

남성 갱년기의 진단과 치료

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LOH

TDS / TRT

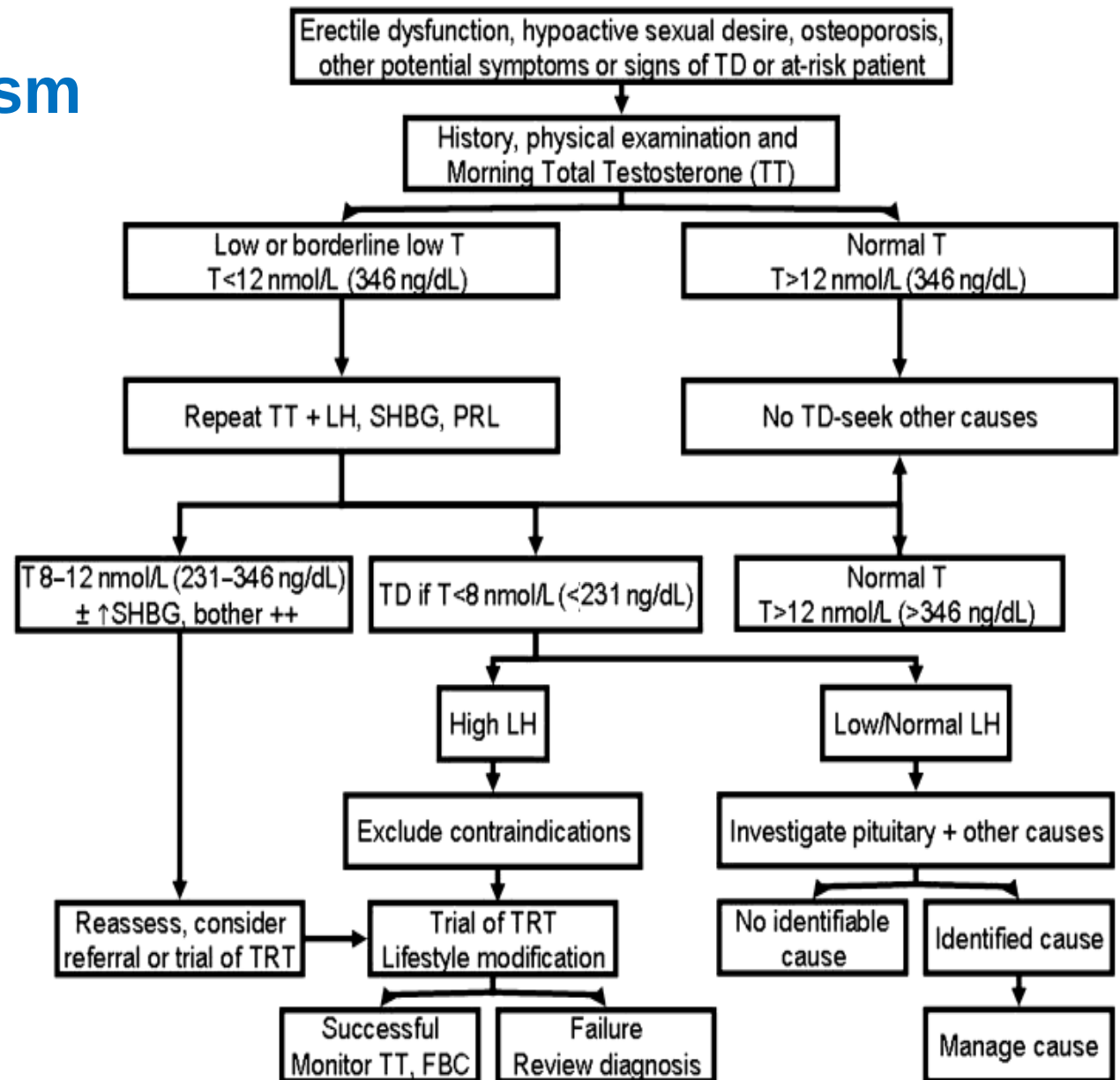
TDS criteria

- a. Primary/ secondary hypogonadism
- b. Late onset hypogonadism /Testosterone deficiency syndrome
- c. Nocturia / LUTS
- d. Secondline Tx of PDE5i resistant pt

TDS

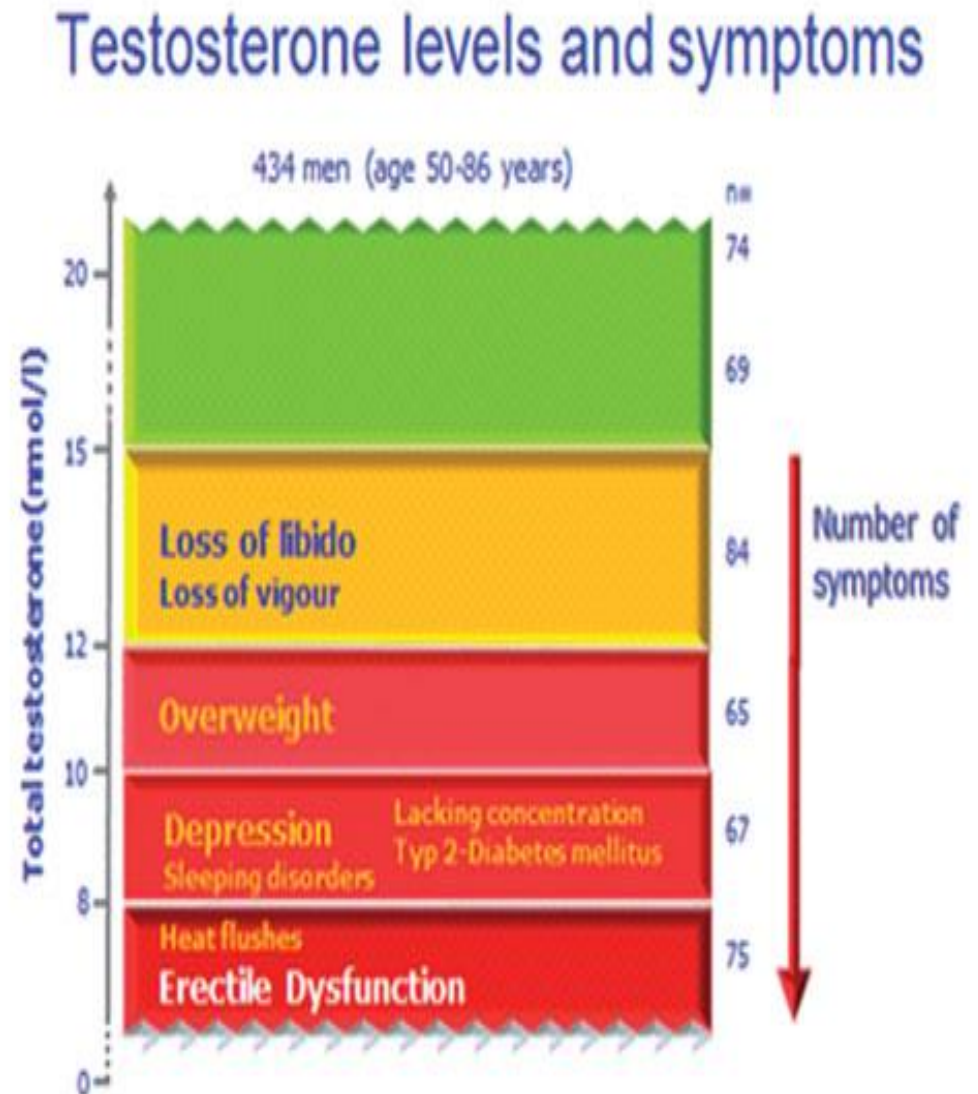
- Andropause
- Late Onset Hypogonadism
- A clinical and biochemical syndrome associated with low level of testosterone, which may adversely affect multiple organ functions and quality of life

Assessment of Hypogonadism



Assessment – Symptom & Sign

Low libido
Poor morning erections
Erectile dysfunction
Depressed mood
Fatigue
Decreased vitality
Cognitive impairment
Insulin resistance
Obesity, abdominal obesity
Metabolic syndrome
Arterial hypertension
Diabetes mellitus type 2
Decreased muscle mass and strength
Decreased bone mineral density and osteoporosis
Use of glucocorticoids, opioids, antipsychotics



Assessment – Lab test

- Serum testosterone
 - Circadian rhythm → 07.00~11.00h
 - Eldery or hypogonadal men : Blunted diurnal variation
- Free testosterone or SHBG
- LH, TSH, Prolactin
- Vit D
- Androgen receptor gene CAG repeat length

Assessment

- PSA, DRE
- BMD
- CBC (hematocrit)

Assessment – Diagnostic Criteria

Total testosterone **<350ng/dL / 300**

Total testosterone **>350ng/dL**

: if **free T < 65~70pg/mL** with one Sx

Young men under 40 with **< 400 ng/dL**

- Increased hypogonadal Sx

50-80 aged men with **< 440 ng/dL**

- TRT: benefits in quality of life & body composition

Secondary Hypogonadism

Disease	Pathophysiology
Hyperprolactinemia	Prolactin-secreting pituitary adenomas (prolactinomas) or drug-induced
Isolated hypogonadotrophic hypogonadism (IHH) (formerly termed idiopathic hypogonadotrophic hypogonadism)	SGnRH deficiency specific (or unknown) mutations affecting GnRH synthesis or action
Kallmann syndrome (hypogonadotrophic hypogonadism with anosmia) (prevalence 1 in 10,000)	GnRH deficiency and anosmia, genetically determined
Secondary GnRH deficiency	Medication, drugs, toxins, systemic diseases
Hypopituitarism	Radiotherapy, trauma, infections, haemochromatosis and vascular insufficiency or congenital
Pituitary adenomas	Hormone-secreting adenomas; hormone-inactive pituitary adenomas; metastases to the pituitary or pituitary stalk
Prader-Willi syndrome (PWS) (formerly Prader-Labhart-Willi syndrome) (prevalence 1 in 10,000 individuals)	Congenital disturbance of GnRH secretion
Congenital adrenal hypoplasia with hypogonadotrophic hypogonadism (prevalence 1 in 12,500 individuals)	X-chromosomal recessive disease, in the majority of patients caused by mutations in the DAX1 gene
Pasqualini syndrome	Isolated LH deficiency

Non-pharmacologic Treatment

- Treatment of sleep apnea
- Weight reduction
- Life-style modification
- Discontinuation of opioid medication

Testosterone Replacement Therapy (TRT): Benefits and potential risks

Benefits

Maintains secondary sexual characteristics

Improves libido and erectile dysfunction

Increases lean/muscle mass and strength

Decreases weight, body fat and visceral obesity

Increases bone mass

Improves energy and vitality

Improves mood and depression^{*}

Coronary vasodilatation, reduces cardiovascular disease risk^{*}

Potential risks

Acne, oily skin

Gynecomastia

Weight gain/fluid retention at initiation of treatment

Lipids (decrease in HDL)

Prostate (benign prostatic hyperplasia and prostate cancer)^{*}

Increased hemoglobin, hematocrit and red cell count

Sleep apnea^{*}

Increased cardiovascular adverse effects^{*}

Risk factors of TRT

- Male Breast cancer
 - there is as yet a lack of strong evidence for this relationship
- Prostate cancer
 - Symptomatic hypogonadal men who have been surgically treated for localised prostate cancer and who are currently without evidence of active disease can be cautiously considered for a TRT
- Cardiovascular disease
 - no substantive evidence that TRT, when replaced to the normal physiological range, is related to the development of major adverse cardiovascular events
 - TRT improves several important modifiable cardiovascular risk factors
 - **should be used with caution in men with pre-existing cardiovascular disease, previous venous thromboembolism or chronic cardiac failure.**

Contraindications against TRT

- Prostate cancer
- Male breast cancer
- Severe sleep apnoea
- Male infertility-active desire to have children
- Haematocrit > 0,54%
- Severe lower urinary tract symptoms due to benign prostatic hyperplasia
- Severe chronic cardiac failure/New York Heart Association Class IV

TRT – Delivery system

Formulation	Administration	Advantages	Disadvantages
Testosterone undecanoate	Oral; 2-6 cps every 6 h	Absorbed through the lymphatic system, with consequent reduction of liver involvement.	Variable levels of testosterone above and below the mid-range [69]. Need for several doses per day with intake of fatty food.
Testosterone cypionate	Intramuscular; one injection every 2-3 weeks	Short-acting preparation that allows drug withdrawal in case of onset of side-effects.	Possible fluctuation of testosterone levels [72, 73].
Testosterone enanthate	Intramuscular; one injection every 2-3 weeks	Short-acting preparation that allows drug withdrawal in case of onset of side-effects.	Fluctuation of testosterone levels [72, 73].
Testosterone undecanoate	Intramuscular; one injection every 10-14 weeks	Steady-state testosterone levels without fluctuation.	Long-acting preparation that cannot allow drug withdrawal in case of onset of side-effects [74].

TRT – Delivery system

Transdermal testosterone	Gel or skin patches; daily application	Steady-state testosterone level without fluctuation.	Skin irritation at the site of application and risk of interpersonal transfer [75, 76].
Sublingual testosterone	Sublingual; daily doses	Rapid absorption and achievement of physiological serum level of testosterone.	Local irritation [80, 81].
Buccal testosterone	Buccal tablet; two doses per day	Rapid absorption and achievement of physiological serum level of testosterone.	Irritation and pain at the site of application [80, 81].
Subdermal depots	Subdermal implant every 5-7 months	Long duration and constant serum testosterone level.	Risk of infection and extrusion of the implants [69, 82, 83].

TRT – Delivery system

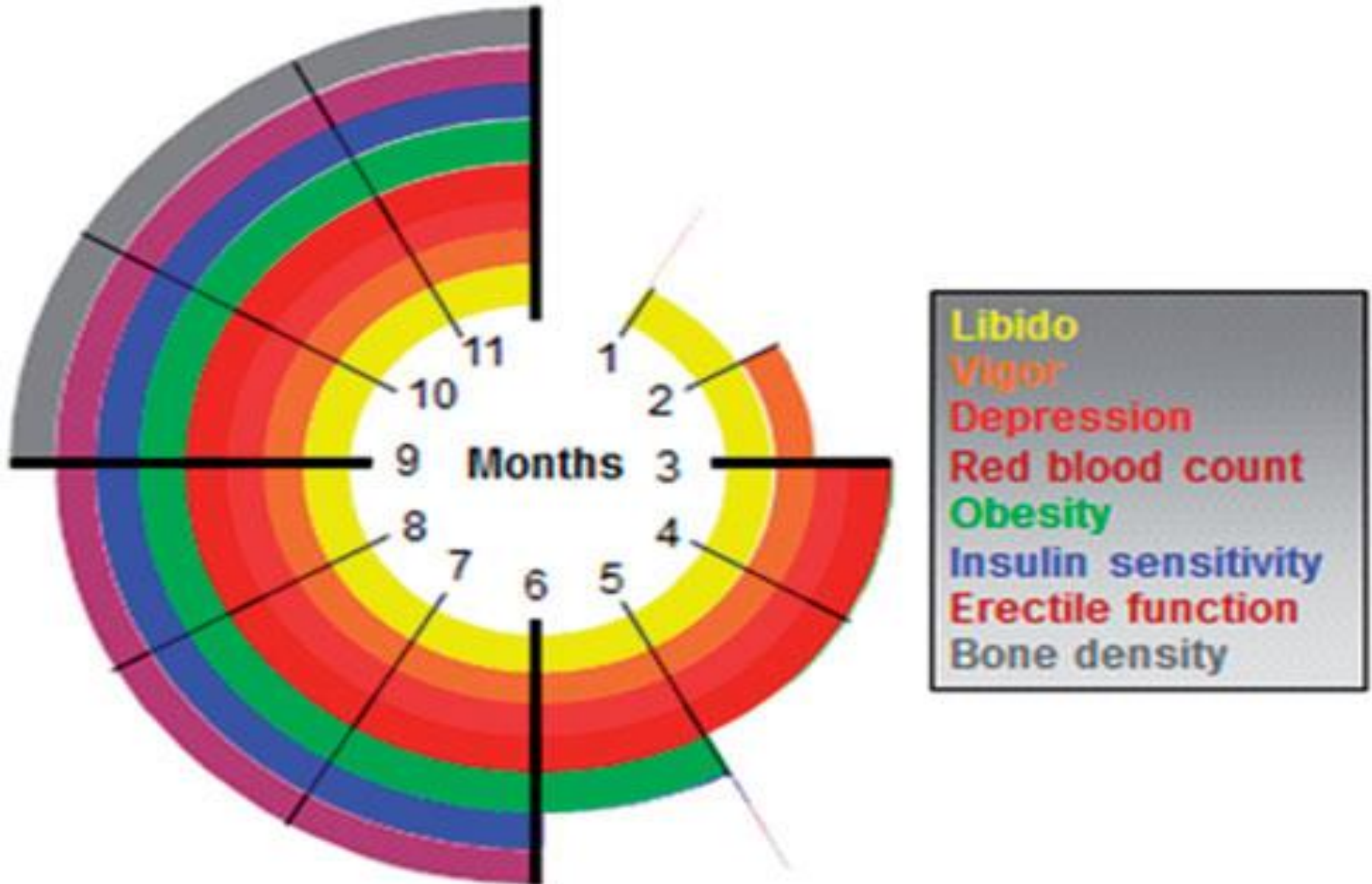
Natesto Nasal gel '나테스토 나잘겔'

/비강용 치료제 / 현대약품



Follow-up

- monitoring of changes in the clinical manifestations



Follow-up

- Testosterone level
 - TRT should restore the serum testosterone level to the mid-normal range of specific age groups
 - Optimal monitoring schedule for serum testosterone level is also dependent on the formulation of TRT used
- Bone density
 - Bone mineral density (BMD) should be monitored only in men whose BMD was abnormal before initiation
 - An increase in lumbar spine BMD may already be detectable after 6 months of TRT

Follow-up

- Haematocrit
 - the most frequent side-effect of TRT
 - clinical significance of a high haematocrit level is unclear
 - The effect of erythropoiesis may become evident at 3 months and peaks at 12 months
- Prostate safety
 - marginal increase in PSA and prostate volume, plateauing at 12 months
- Cardiovascular monitoring
 - Caution should be used in men with pre-existing cardiovascular disease
 - In men with chronic heart failure TRT can result in fluid retention and an exacerbation of the condition

Follow-up: EAU recommendations

- The response to treatment should be assessed 3, 6 and 12 months after the onset of treatment, and thereafter annually.
- Haematocrit should be monitored at 3, 6 and 12 months and thereafter annually. The testosterone dosage should be decreased, or therapy discontinued if the haematocrit increases above 0,54.
- Prostate health should be assessed by digital rectal examination and PSA before the start of TRT. Follow-up by PSA at 3, 6 and 12 months and thereafter annually.
- Men with cardiovascular diseases should be assessed for cardiovascular symptoms before TRT is initiated. There should be close clinical assessment during TRT.

A Point to be Considered

- Obesity c type 2 DM & Hypogonadism
- Vit D & Testosterone

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TRT – 전제 조건 precondition

- 근력 운동 exercise of muscle
- **근력 강화 운동** strength exercise
- **근력 강화 운동 프로그램** muscle strengthening program

【 남성호르몬 / 테스토스테론 】

- ♂ 근육운동
- ♂ 스트레스 / 코티솔 문제
- ♂ 단백질 탄수화물 지방 - 균형식사
- ♂ 햇볕 Vit D
- ♂ 수면
- ♂ 비타민 미네랄 - 마그네슘 아연
- ♂ 생강
- ♂ 건강수칙 (성생활- 술) / 에스트로겐
- ♂ 병용 약물 문제
- ♂ 과체중

【 남성호르몬 / 테스토스테론 】

- ♂ **근력운동:** 근육량을 늘리는 운동
- ♂ **과체중:** 복부비만 (대사증후군)
- ♂ **수면부족** **생활습관의 변화**
- ♂ **햇볕** **Vit D 보충**
- ♂ **단백질 탄수화물 지방 – 균형식사**

굴에 풍부한 아연

연어/ 버섯류/ 비타민 D

장어/ 브라질너트

토마토, 양배추 브로콜리