

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



# MOTTO AND VISION



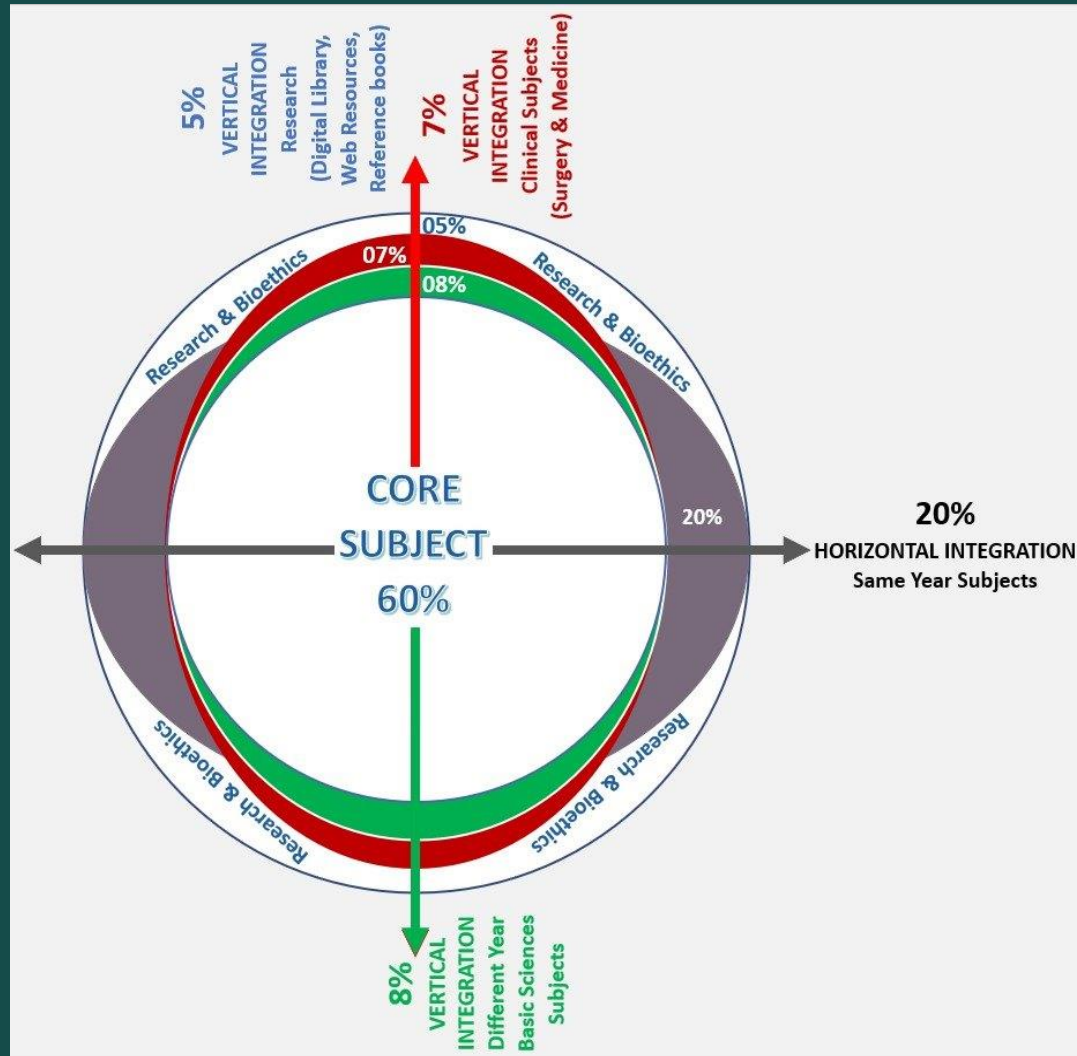
To impart evidence based research oriented medical education

To provide best possible patient care

To inculcate the values of mutual respect and ethical practice of medicine



# PROFESSOR UMAR MODEL OF INTEGRATED LECTURE





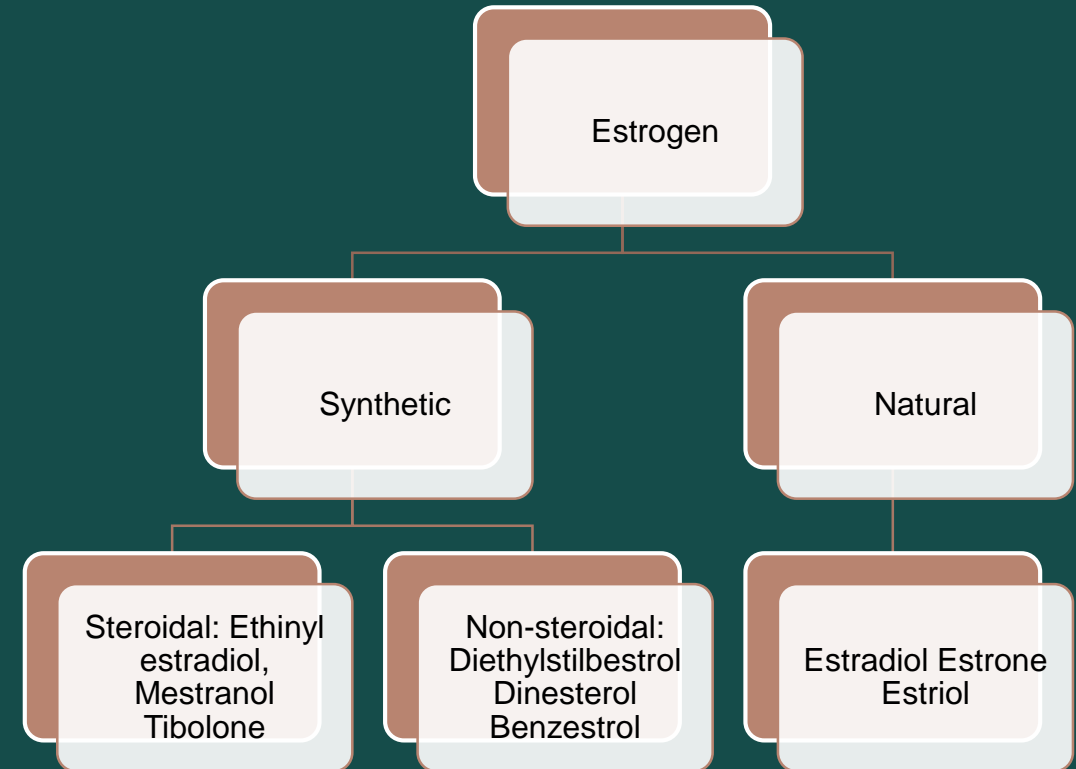
# ESTROGENS AND ANTIESTROGENS

DR MEMUNA KANWAL

Sources: Bertram G. Katzung Basic &  
Clinical Pharmacology 15th Edition

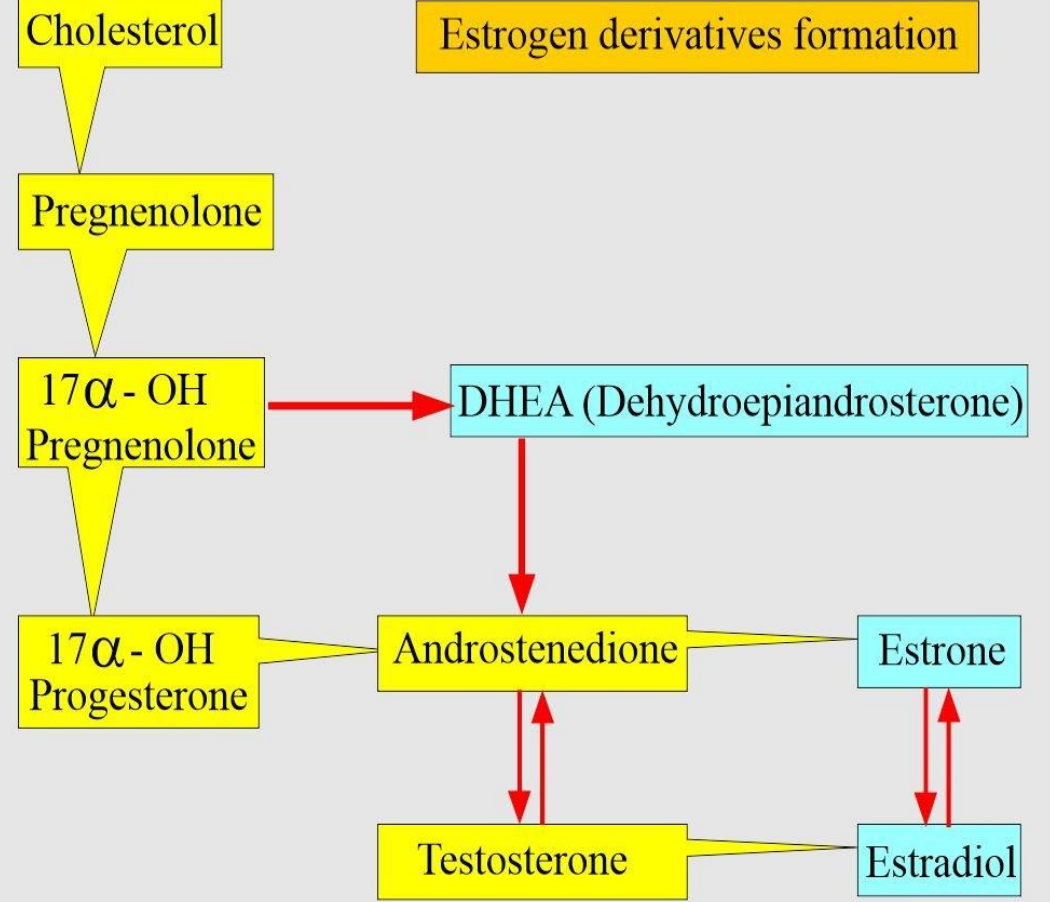
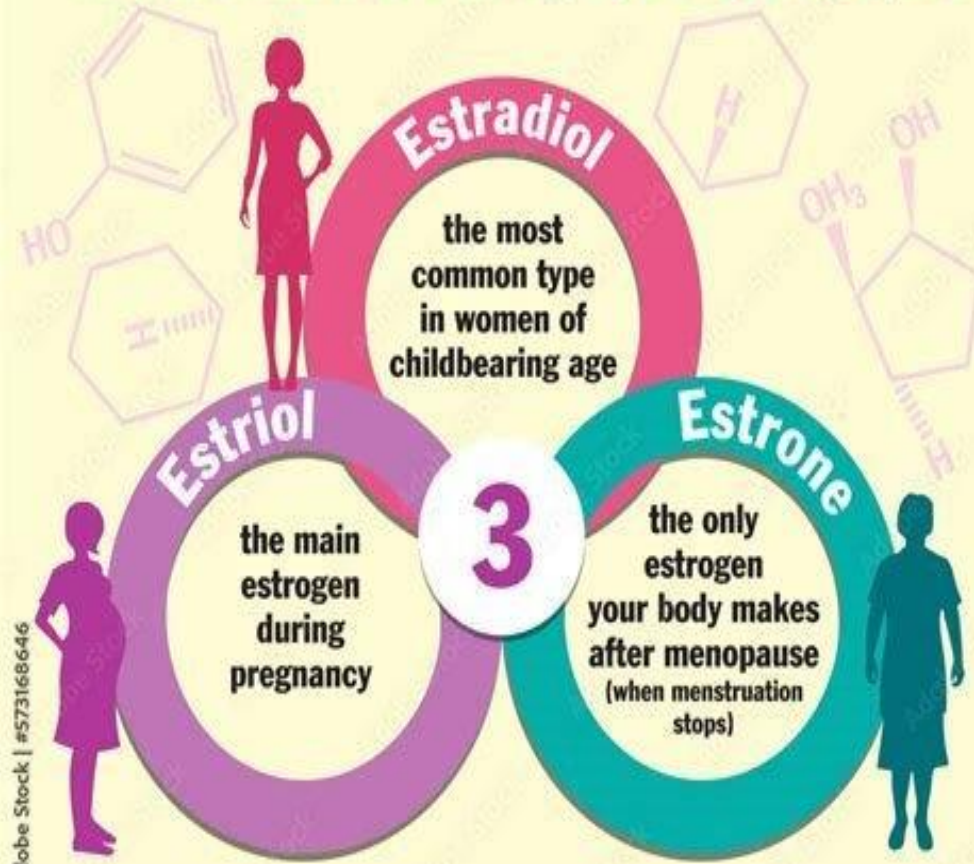
# WHAT IS ESTROGEN?

- It's a female gonadal hormone
- Sites of estrogen production

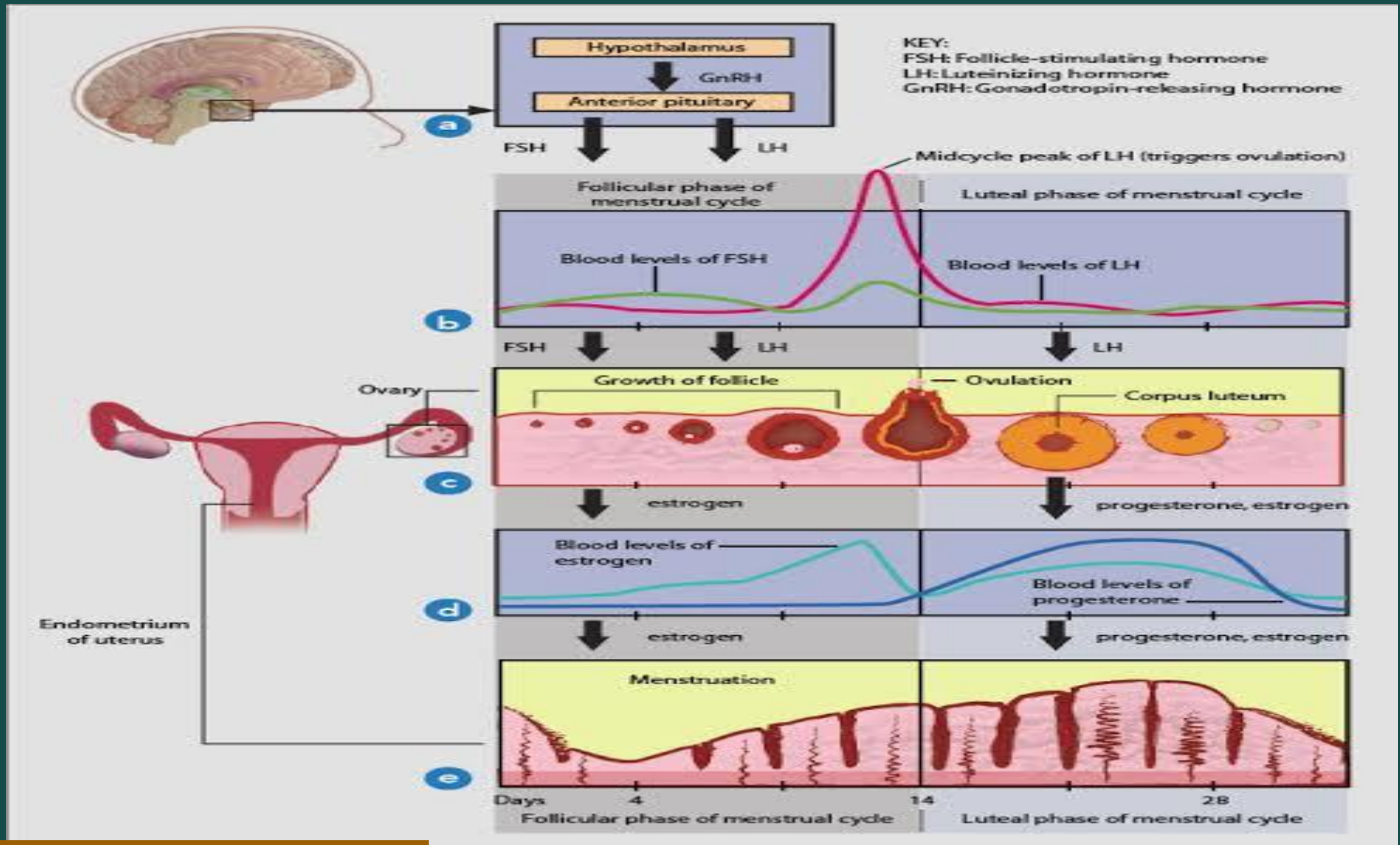




## THREE MAIN TYPES OF ESTROGEN

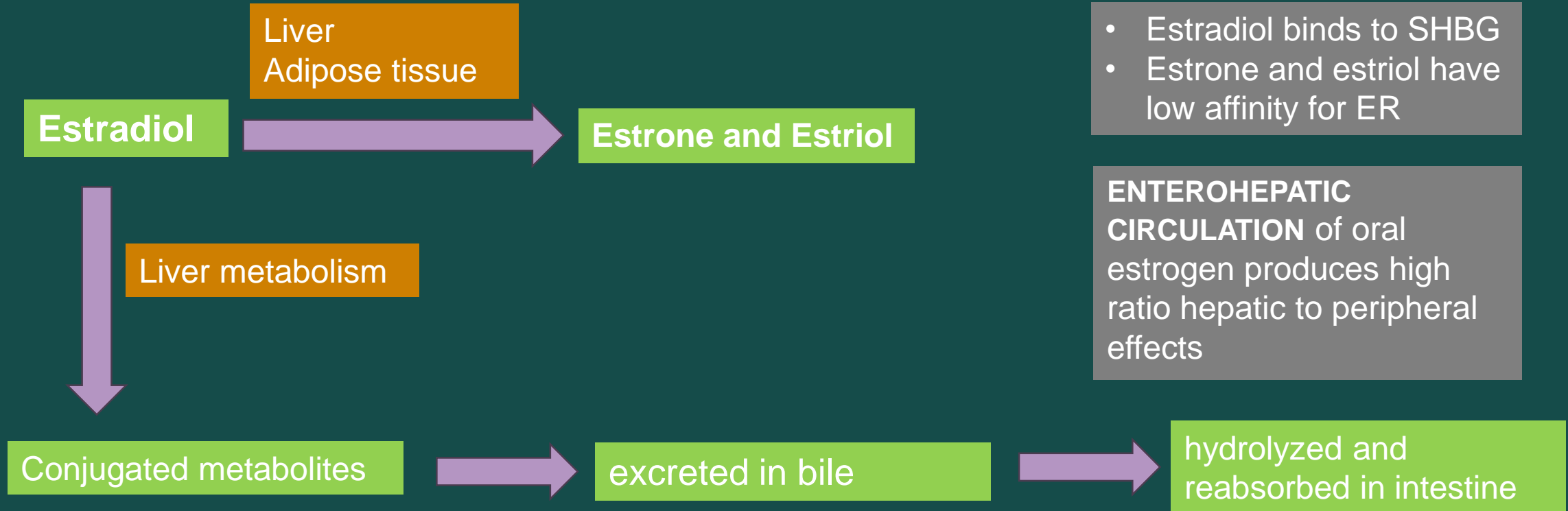


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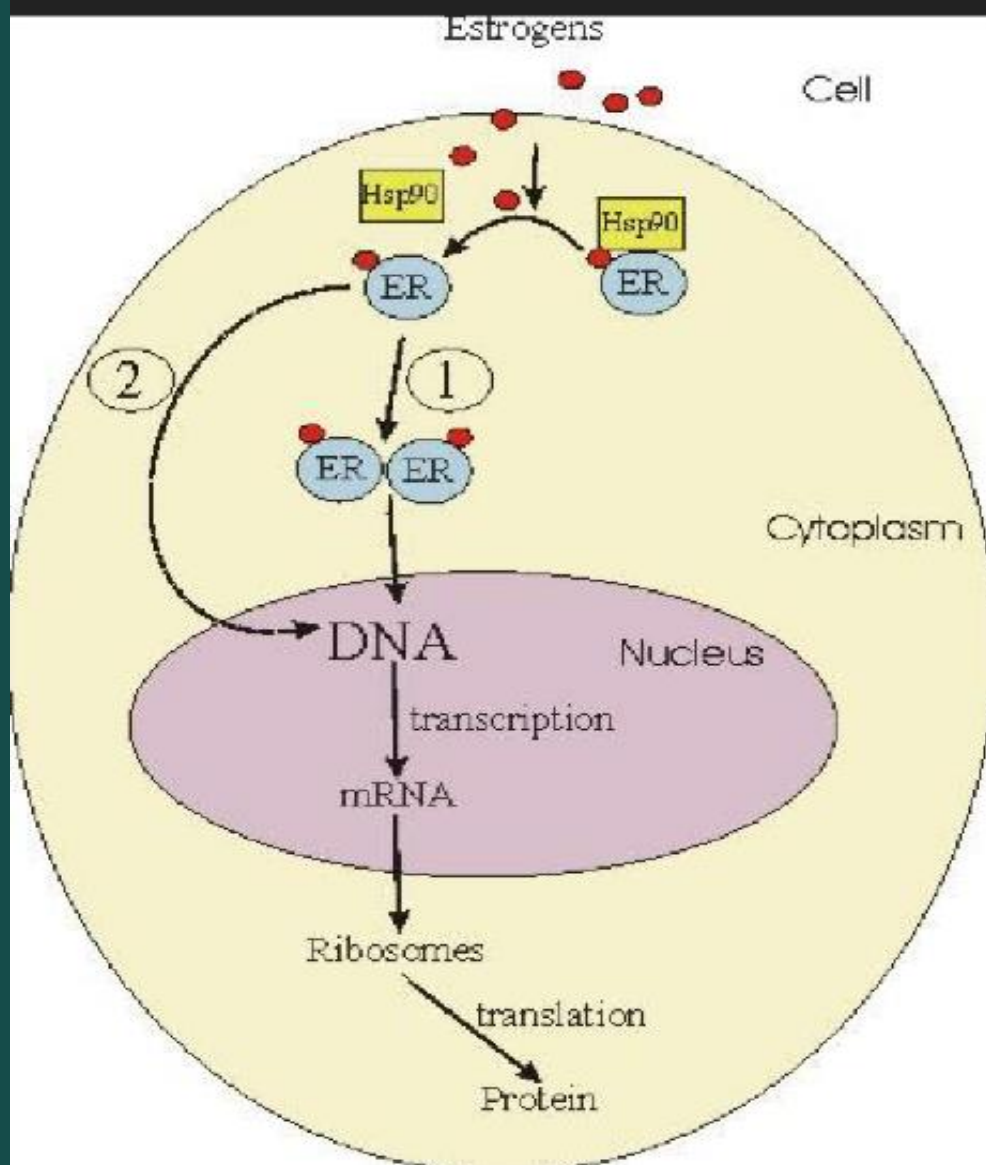




# PHARMACOKINETICS







# MECHANISM OF ACTION

ER alpha: induce transcription  
Predominant in uteruses, vagina, breast, blood vessels  
ER beta: have repressor domain  
Predominant in prostate and ovaries, bone, brain

# ACTIONS OF ESTROGEN ON BODY

## Female maturation

- Develops vagina, uterus, fallopian tubes in female
- Secondary sexual characteristics

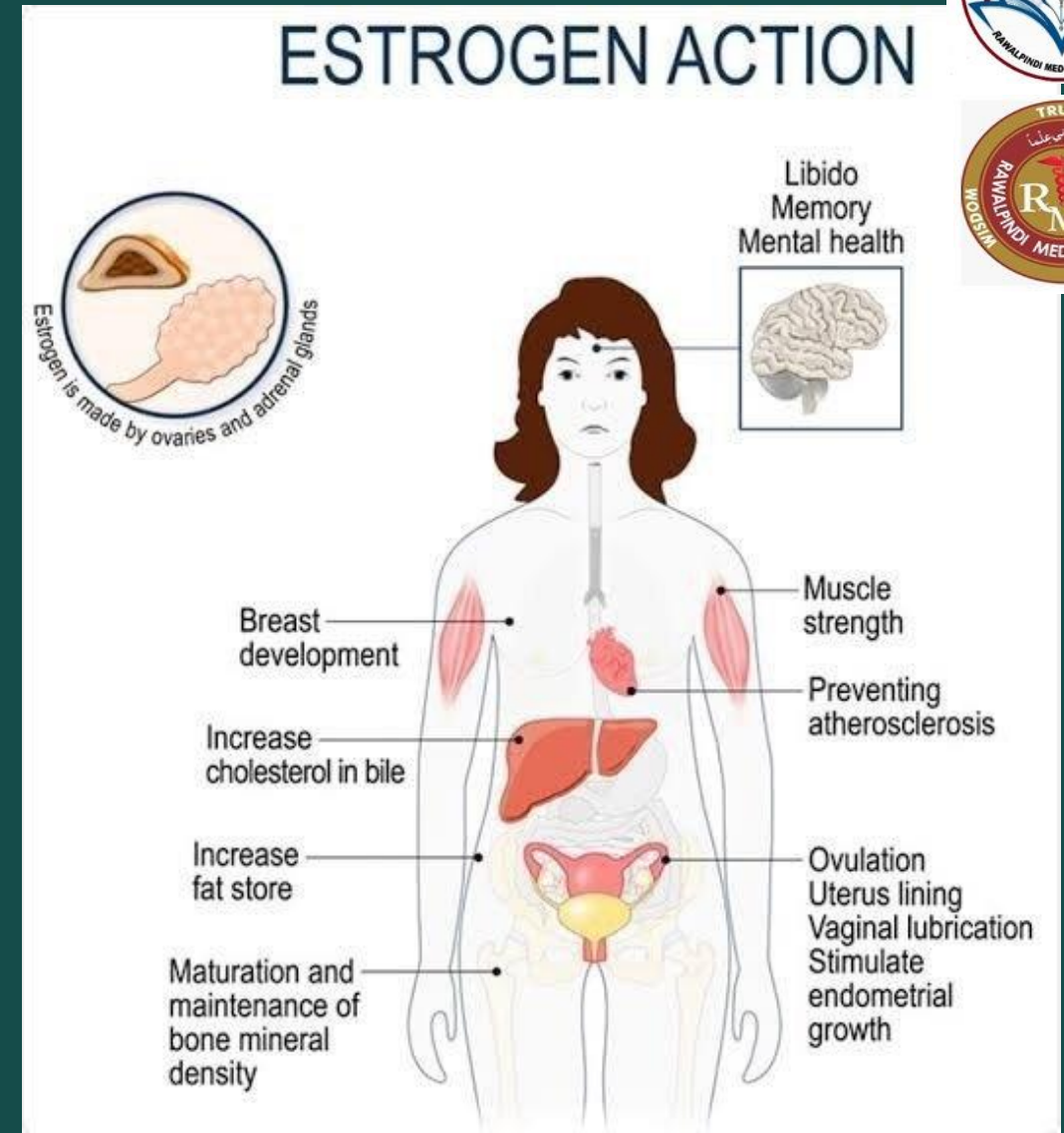
## Endometrial effects

## Effects on blood coagulability

## Effects on bones

## Metabolic effects

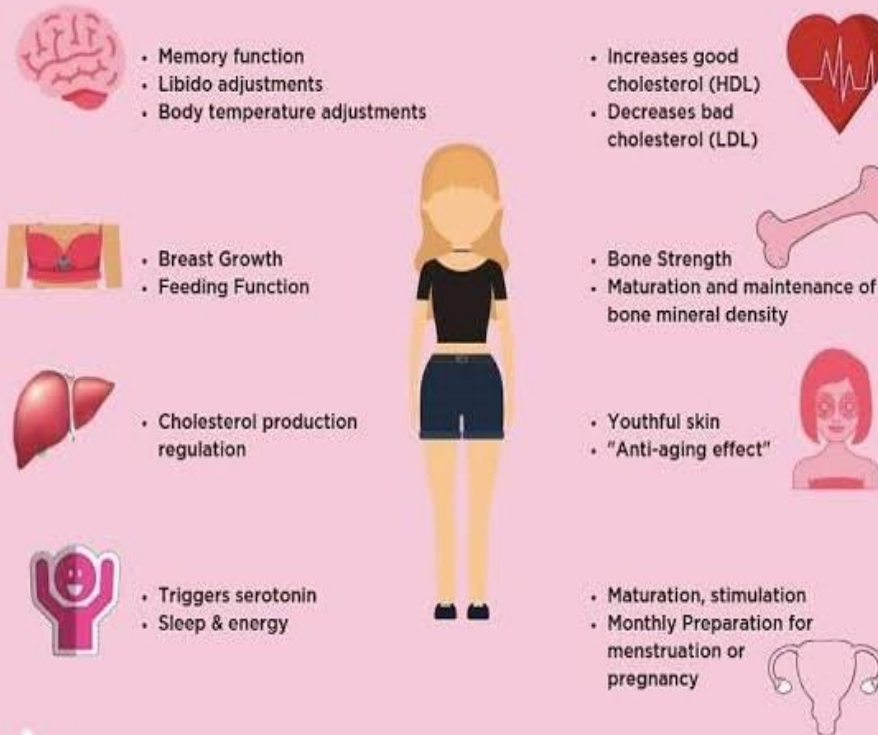
- Effects on proteins
- Effects on lipids





# ACTIONS OF ESTROGEN ON BODY

## Superpowers of Oestrogen



- Effects on brain
- Effects on skin
- Effects on liver

# CLINICAL USES OF ESTROGEN

- Primary hypogonadism
- Contraception
- Hormone replacement therapy
- Osteoporosis after menopause
- Senile vaginitis





# ADVERSE EFFECTS OF ESTROGEN



Nausea, headache

Breast tenderness

Postmenopausal uterine bleeding

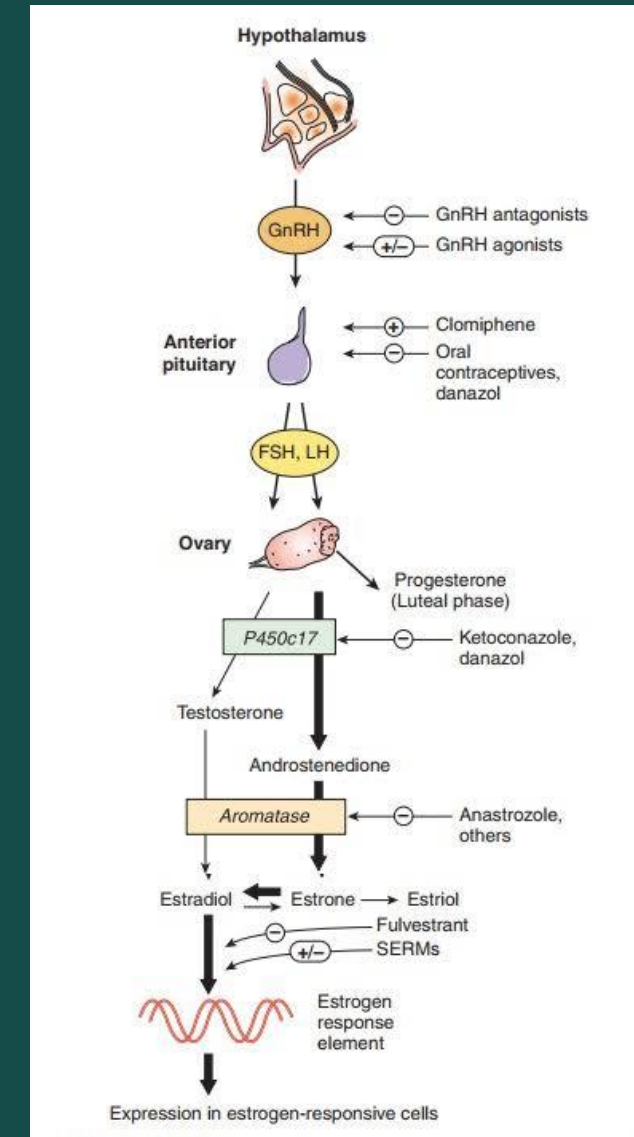
Peripheral edema, hypertension

Increased risk of **THROMBOEMBOLISM**

Increased risk of CA endometrium, and breast CA

# ANTIESTROGENS

- Selective Estrogen Receptor Modulators
- Pure Estrogen Receptor Antagonists
- Synthesis Inhibitors



# SELECTIVE ESTROGEN RECEPTOR MODULATORS

Mixed estrogen agonists that have agonist effects in some tissues and act as partial agonists or antagonists in other tissues

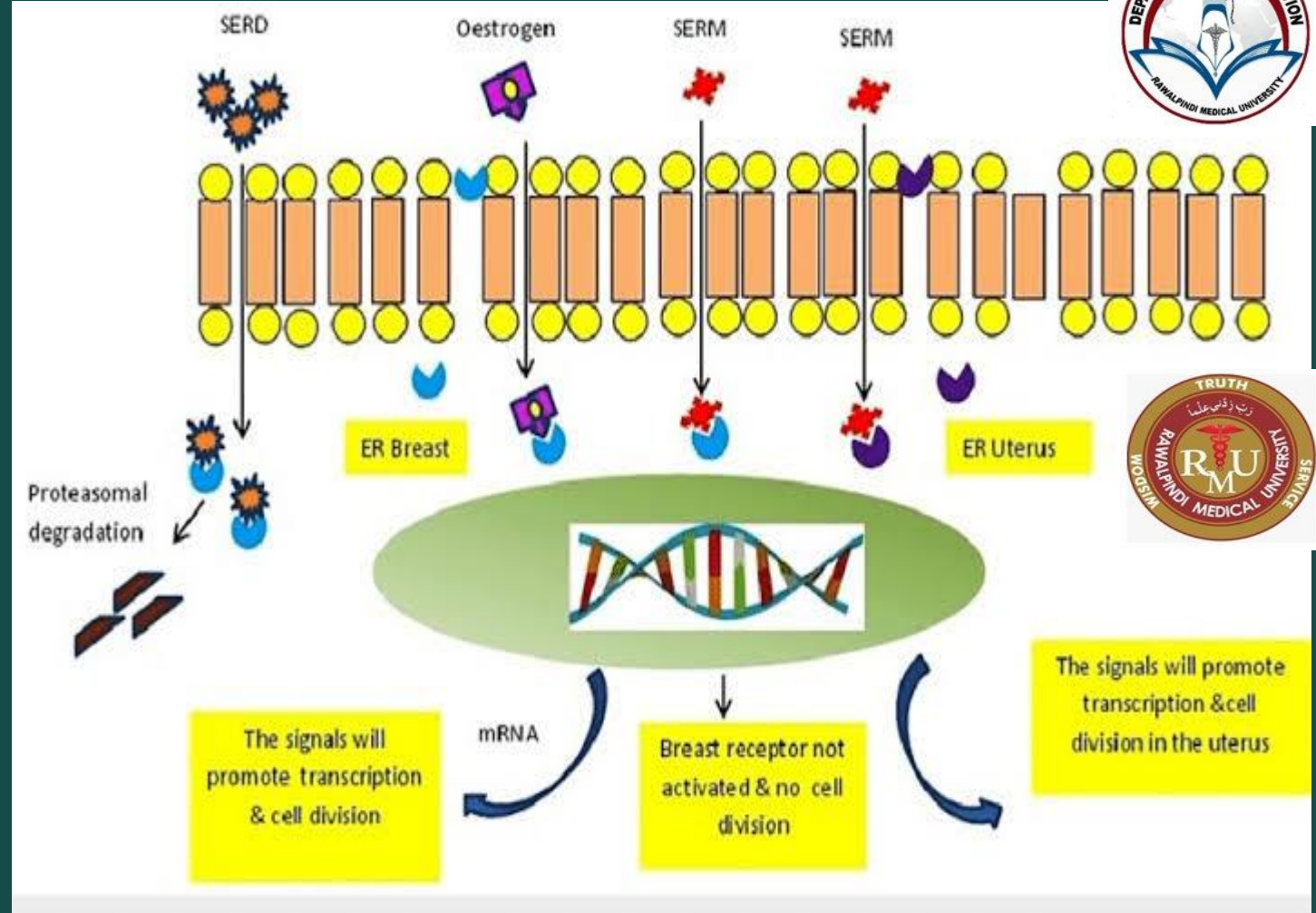
Tamoxifen

Raloxifene

Toremifene

Bezedoxifene

Clomiphene



# TAMOXIFEN

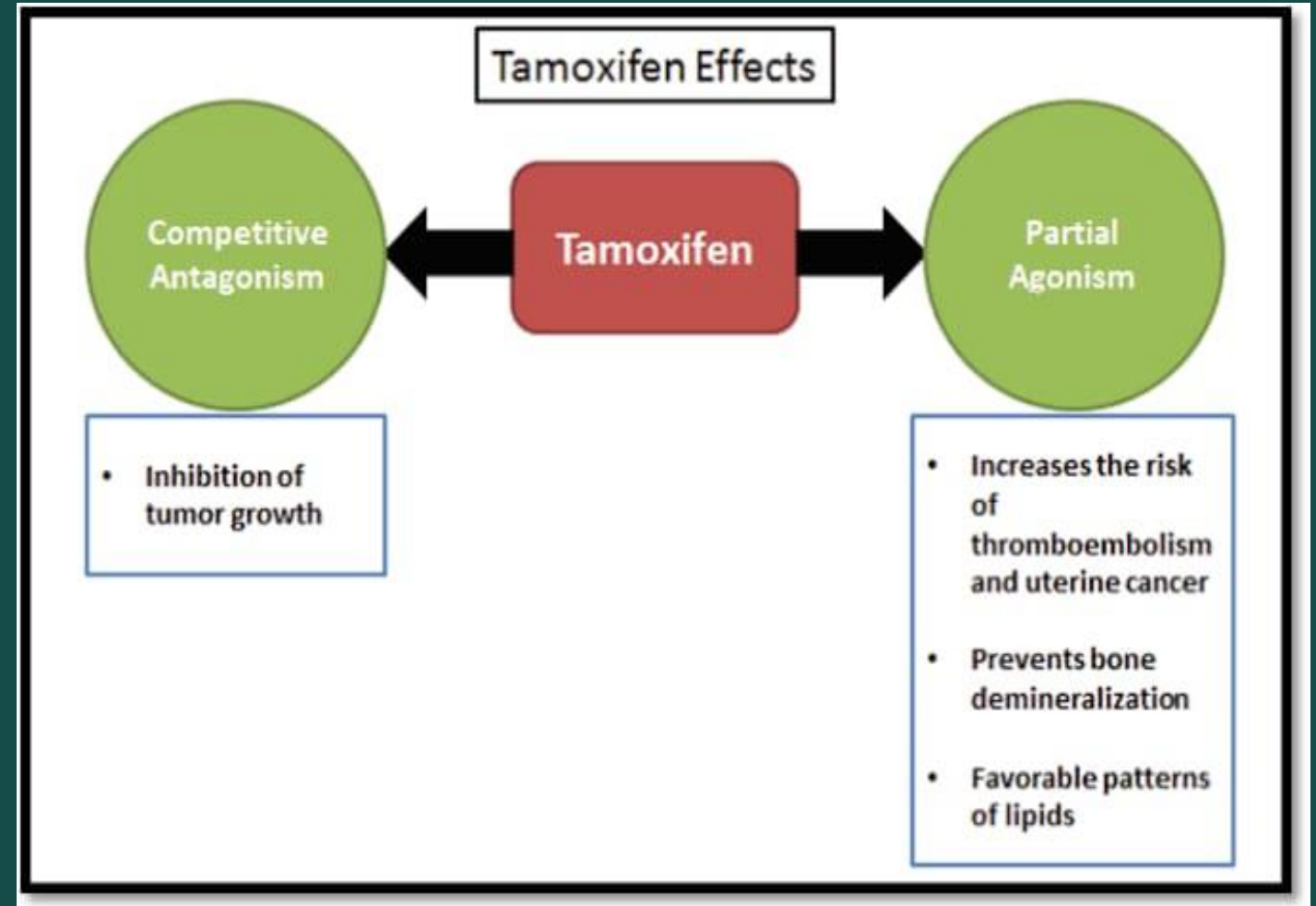
- **AGONIST EFFECTS**

- Endometrial receptors
- Increased risk of VTE
- Bone

- **ANTAGONIST EFFECTS**

- Breast
- Hot flushes

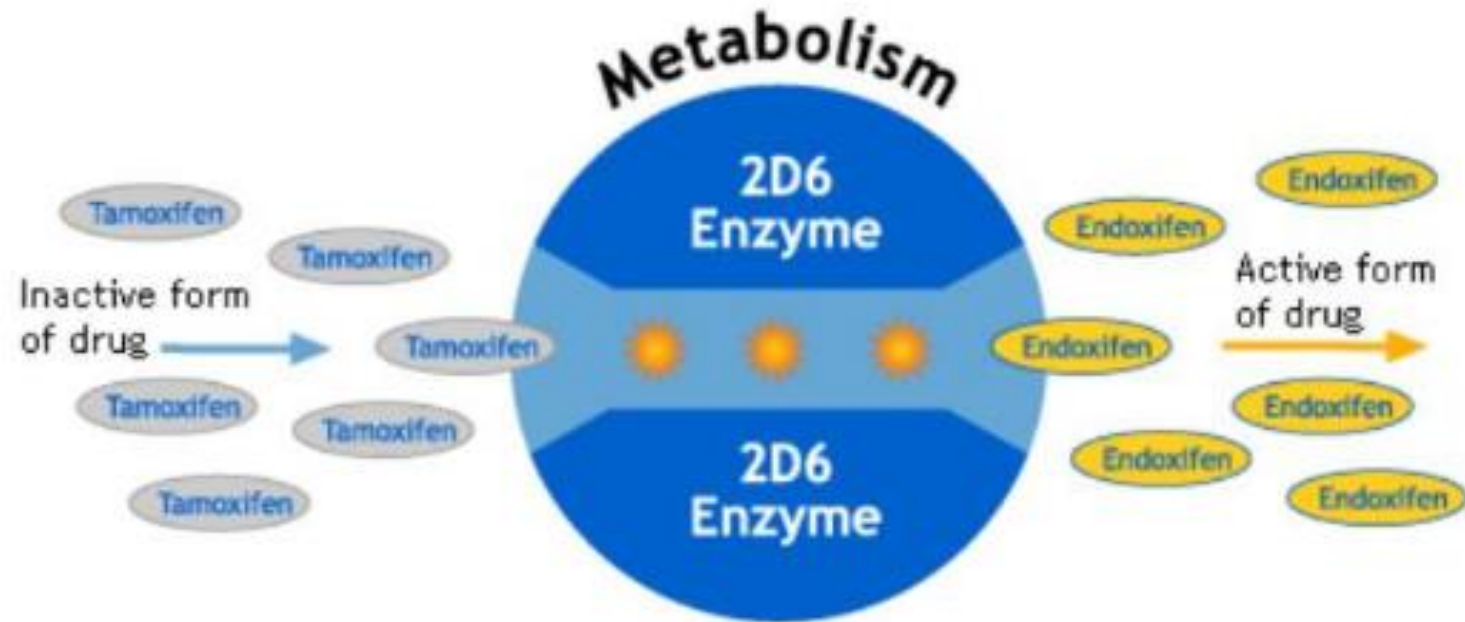
Toremifene is similar to tamoxifen





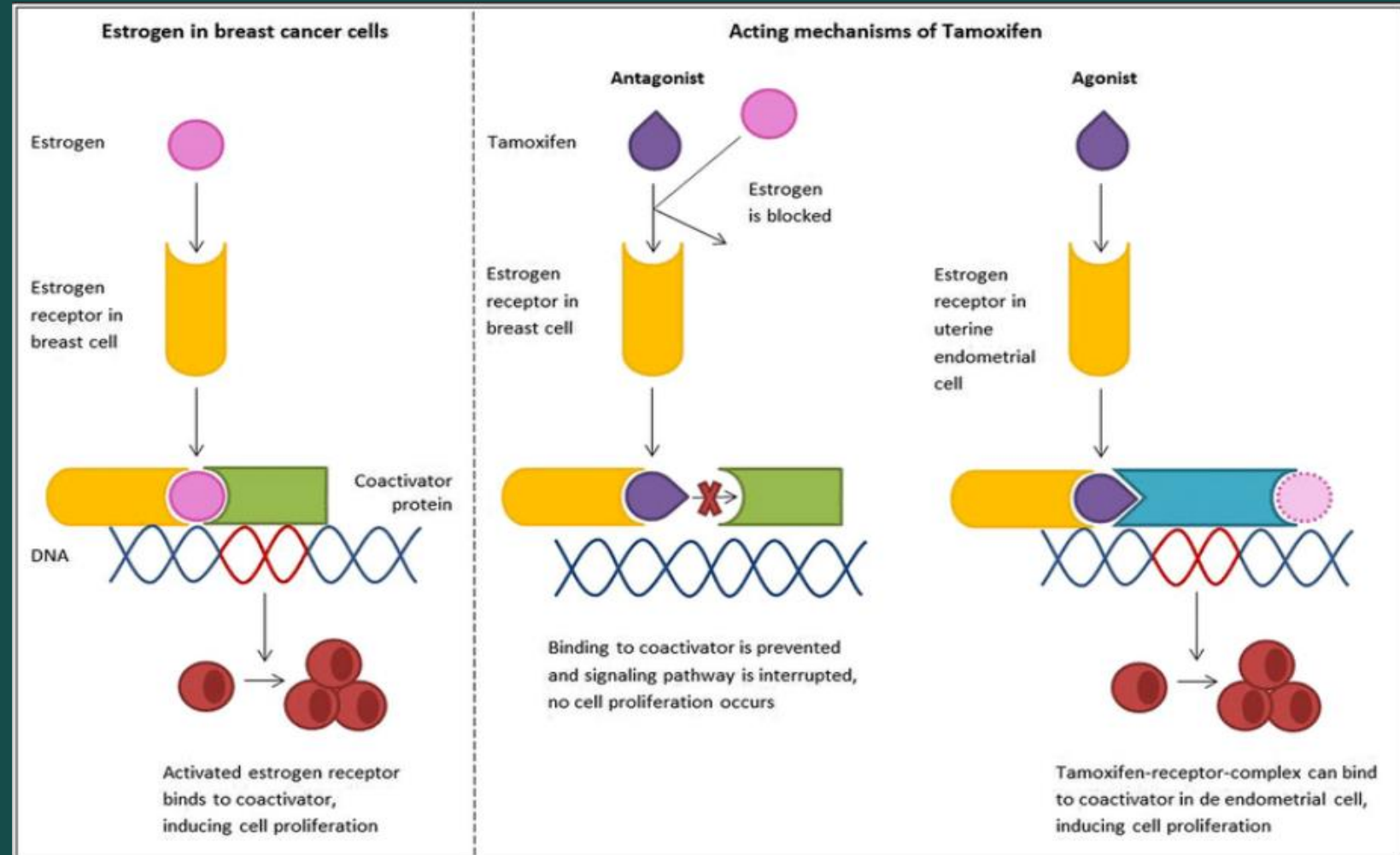
# TAMOXIFEN METABOLISM

- Metabolised in liver
- Role of pharmacogenetics in tamoxifen Metabolism?



# CLINICAL USES OF TAMOXIFEN

- Treatment of hormone responsive breast cancer
- Prophylaxis of breast CA in high risk patients



# RALOXIFENE

**AGONIST:** at bone, increased risk of VTE

**ANTAGONIST:** at breast, hot flushes

**No effect on endometrial tissue**

## Clinical uses

- Prevention and treatment of osteoporosis in postmenopausal women
- Prophylaxis of breast cancer in high risk women



# BAZDOXIFENE

Used for prevention of osteoporosis in postmenopausal women

Used to treat vasomotor symptoms associated with menopause

Antagonist effects in breast and uterus

Increased risk of VTE





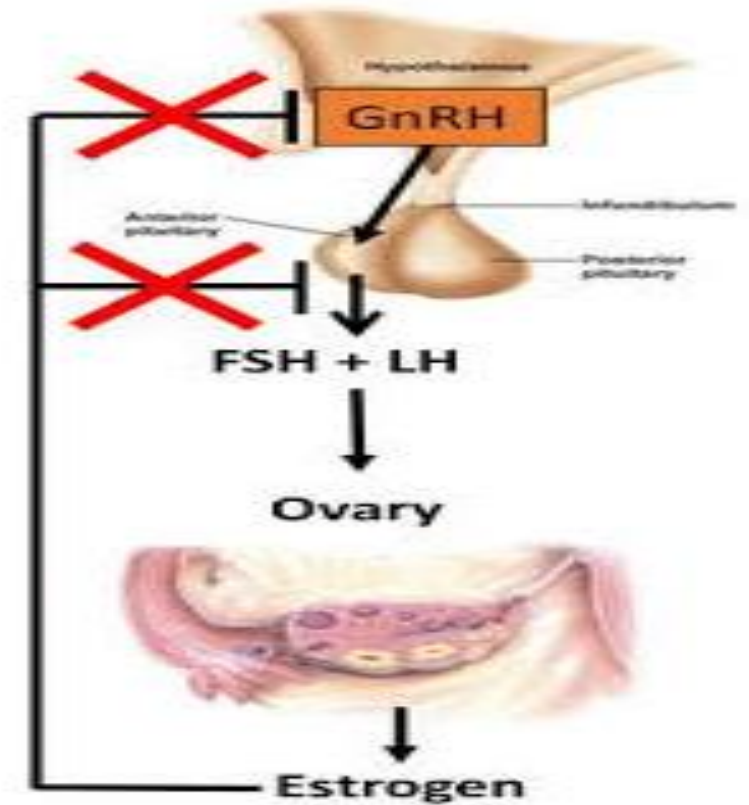


# SERMS COMPARISON

	BONE	ENDOMETRIUM	BREAST	VASOMOTOR SYMPTOMS	VTE
<b>TAMOXIFEN</b>	Agonist	Agonist	Antagonist	Increased	Increased
<b>RALOXIFENE</b>	Agonist	No Effect	Antagonist	Increased	Increased
<b>BAZDOXIFENE</b>	Agonist	Antagonist	Antagonist	Reduced	Increased

# CLOMIPHENE

- Agonist at ovary
- Antagonist at hypothalamus and anterior pituitary
- **Mechanism of action**
  - Prevent estrogen negative feedback of HP-Gonadal axis
  - Promote increased expression of GnRH and gonadotrophins
  - Increased production of FSH and LH
  - Increased follicular development and ovulation



# CLOMIPHENE



## Uses

- Female infertility due to anovulation

## Adverse effects

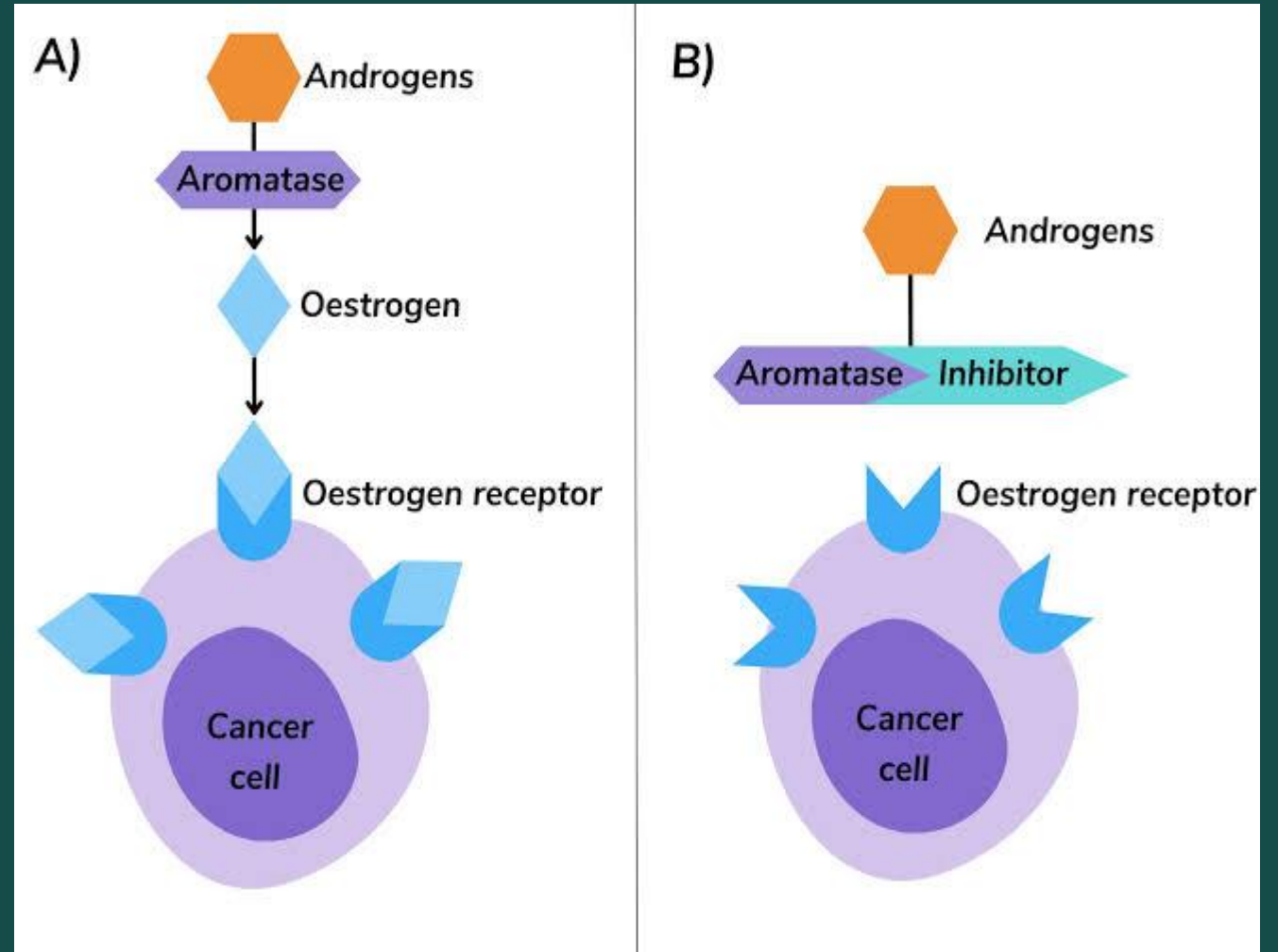
- Multiple pregnancies
- Hot flashes

# SYNTHESIS INHIBITORS

- **Aromatase Inhibitors**

- Anastrozole, Letrozole, Fadrozole
- Exemestane: irreversible inhibitor

- **Uses:** CA breast resistant to tamoxifen





# SYNTHESIS INHIBITOR: DANAZOL

Weak agonist of progestin, androgen & glucocorticoid receptors

## Mechanism of action

- Inhibit midcycle LH surge
- Binds to and translocate androgen receptors into nucleus to initiate androgen specific RNA synthesis
- inhibit cytochrome P450 enzymes involved in gonadal steroid synthesis
- ETHISTERONE: its metabolite has both progestational and mild androgenic effects



# DANAZOL

Long half life: 15 hours

Excreted in feces and urine

**Uses:** Endometriosis, Fibrocystic disease of breast

**Adverse effects:**

- Weight gain, edema, decreased breast size, acne and oily skin
- Deepening of voice, hirsutism, headache, hot flushes, changes in libido
- May cause adrenal suppression

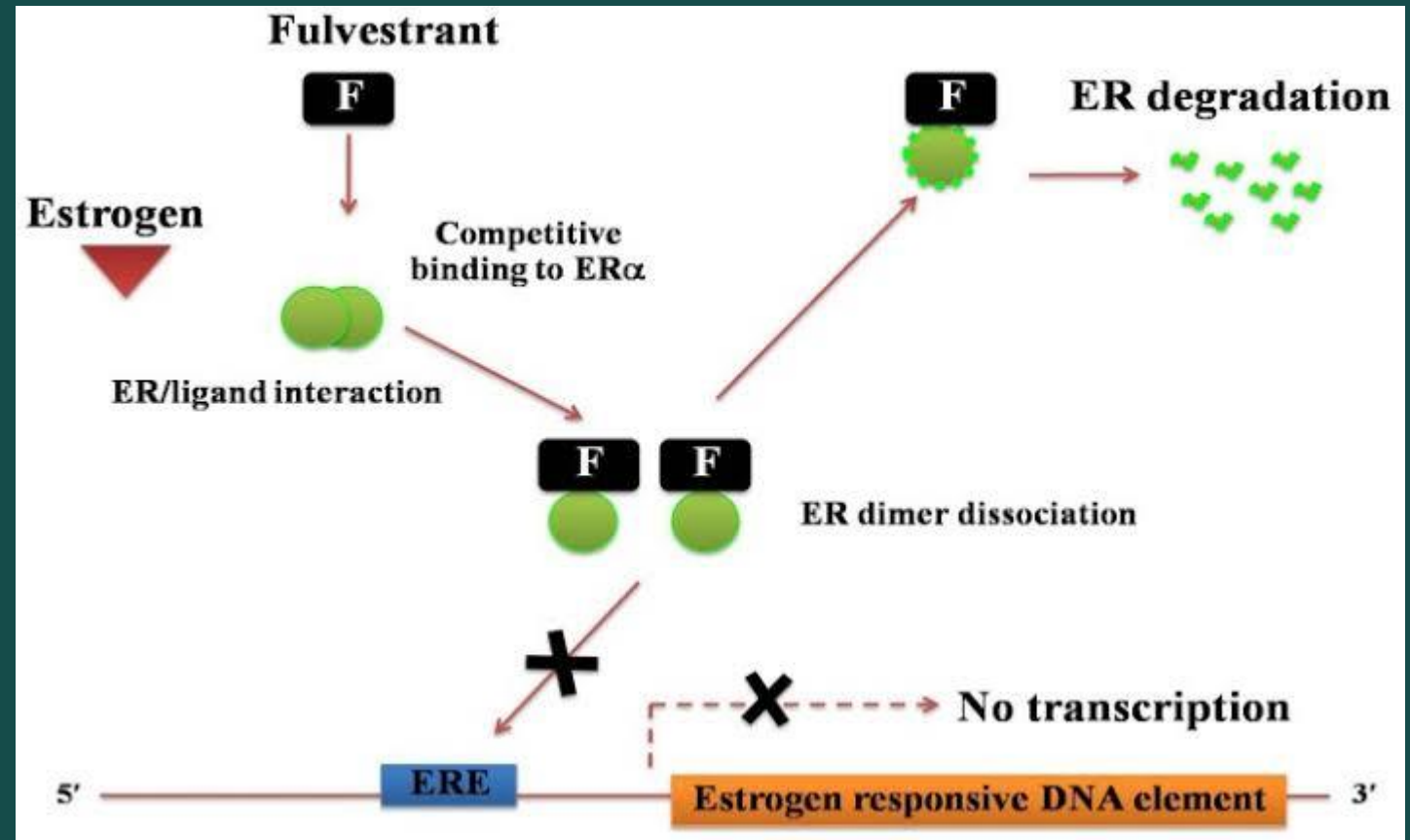
Used with caution in hepatic dysfunction

Contraindicated in pregnancy and lactation

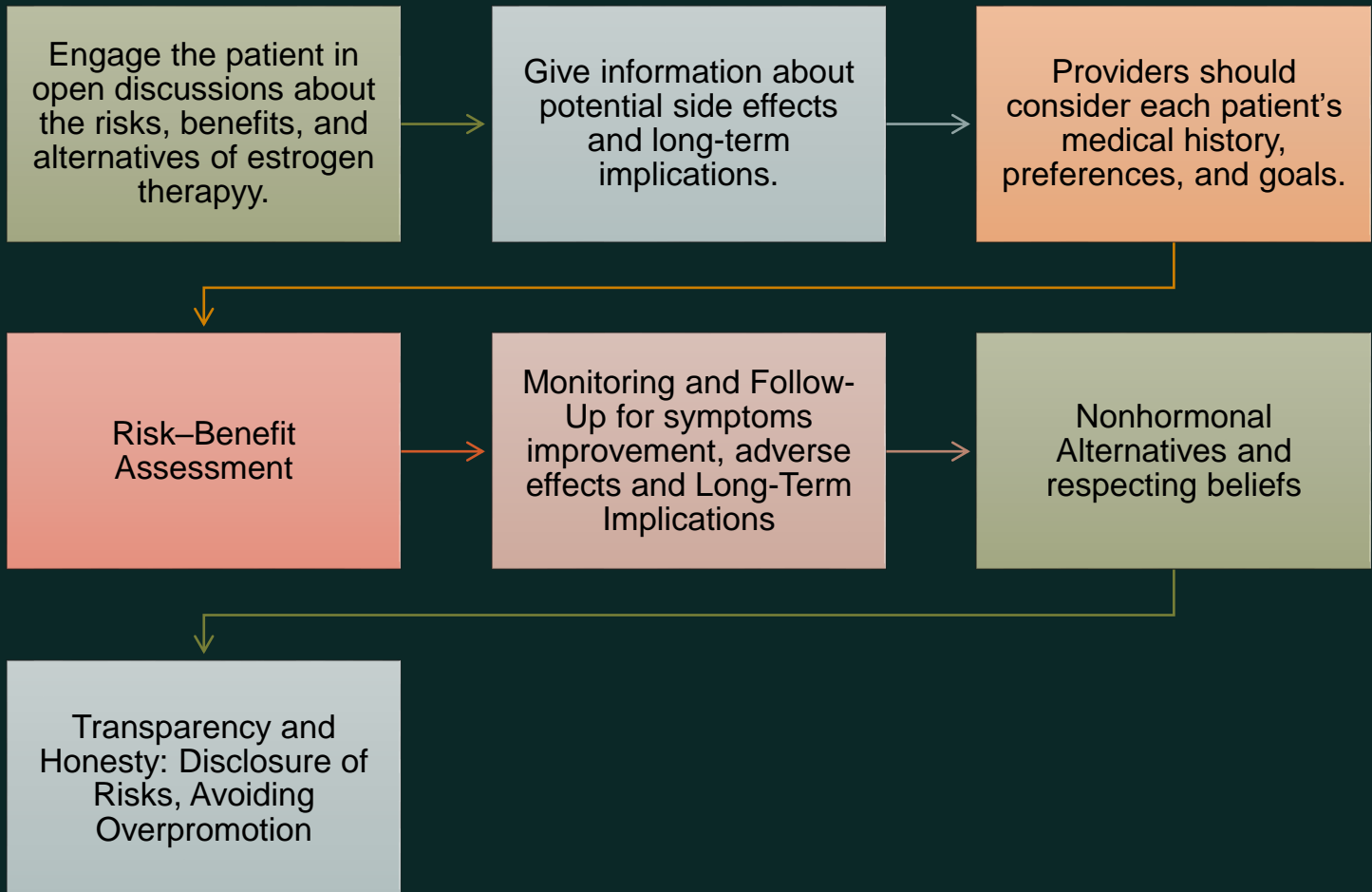


# PURE ESTROGEN RECEPTOR ANTAGONISTS

- Fulvestrant
- Treatment of CA breast resistant to tamoxifen



# BIOETHICAL CONSIDERATIONS





# HOW TO ASSESS DIGITAL LIBRARY

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Go to the website of HEC National Digital Library.

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On Home Page, click on the INSTITUTES.

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A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL.

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Select your desired Institute.

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A page will appear showing the resources of the institution

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Journals and Researches will appear

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You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal.





# FURTHER READING

Sriprasert I, Kono N, Karim R, Hodis HN, Stanczyk FZ, Shoupe D, Mack WJ. Factors associated with serum estradiol levels among postmenopausal women using hormone therapy. *Obstetrics & Gynecology*. 2020 Oct 1;136(4):675-84.

Clusan L, Le Goff P, Flouriot G, Pakdel F. A closer look at estrogen receptor mutations in breast cancer and their implications for estrogen and antiestrogen responses. *International journal of molecular sciences*. 2021 Jan 13;22(2):756.



# END OF LECTURE ASSESSMENT

- Which of the following is not an estrogen preparation
- Mestranol
- Ethinyl estradiol
- Estrone
- Norethindrone
- Estradiol acetate
- In women with CA breast resistant to tamoxifen which drug is used
- Fulvestrant
- Bazedoxifene
- Raloxifene
- Mifepristone
- Danazol



# END OF LECTURE ASSESSMENT

- Which of the following drugs is approved for prevention and treatment of osteoporosis in postmenopausal women
  - Clomiphene
  - Letrozole
  - Tamoxifen
  - Bazedoxifene
  - Raloxifene
- Which of the following SERMs is used for ovulation induction
  - Clomiphene
  - Anastrozole
  - Tamoxifen
  - Raloxifene
  - Danazol

THANK  
YOU