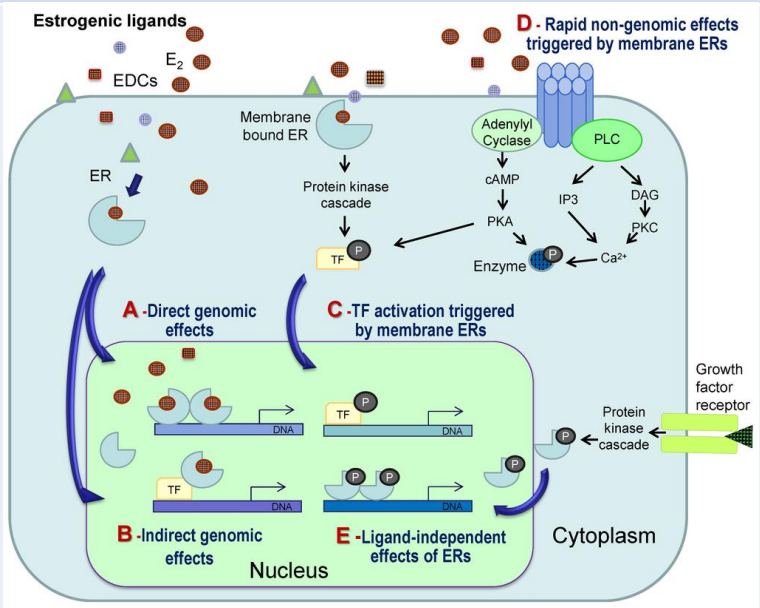
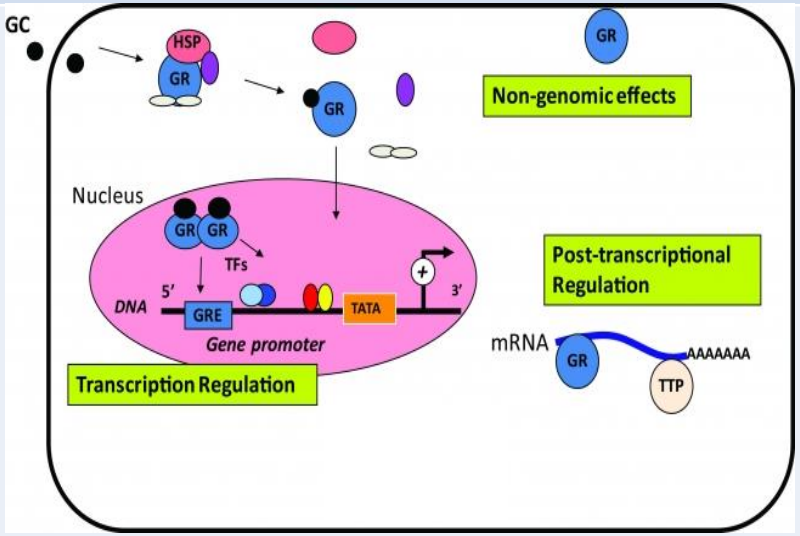
Female reproductuctive system 2

Ovarian hormones:

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ • Other systemic actions	

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Forms: estradiol, estrone, estriol Cholesterol ___ LH (theca cells) ___ androstenedione Androstenedione ___ aromatase +FSH ___ estradiol (granulosa cells) Growing follicles, graafian follicle, corpus luteum Placenta Adrenal cortex Ovarian stroma cells Adipose tissue, bone and brain 2 peaks: • Maximum pre-ovulatory peak 380ug/day • Moderate luteal peak 250ug/day	Corpus luteum, small amount by the follicular cells Placenta Adrenal cortex 1 peak: • Mid-luteal peak 18ng/ml (20 folds!)

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism:	
2% free 98% bound: albumin 60% sex hormone binding globulin 38% • Conjugation in the liver to glucuronide and sulfate----excretion in urine and in bile to a lesser extent • Converted to lesser potent estrone and estriol	2% free 98% bound: albumin 80% sex hormone binding globulin 18% Metabolised in liver Converted to pregnandiol----- excretion in urine

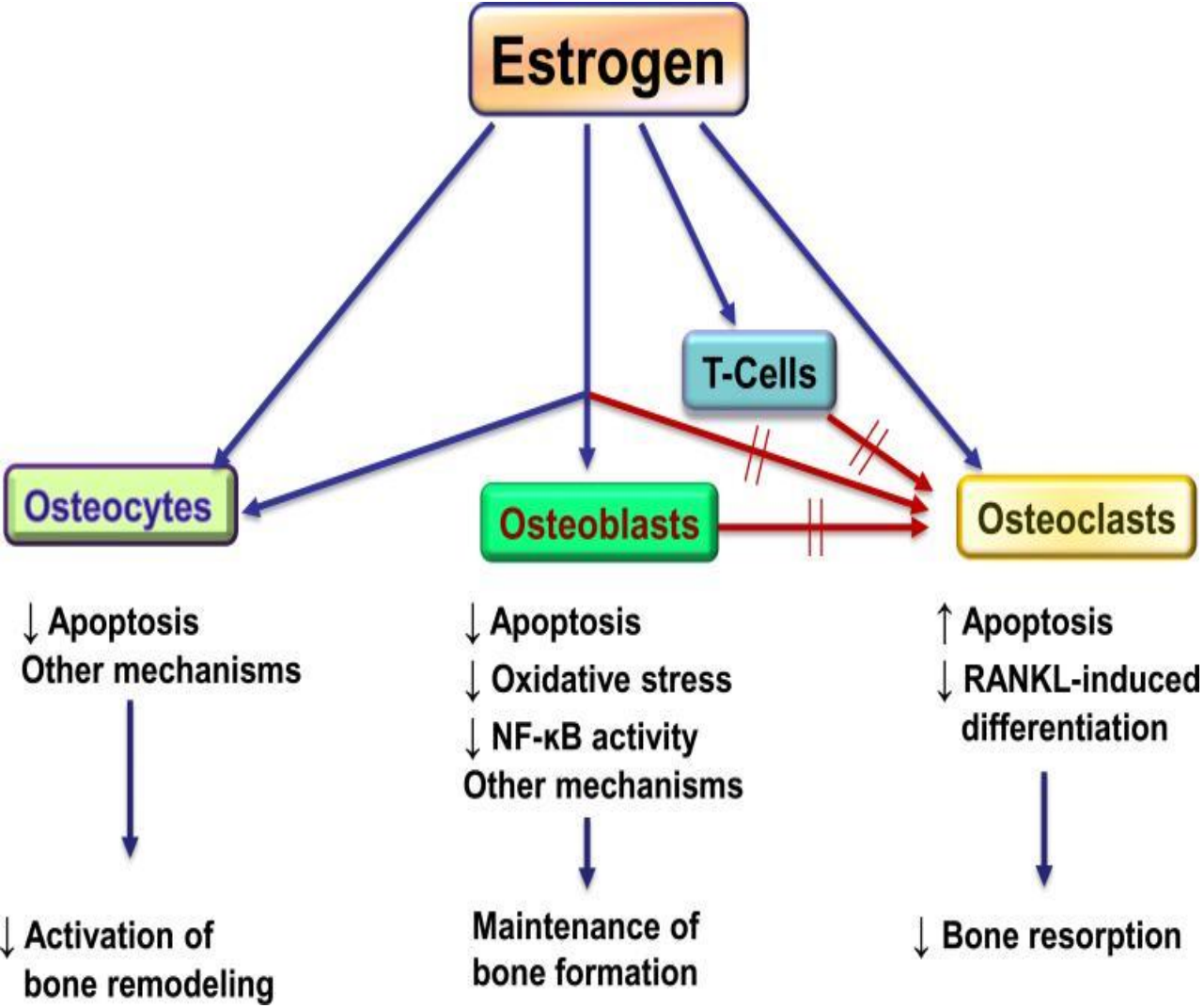
ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Genomic: ER alpha and beta  Non genomic: GPR 30 ------- Ca2+ and NO	Genomic: Receptors A & B  Non genomic: MPRs Cytoplasmic fraction of nuclear receptor

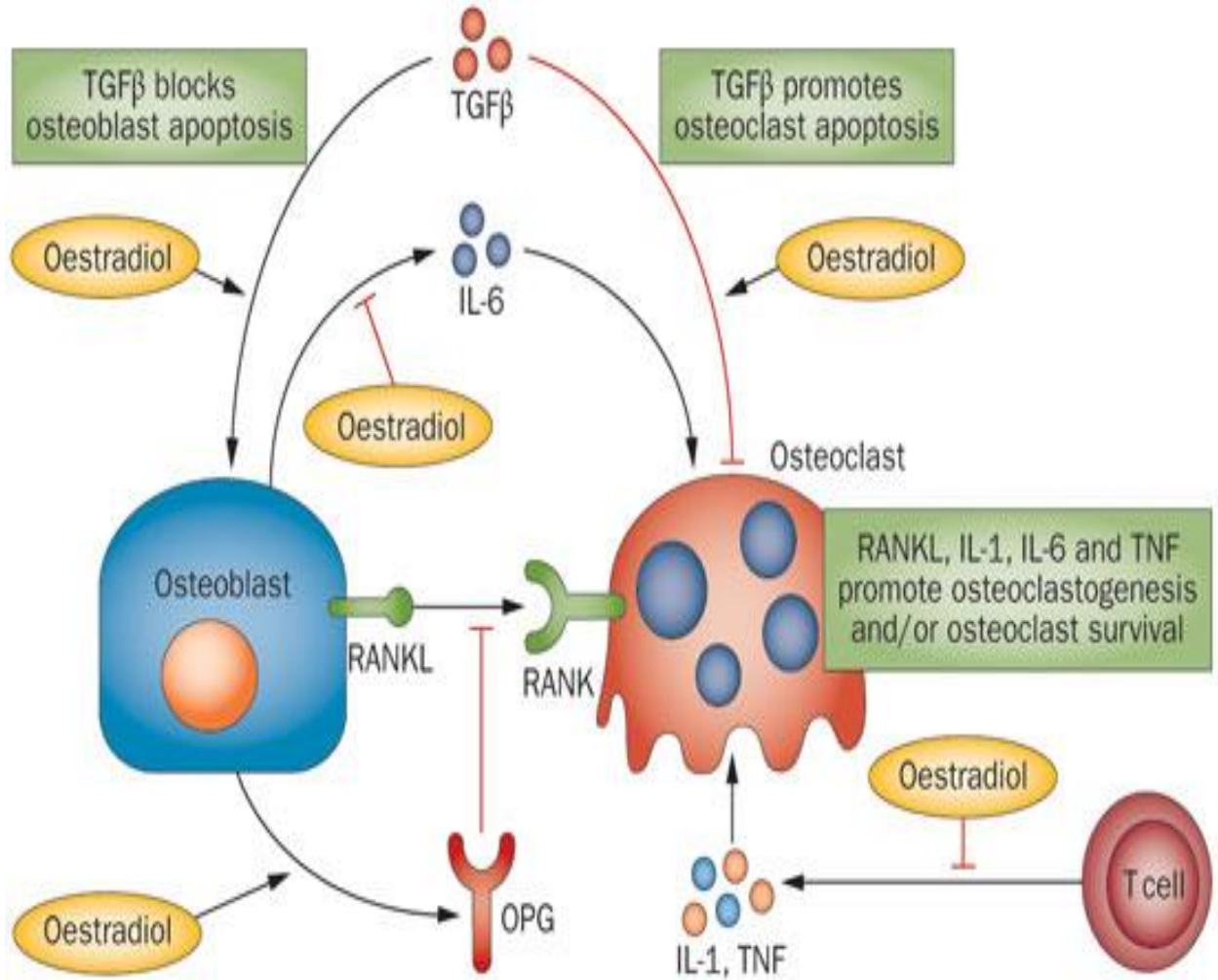
ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: On primary sex organs:	
• Growth of ovarian follicles • LH surge therefore ovulation and corpus luteum formation	• Regulate folliculogenesis

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ	
Uterus: **Endometrium:** Regeneration of the functional layer (proliferative phase) **Myometrium:** Increase blood flow Increase contractile proteins Increase excitability and spontaneous contractility Increase number and sensitivity to oxytocin **Cervix:** thin alkaline mucus (sperm transport) **Vagina**: stratification glycogen deposition and lactic acid production **Fallopian tubes**: motility of tube activity and number of cilia **Mamary glands**: growth of ducts nipples and areola deposition of fats blood flow	**Uterus:** **Endometrium:** secretory phase- help implantation and placenta formation- convert endometrial cells into secreting decidual cells **Myometrium:** decrease excitability and inhibit contractility decrease number of estrogen receptors Decrease sensitivity to oxytocin action **Vagina**: thick vaginal secretion epithelial proliferation with leucocytic infiltration **Fallopian tubes**: secretion of mucus necessary for the nutrition of fertilized ovum **Mamary glands**: development of lobules and alveoli differentiation of estrogen prepared ductal tissue supports the secretory function during lactationv

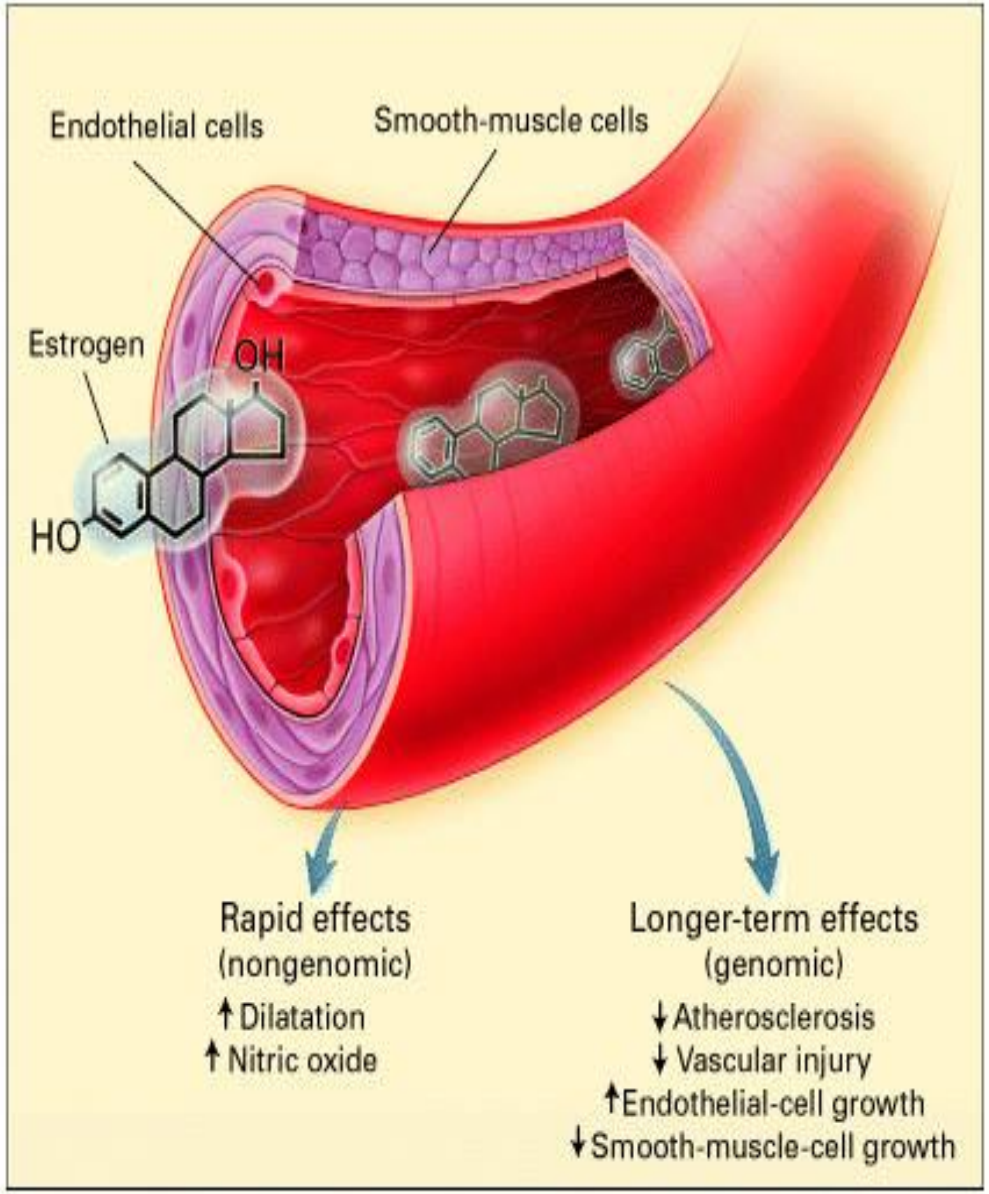
ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ • On secondary sex characters	
• **BODY CONFIGURATION** • **VOICE:** keep children voice • **HAIR:** less body/more scalp hair distribution of pubic hair (growth of pubic and axillary hair due to androgen) • **SKIN:** inhibit acne and comedones • **BEHAVIOR**	

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ • Other actions	
• Secondary sex characters • **Bones:** anabolic- antiosteoporotic- maturation of ossific centers and union of epiphysis • Cardiovascular • CNS • Endocrine glands	• Thermogenic effect • Respiration • CNS

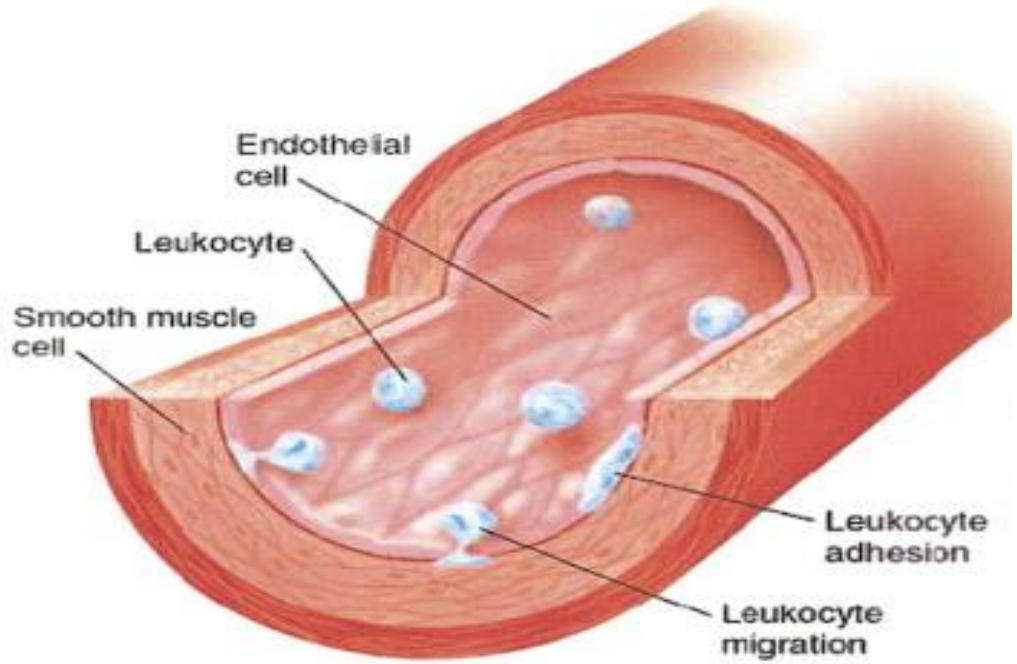

Estrogen
T-Cells
Osteocytes
Osteoblasts
Osteoclasts
↓ Apoptosis
Other mechanisms
↓ Activation of bone remodeling
↓ Apoptosis
↓ Oxidative stress
↓ NF-κB activity
Other mechanisms
Maintenance of bone formation
↑ Apoptosis
↓ RANKL-induced differentiation
↓ Bone resorption


TGFβ blocks osteoblast apoptosis
TGFβ
TGFβ promotes osteoclast apoptosis
Oestradiol
IL-6
Oestradiol
Oestradiol
Osteoclast
Osteoblast
RANKL
RANK
RANKL, IL-1, IL-6 and TNF promote osteoclastogenesis and/or osteoclast survival
Oestradiol
T cell
OPG
Oestradiol
IL-1, TNF

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ • Other actions	
• Secondary sex characters • Bones • **Cardiovascular:** antiatherosclerosis • CNS • Endocrine glands	• Thermogenic effect • Respiration • CNS



Early atherogenesis



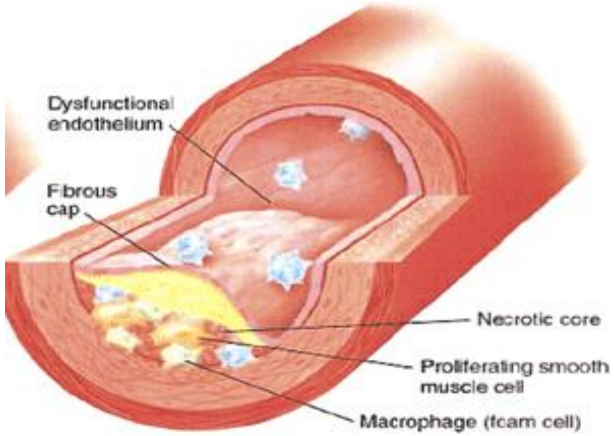
Beneficial effects of HRT

↑ Vasodilation	↓ Inflammatory activation
↑ Nitric oxide	↑ Nitric oxide
↓ Endothelin	↓ CAMs
↑ Cox-2	↓ MCP-1, TNF-α

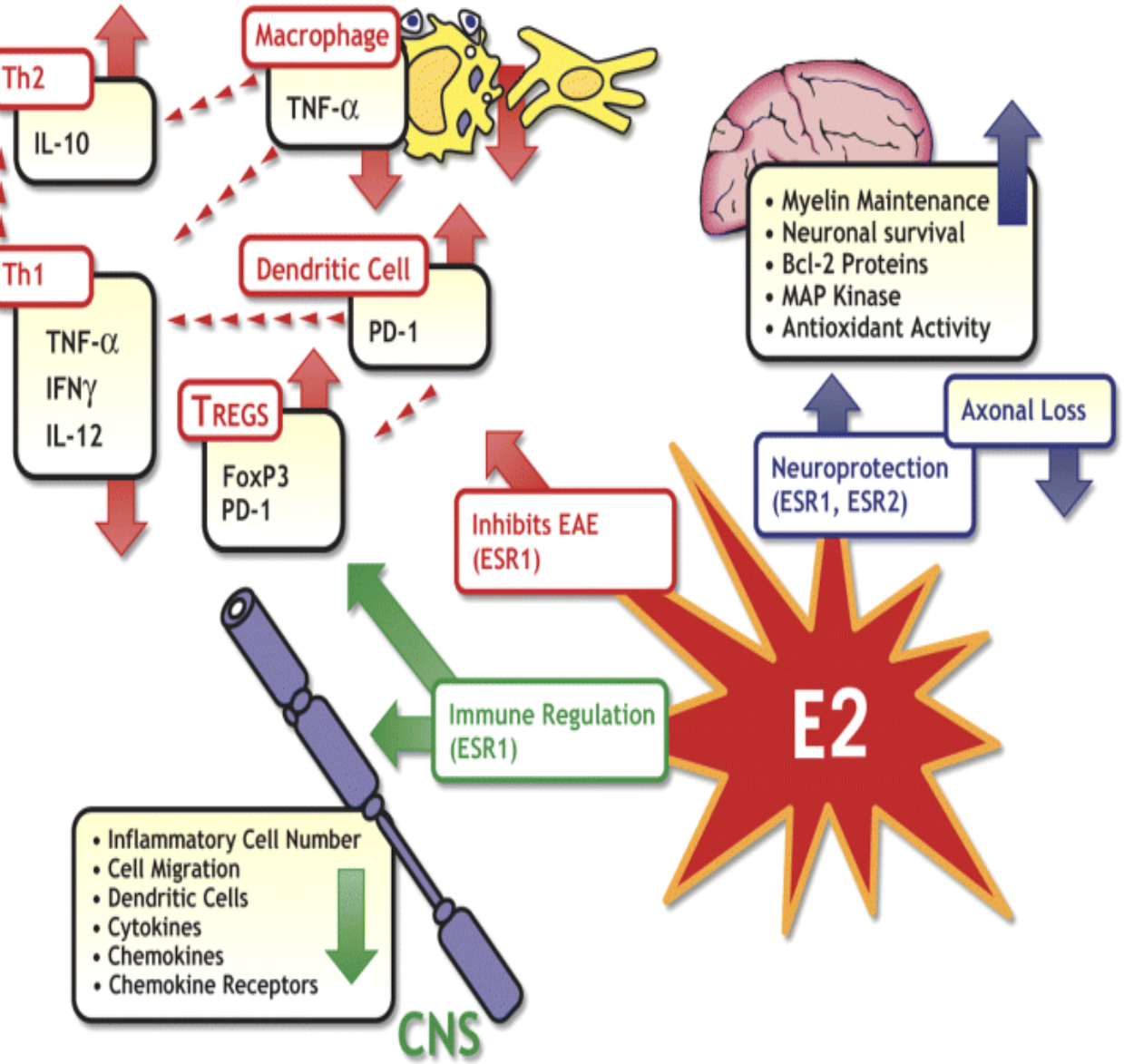
↓ Lesion progression

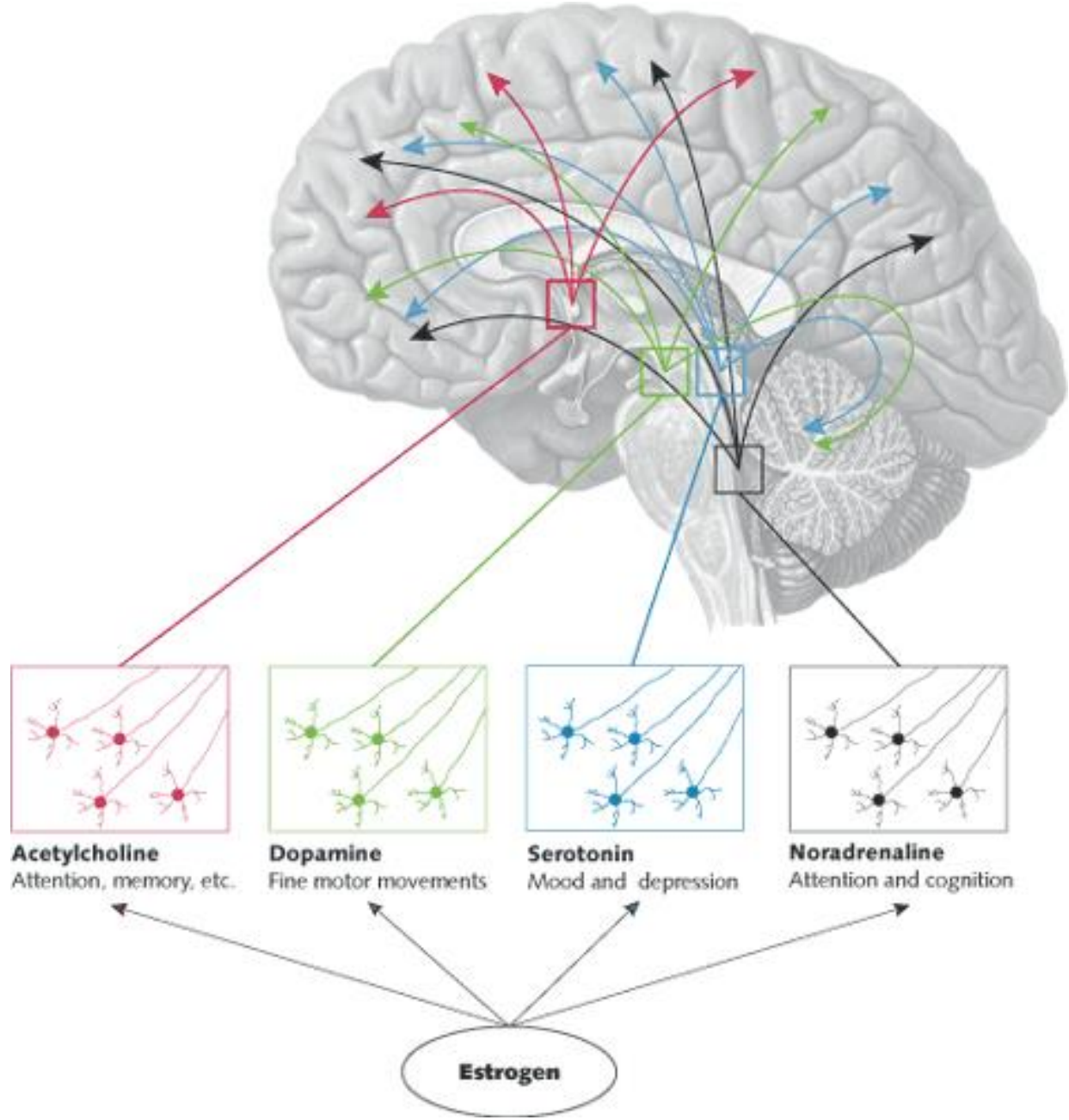
↑ Nitric oxide	↓ Platelet activation
↓ Inflammatory cell adhesion	↓ VSMC proliferation
↓ LDL oxidation/binding	

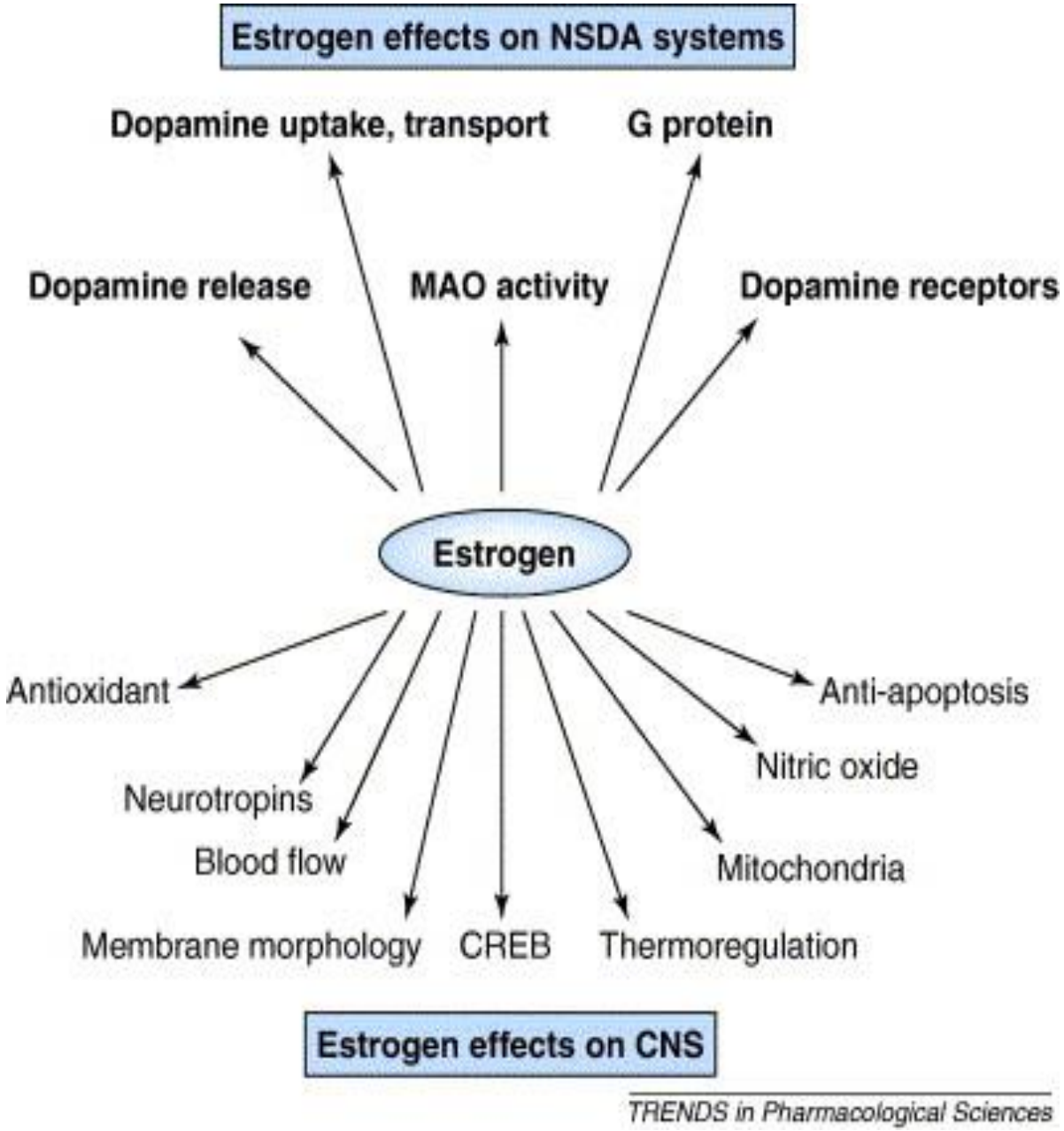
Established atherosclerosis

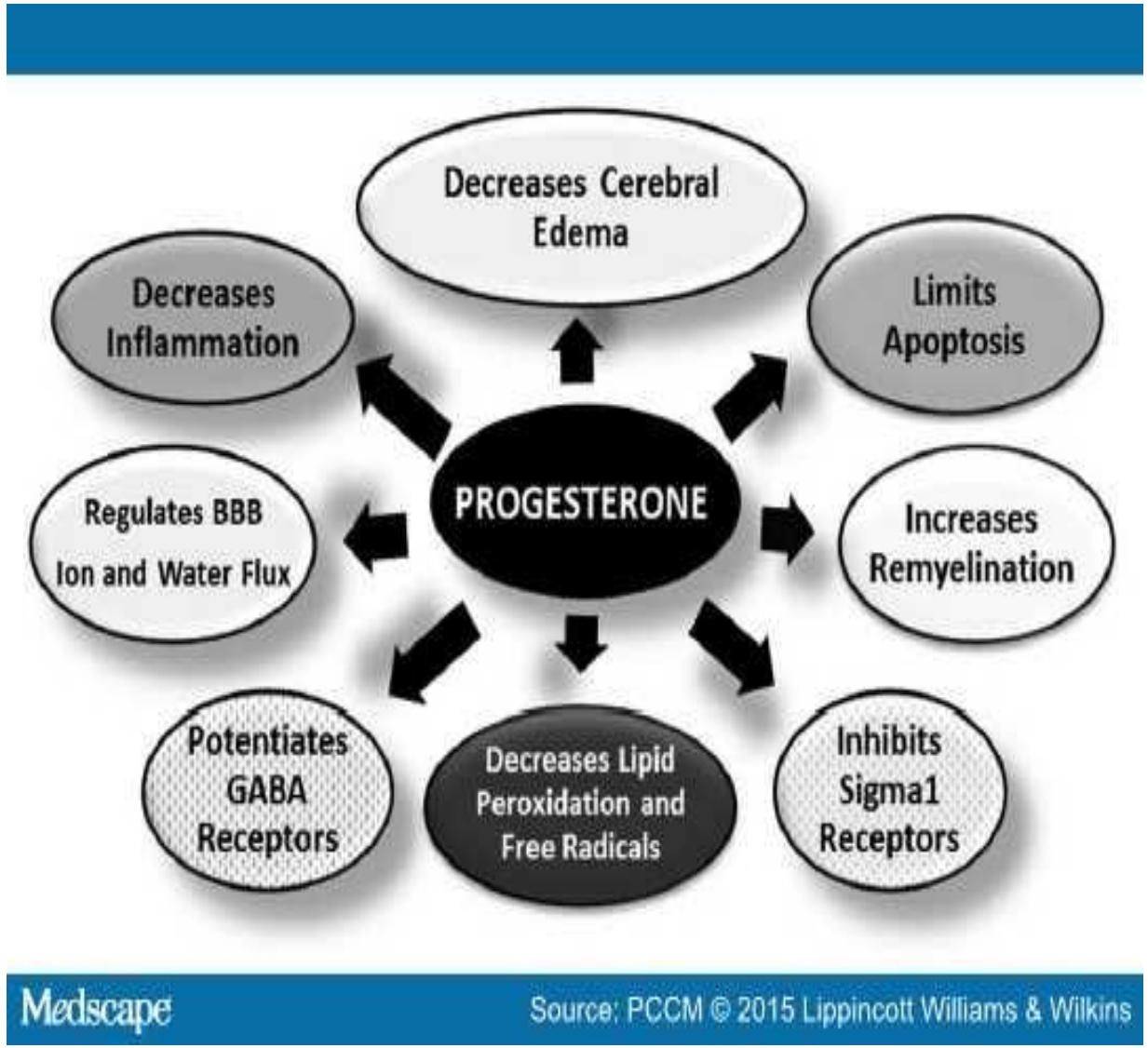


ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ • Other actions	
• Secondary sex characters • Bones • Cardiovascular • **CNS:** neuroprotection- cognitive functions • Endocrine glands	• Thermogenic effect • Respiration • **CNS:** neuroprotection- BBB


Th2
IL-10
Macrophage
TNF-α
Th1
TNF-α
IFNγ
IL-12
Dendritic Cell
PD-1
TREGS
FoxP3
PD-1
• Myelin Maintenance
• Neuronal survival
• Bcl-2 Proteins
• MAP Kinase
• Antioxidant Activity
Axonal Loss
Neuroprotection
(ESR1, ESR2)
Inhibits EAE
(ESR1)
Immune Regulation
(ESR1)
E2
• Inflammatory Cell Number
• Cell Migration
• Dendritic Cells
• Cytokines
• Chemokines
• Chemokine Receptors
CNS


Acetylcholine
Attention, memory, etc.
Dopamine
Fine motor movements
Serotonin
Mood and depression
Noradrenaline
Attention and cognition
Estrogen


Estrogen effects on NSDA systems
Dopamine uptake, transport
G protein
Dopamine release
MAO activity
Dopamine receptors
Estrogen
Antioxidant
Anti-apoptosis
Nitric oxide
Neurotropins
Blood flow
Mitochondria
Membrane morphology
CREB
Thermoregulation
Estrogen effects on CNS
TRENDS in Pharmacological Sciences


Decreases Cerebral Edema
Decreases Inflammation
Limits Apoptosis
Regulates BBB Ion and Water Flux
PROGESTERONE
Increases Remyelination
Potentiates GABA Receptors
Decreases Lipid Peroxidation and Free Radicals
Inhibits Sigma1 Receptors
Medscape
Source: PCCM © 2015 Lippincott Williams & Wilkins

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ • Other actions	
• Secondary sex characters • Bones • Cardiovascular • CNS • **Endocrine glands:** regulate gonadotropins secretion- stimulate angiotensinogen, thyroxine binding globulin, CBG	• Thermogenic effect • Respiration • CNS

ESTROGEN	PROGESTERONE
Synthesis and secretion	
Transport and metabolism	
Mechanism of action	
Actions: • On primary sex organs • On secondary sex organ • Other actions	
• Secondary sex characters • Bones • Cardiovascular • CNS • Endocrine glands	• **Thermogenic effect:** 0.5°C (central effect) • **Respiration:** ↑RR→ ↓PCO_2 • **CNS:** neuroprotection- BBB

Abnormalities in ovarian functions

PRIMARY

SECONDARY

Hypo
Hypogonadism

Prepubertal

Primary ammenorhea and sterility

Secondary sex organs infantile

Secondary sex characters absent

Delayed epiphysead closure

Postpubertal

Secondary amenorrhea

Secondary sex organs regress

Secondary sex characters regress

Osteoporosis and muscle wasting

Hyper
Ovarian Hypersecretion

Prepubertal

Precocious sexual developementl

Postmenopausal

rare

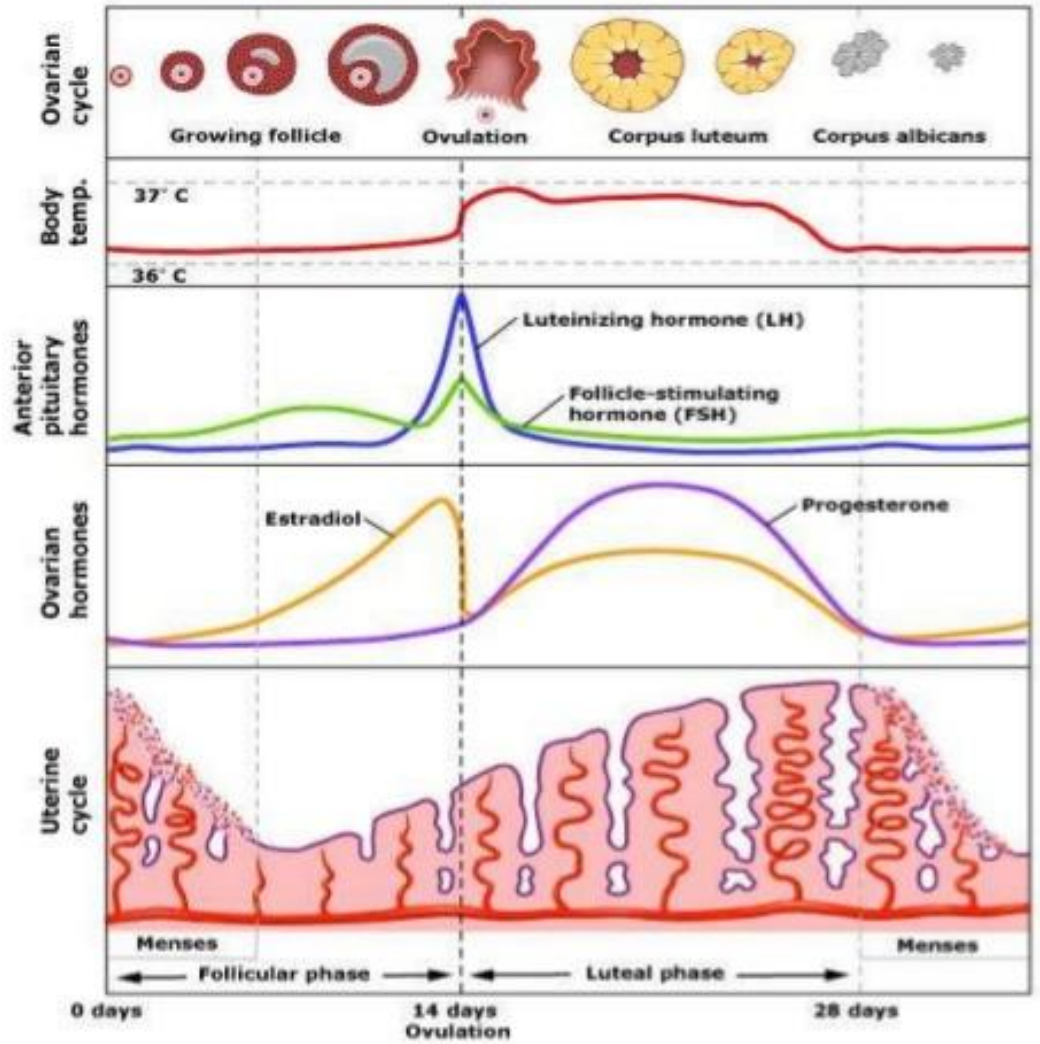
Anovulatory cycles

- Causes:

1. Lack of enough LH
2. Lack of ovarian response to LH
3. Decrease GnRH

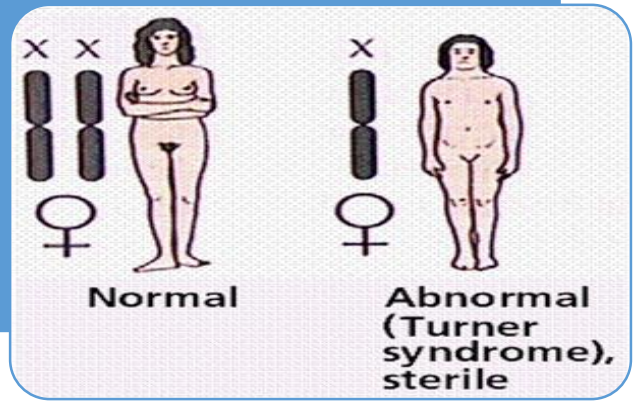
(lactation, emotional stress….)

- When?
- Diagnosis:



Amenorrhea

Primary



Secondary

Physiological

- Pregnancy
- Menopause
- Lactation
- Emotional stress

Pathological

- Hypothalamic
- Pituitary
- Ovarian
- Systemic diseases