 40kg/m^2

- 30세 이상
- 유산 또는 조산의 병력
- 난임

Subclinical Hypothyroidism

SCH – Reproduction

Prevalence in infertile women : 1 – 43 %

First author (Ref.)	Prevalence of SCH in patients	Prevalence of SCH in controls	SCH was defined as	Type of study
Bohnet (168)	11% (20/185)	No controls	Basal TSH >3 mU/liter or peak TSH[c] >15 mIU/liter	P
Gerhard (170)	43% (80/185)[a]	No controls	Peak TSH[c] >20 mIU/liter	P
Shalev (171)	0.7% (3/444)	No controls	Basal TSH >4.5 mIU/liter	R
Grassi (172)	4.6% (6/129)	No controls	Basal TSH >4.5 mIU/liter	P
Arojoki (173)	1.3% (4/299)	2–3%[b]	Basal TSH >5.5 mIU/liter	R
Poppe (155)	0.9% (4/438)	<1%	Basal TSH >4.2 mIU/liter	P
Raber (174)	34% (96/283)	No controls	Basal TSH >4 mIU/liter or peak TSH[c] >15 mIU/liter	P
Abalovich (175)	13.9% (34/244)	3.9% (6/155)	Basal TSH >4.22 mIU/liter, stimulating TSH >26.6 mIU/liter	R

Poppe et al. Nat Clin Pract Endocrinol Metab 2008

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

SCH – Reproduction

- Infertile women with normal TSH levels (0.4–4.5 μIU/mL)
- Retrospective study
- N=225

Table 1 Patient characteristics of 225 women who underwent work up for in vitro fertilization

	All ($n = 225$)	TSH < 3μIU/mL ($n = 199$)	TSH ≥ 3μIU/mL ($n = 26$)	*P*-value
Female age (years)	38.4 ± 5.0	38.3 ± 5.1	38.9 ± 4.4	0.67
TSH (μIU/mL)	1.8 ± 0.9	1.6 ± 0.6	3.5 ± 0.5	
Thyroid autoimmunity (%)	11.1 %	9.0 %	26.9 %	0.01
Thyroid peroxidase antibodies (%)	11.1 %	9.0 %	26.9 %	0.02
Thyroglobulin antibodies (%)	1.8 %	1.0 %	0.8 %	0.10
AMH (ng/mL)	1.3 ± 2.0	1.4 ± 2.0	0.8 ± 1.8	0.02
Positive Thyroid autoimmunity	0.9 ± 1.3	1.1 ± 1.5	0.5 ± 0.6	0.45
Negative Thyroid autoimmunity	1.4 ± 2.1	1.4 ± 2.1	0.9 ± 2.1	0.04

Values are presented as means ± standard deviation

Weghofer et al. Reprod Biol Endocrinol 2016

SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

SCH – Pregnancy outcome

- in thyroid antibody negative women

  with TSH levels 2.5 – 5.0 in 1st trimester

  - Increased pregnancy loss rate

Negro et al. J Clin Endocrinol Metab. 2010

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

SCH – IVF outcomes

Table III. Mean Hormone Levels by First Cycle Pregnancy Outcomes

		Prolactin (ng/mL)		TSH (μIU/mL)	
	Number	Mean	SD	Mean	SD
Clinical pregnancy					
Yes	151	15.9	8.6	2.2	2.2
No	358	16.0	9.4	2.1	3.1
p value		0.78		0.21	
Detailed outcome					
Failed retrieval	50	14.8	9.4	1.8	1.2
Failed fertilization	22	17.2	8.2	5.1	11.6
Failed implantation	285	16.1	9.5	1.9	1.2
SAB	22	16.3	10.7	2.7	3.0
Liveborn	126	15.7	8.2	2.1	2.1
p value		0.721		0.004	
Fertilization rate					
<50%	141	16.6	8.6	2.5	4.7
≥50%	305	15.7	9.1	2.0	1.7
p value		0.23		0.05	

- PRL, TSH prior to IVF
- Prospective study
- N=509

Cramer et al. J Assist Reprod Genet 2003

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

SCH

Treatment in women with SCH

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

Treatment of SCH – IVF outcomes

Characteristics	Group A (levothyroxine treatment) (n = 35)	Group B (placebo) (n = 35)	*P* value
No. oocytes retrieved, mean (SD)	6.2 (0.7) (range, 5.5-8.3)	6.1 (0.9) (range, 5.2-8.8)	.450
No. of metaphase II at time of injection	29	14	.019
Miscarriage, %	9	13	.031
Fertilization, %	51.9	18.8	.015
Pregnancy, %	35	10	.021
Delivery, %	26	3	.017

- LT4 50 – 100 μg (one month before ART)
- RCT
- N=70

Rahman et al. Endocr Pract 2010

SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Treatment of SCH – IVF outcomes

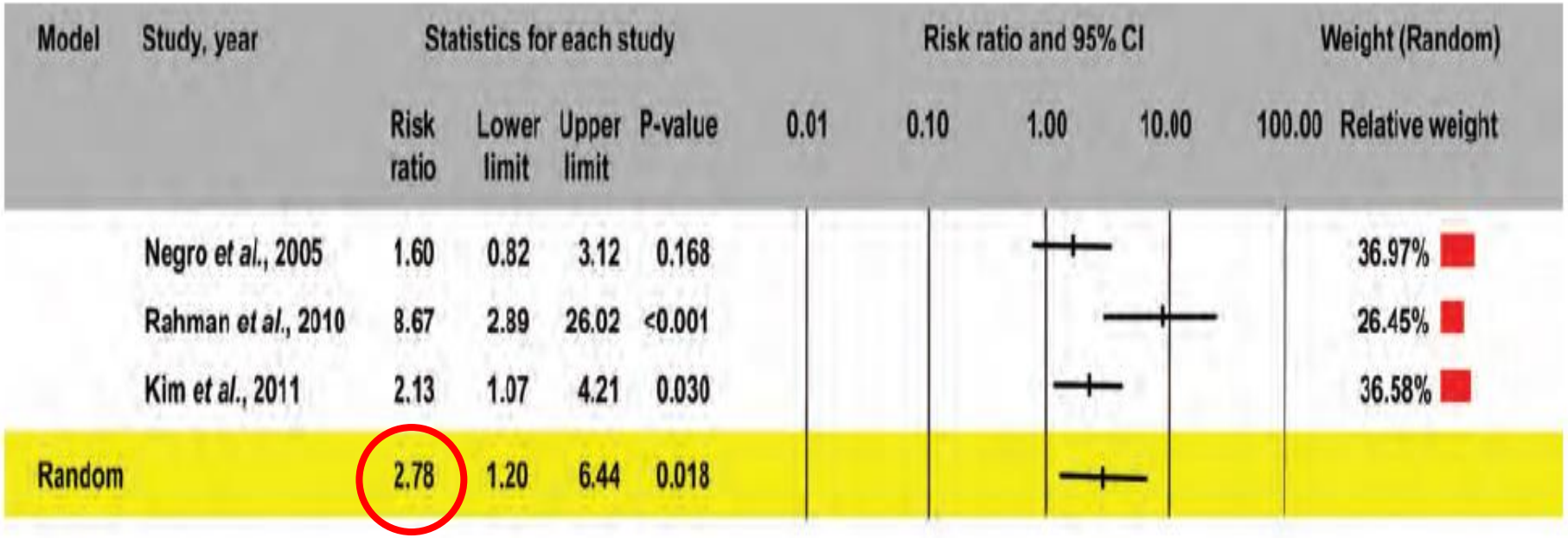
- LT4 50 μg
  (from the 1st day of COS)
- Prospective, randomized trial
- N=64

Factor	LT4 treatment	Control	*P* value
No. of oocytes retrieved	9.3 ± 3.9	9.2 ± 3.2	NS[b]
No. of mature oocytes	8.2 ± 3.4	7.5 ± 2.6	NS[b]
No. of fertilized oocytes	8.1 ± 3.4	7.2 ± 2.3	NS[b]
No. of grade I, II embryos	3.3 ± 1.6	2.2 ± 1.3	.007[b]
No. of embryos transferred	2.9 ± 0.5	2.9 ± 0.4	NS[b]
No. of embryos cryopreserved	2.5 ± 2.7	1.8 ± 2.3	NS[b]
Embryo implantation rate, % (n)	26.9 (25/93)	14.9 (14/94)	.044[a]
Clinical PR per cycle initiated, % (n)	53.1 (17/32)	37.5 (12/32)	NS[a]
Miscarriage rate, % (n)	0 (0/17)	33.3 (4/12)	.021[a]
Live birth rate per cycle initiated, % (n)	53.1 (17/32)	25.0 (8/32)	.039[a]

Kim et al. Fetril Steril 2011

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

Treatment of SCH – IVF outcomes



Delivery rate 증가

Velkeniers et al. Hum Reprod Update 2013

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

SCH – Summary

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

		TSH	
Pregnancy	• infertility	> 2.5 mIU/L	Level C
	• **miscarriage**	2.5 – 4 mIU/L	Level C
		> 4 mIU/L	Level B
Adverse Obstetric Outcomes	• placental abruption • preterm birth • fetal death • PPROM	2.5 – 4 mIU/L	no data
		> 4 mIU/L	Level B
Developmental Outcomes in Children	• impaired school performance • lower IQ	2.5 – 4 mIU/L	no evidence
		> 4 mIU/L	Level B

Practice Committee of the ASRM. Fertil Steril 2015

SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Treatment of SCH – Summary

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

		TSH	Outcomes	
Pregnancy Outcomes	• **pregnancy rates** • **miscarriage rates**	**> 4 mIU/L**	**Improvement**	Level B
Developmental Outcomes in Children	• impaired school performance • lower IQ		No improvement	Level B

Practice Committee of the ASRM. Fertil Steril 2015

SNUH SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

Thyroid Autoimmunity

Thyroid Ab

- Thyroid Peroxidase Antibodies (**TPO Ab**)

  (formerly known as microsomal Antibodies)

  - Correlate with the development of hypothyroidism

- TSH Receptor Antibodies (TSHR Ab)

  - Used in the diagnosis and monitoring of Graves'

- Thyroglobulin Antibodies (TG Ab)

  - Does not correlate with hypothyroidism

Thyroid autoimmunity

- 8–14% among all women at reproductive age

- **Risk of developing hypothyroidism ↑**
  - TPO-Ab (+) & SCH : 4% per year
  - either alone : 2–3% per year

Rushworth et al. Hum Reprod 2000
Vanderpump et al. Thyroid 2002

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

TAI – Reproductive outcomes

- Meta-analysis
- Euthyroid
- Thyroid antibody (+) vs. (-)

  - **Unexplained subfertility** : OR 1.47 [1.06, 2.02]
  - **Miscarriage** : OR 3.73 [1.83, 7.60]
  - **Recurrent miscarriage** : OR 2.26 [1.46, 3.50]
  - **Preterm delivery** : OR 1.93 [1.08, 3.47]

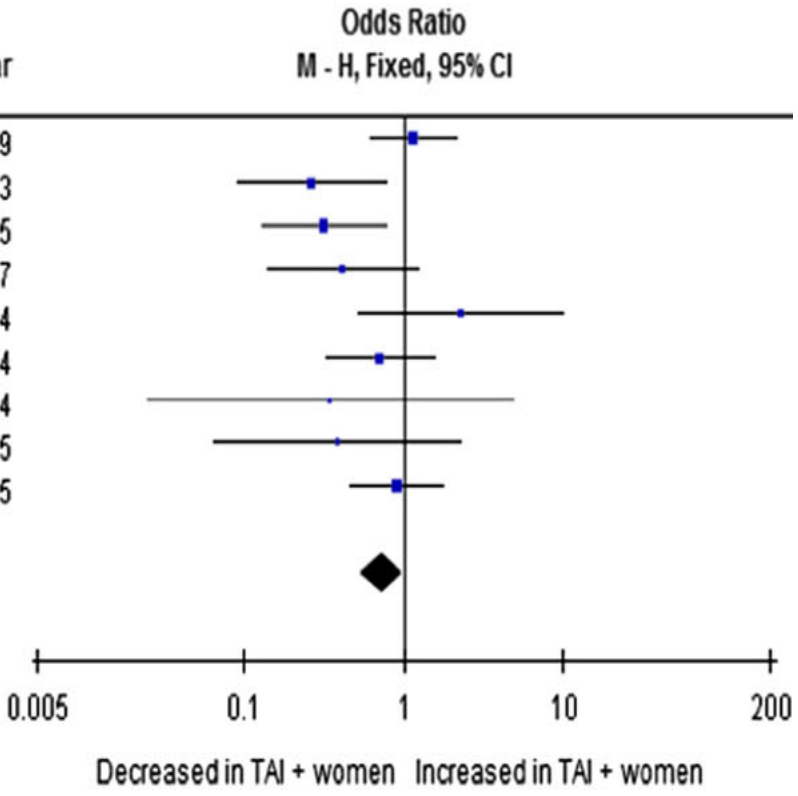
Boogaard et al. Hum Reprod Update 2011

TAI – IVF/ICSI outcomes

Study or Subgroup	TAI + women Events	Total	TAI - women Events	Total	Weight	Odds Ratio M - H, Fixed, 95% CI	Year
Kutteh 1999	78	92	396	478	20.6%	1.15 [0.62, 2.14]	1999
Poppe 2003	8	17	67	87	12.3%	0.27 [0.09, 0.78]	2003
Negro 2005	10	21	236	318	16.2%	0.32 [0.13, 0.77]	2005
Negro 2007	16	21	207	234	8.6%	0.42 [0.14, 1.23]	2007
Tan 2014	43	45	272	301	3.3%	2.29 [0.53, 9.96]	2014
Chai 2014	29	40	151	192	15.2%	0.72 [0.33, 1.55]	2014
Mintziori 2014	4	5	23	25	1.6%	0.35 [0.03, 4.80]	2014
Litwicka 2015	6	8	54	61	3.3%	0.39 [0.07, 2.31]	2015
Łukaszuk 2015	35	50	169	235	18.8%	0.91 [0.47, 1.78]	2015
Total (95% CI)		**299**		**1931**	**100.0%**	**0.73 [0.54, 0.99]**	
Total events	229		1575				

Heterogeneity: $Chi^2 = 13.49$, $df = 8$ ($P = 0.10$); $I^2 = 41\%$

Test for overall effect: $Z = 2.03$ ($P = 0.04$)



Live birth rate 감소

Busnelli et al. Human Reprod Update 2016

SNUH
SEOUL NATIONAL UNIVERSITY BUNDANG HOSPITAL

TAI – IVF/ICSI outcomes

- Number of oocytes : SMD 0.10 [-0.09–0.29]
- Fertilization rate : OR 1.11 [0.97–1.27]
- Implantation rate : OR 0.98 [0.73–1.32]
- Clinical pregnancy rate : OR 0.90 [0.77–1.06]
- **Miscarriage rate** : OR 1.44 [1.06–1.95]
- **Live birth rate** : OR 0.73 [0.54–0.99]

Busnelli et al. Human Reprod Update 2016

Thyroid autoimmunity

Treatment in euthyroid women with TAI

Treatment of TAI
– Pregnancy outcomes

유산 감소

- LT4 0.5 – 1 μg/kg
  (from the 1st visit)
- Double-blind RCT
- N=984

조산 감소

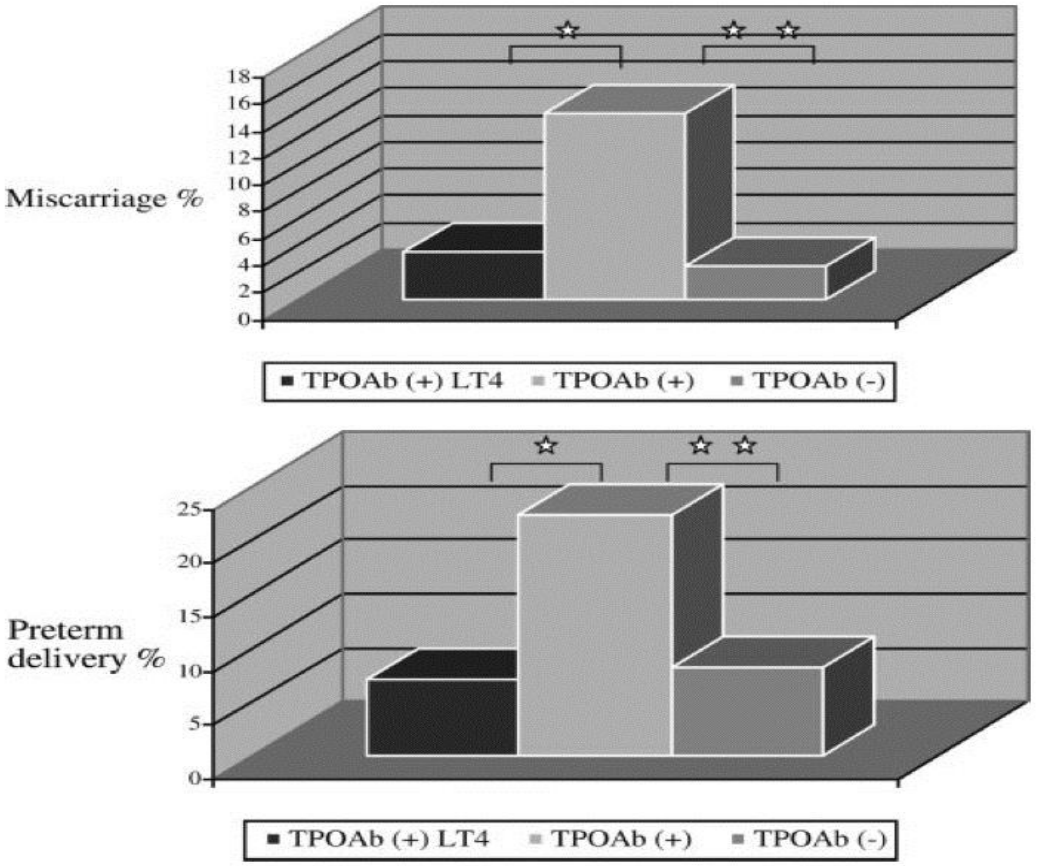


FIG. 4. Percentage of miscarriages (*top*) and premature deliveries (*bottom*) in group A ($TPOAb^+$ treated with LT_4), group B ($TPOAb^+$), and group C ($TPOAb^-$). ☆, $P < 0.05$; ☆ ☆, $P < 0.01$.

Negro et al. J Clin Endocrinol Metab 2006

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

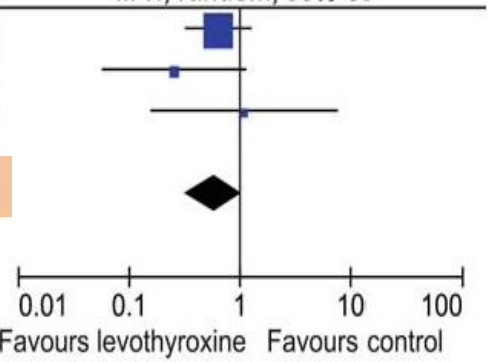
TAI – Treatment outcomes

(a)

Study or subgroup	Levothyroxine Events	Total	Control Events	Total	Weight	Risk ratio M-H, random, 95% CI
Negro, 2005	8	24	11	21	74.5%	0.64 [0.32, 1.28]
Negro, 2006	2	57	8	58	16.0%	0.25 [0.06, 1.15]
Revelli, 2009	3	11	1	4	9.5%	1.09 [0.15, 7.69]
Total (95% CI)		**92**		**83**	**100.0%**	0.58 [0.32, 1.06]
Total events	13		20			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.72$, df = 2 ($P = 0.42$); $I^2 = 0\%$

Test for overall effect: $Z = 1.78$ ($P = 0.07$)



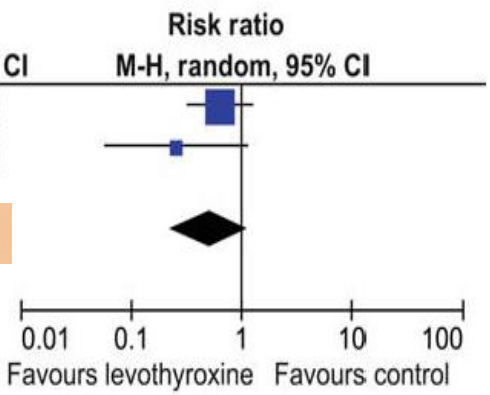
(b)

RCTs only

Study or subgroup	Levothyroxine Events	Total	Control Events	Total	Weight	Risk ratio M-H, random, 95% CI
Negro, 2005	8	24	11	21	74.9%	0.64 [0.32, 1.28]
Negro, 2006	2	57	8	58	25.1%	0.25 [0.06, 1.15]
Total (95% CI)		**81**		**79**	**100.0%**	0.51 [0.22, 1.15]
Total events	10		19			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 1.30$, df = 1 ($P = 0.25$); $I^2 = 23\%$

Test for overall effect: $Z = 1.63$ ($P = 0.10$)



유산 감소

Vissenberg et al. Hum Reprod Update 2012

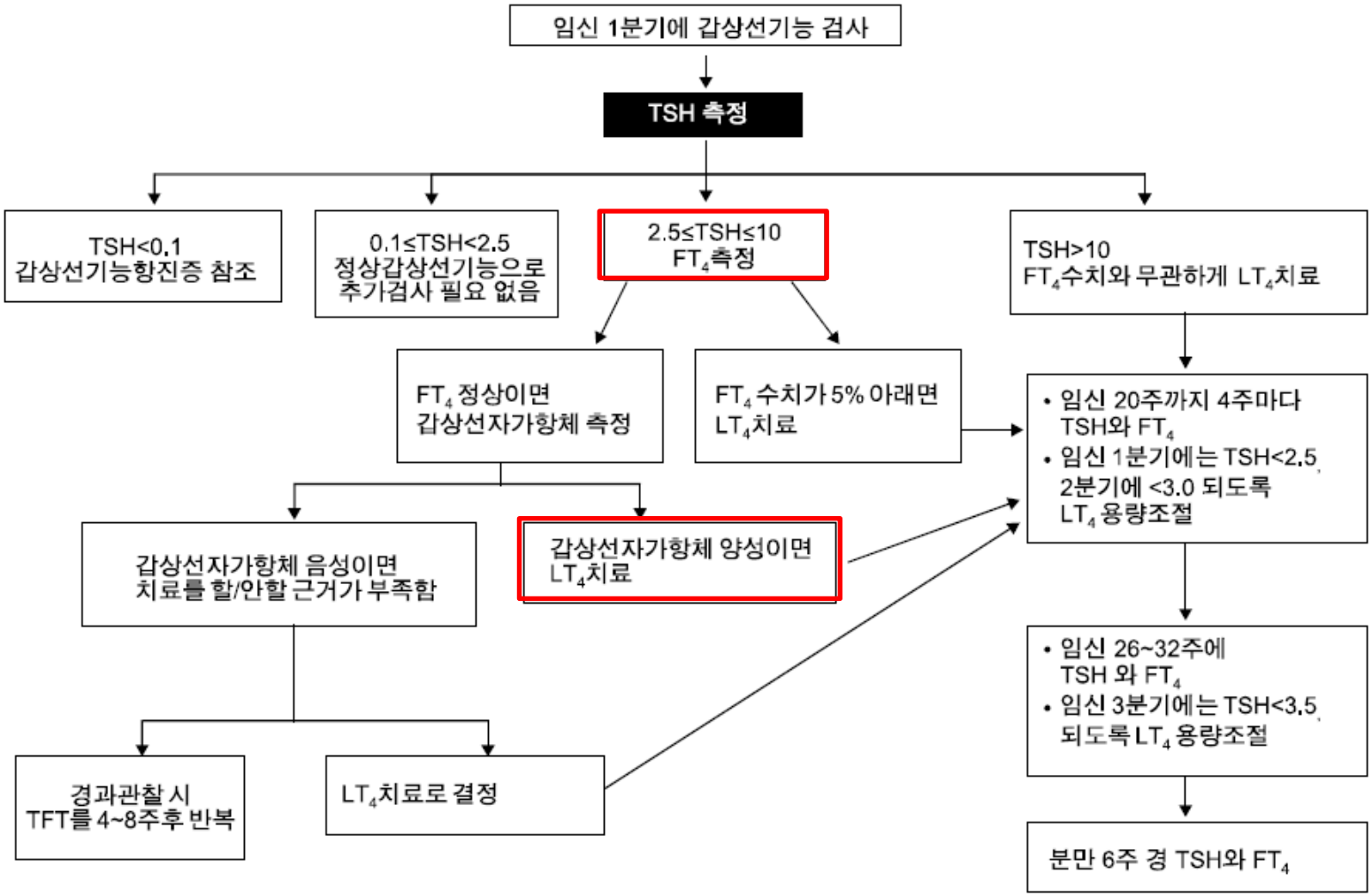
SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

Summary

TSH < 2.5 mIU/L	TPO-Ab (+) particularly when there is a history of miscarriage or past history of hypothyroidism	treating with LT4	Grade B BEL 2
TSH 2.5 – 4 mIU/L		testing TPO-Ab	Grade C
	planning a pregnancy including ART in the immediate future	treating with LT4	Grade B BEL 2
	TPO-Ab (+)	treating with LT4	Grade B
TSH > 4.0 mIU/L		treating with LT4	Grade B


skkim@snubh.org

임신 1분기 갑상선 기능검사 알고리즘



이가희 외, 임신 중 및 산후 갑상선 질환의 진단 및 치료 권고안, 대한갑상선학회 2014

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL

TAD – Treatment

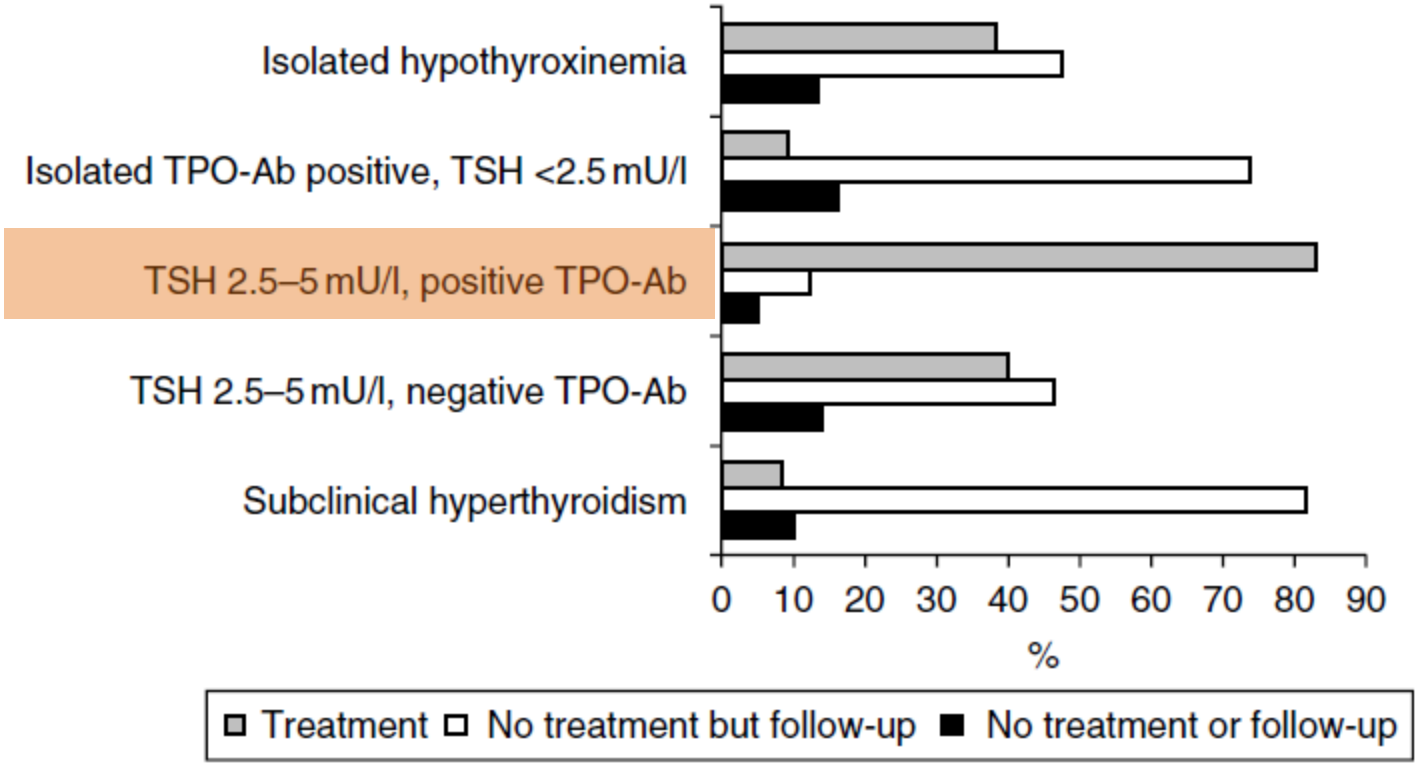


Figure 1 Percentage of responders recommending treatment, follow-up only or no action for various outcomes following thyroid screening in pregnancy.

Vaidya et al. Eur J Endocrinol 2012

SNUH
SEOUL NATIONAL UNIVERSITY
BUNDANG HOSPITAL