



# Drugs of Reproductive Block FINAL



This is NOT for studying just to review the lectures  
Good Luck!

This work includes the following lectures:

1. Medications affecting erectile dysfunction
2. Oral and other forms of contraception
3. Drugs inducing ovulation
4. Tocolytics and oxytocin
5. Teratogens and drugs of abuse in pregnancy
6. Hormonal replacement therapy
7. Drugs affecting breast milk and lactation
8. Drugs used in STDs



# FEW IMPORTANT NOTES

1. Know the differences between classes of drugs (or even drugs within the same class) with the same therapeutic use. You will find it in [this color](#)
2. You will find what doctors focused most about in this color (dark red),
3. SAQ is most likely from Drugs Affecting Erectile Dysfunction, Teratogens, Drugs Inducing Ovulation and Treatment of STDs. study them well!
4. Good luck!



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# Drugs of Reproductive Block

## Medications Affecting Erectile Dysfunction

### Drugs adversely causing ED

#### Central acting drugs

Drug	Key Point	C.I
<b>Antidepressants</b>	<b>M.O.A:</b> decrease 5HT uptake which lead to ↑5HT in synapse act on 5HT2 → decrease dopamine release → decrease arousal <b>Treatment of:</b> premature ejaculation	ED
<b>Antipsychotics</b>	<b>M.O.A:</b> DA (dopamine) antagonist → hyperprolactinemia	ED
<b>Antiepileptics</b> (phenytoin)	<b>M.O.A:</b> have GABA effect (inhibitory neurotransmitter) →. antagonize excitatory Amino acid → increase sedation → decrease arousal.	ED

#### Antihypertensives

<b>Methyldopa, reserpine</b>	<b>M.O.A:</b> decrease DA by depleting dopamine → decrease arousal (centrally)	ED
<b>Clonidine</b>	<b>M.O.A:</b> (α2 agonist) decrease arousal centrally, Vasoconstriction peripherally by anticholinergic action (blocking alpha receptors) → ED	ED
<b>β2 blockers</b>	<b>M.O.A:</b> -ve vasodilating β2 → potentiate α1 effect (vasoconstriction)	ED

#### Anti-androgens

<b>Finasteride</b>	<b>M.O.A.:</b> α reductase inhibitor (prevent production of active testosterone ) → <u>irreversible erectile dysfunction</u>	ED
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#### Others:

Cyproterone acetate, cimetifine (high doses), ketoconazole, spironolactone, estrogen-containing medications

ED

#### Habituating agents

<b>Smoking</b>	Causes vasoconstriction and penile venous leakage	ED
<b>Alcohol</b>	<u>Small amounts:</u> increase desire + decrease anxiety + vasodilatation <u>Large amount:</u> increase sedation + decrease desire <b>Chronic alcoholism</b> → hypogonadism	ED

### Drugs treating ED (ORAL)

#### Selective PDE5 inhibitors (oral)

<b>Sildenafil</b> <b>Vardenafil</b> <b>Tadalafil</b> <b>Avanafil</b>	<b>M.O.A.:</b> inhibit <b>PDE5</b> → prevent breakdown of <b>cGMP</b> → pertain vasodilatation → erection. They do not affect the libido, so sexual stimulation is essential. <b>Indications:</b> ED (1st line therapy), BPH & premature ejaculation. <b>P.K:</b> <b>metabolized in the liver</b> , food interact with <b>sildenafil</b> & <b>vardenafil</b> (taken on empty stomach), and <b>Avanafil</b> has the advantage of been given 30 mins before intercourse. <b>Selectivity:</b> Tadalafil > vardenafil > sildenafil. <b>ADRs:</b> priapism if erection lasts longer than 4 hrs. <b>Sildenafil:</b> abnormal vision. <b>Vardenafil:</b> Q-T prolongation. <b>Tadalafil:</b> myalgia & back pain, ↓ sperm function	<u>Nitrates</u>
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# Medications Affecting Erectile Dysfunction cont.

## Drugs treating ED (ORAL)

### Other oral drugs

Drug	Key Point	C.I
1. Testosterone 2. Apomorphine 3. Oral Phentolamine 4. Yohimbine 5. Trazodone	1. Promote desire 2. Dopamine agonist on D2 receptors, Centrally acting., safe with <u>nitrates</u> . 3. $\alpha$ 1 blocker 4. Has many CVS side effects 5. Antidepressant → priapism	-

## Drugs treating ED (TOPICAL)

### Cream combination

Drug	Key Point	C.I
20% papaverine 2% minoxidil 2% nitroglycerine	<b>Disadvantages:</b> Low efficacy / no FDA approval Female partner can develop hypotension, headache due to vaginal absorption	-

## Drugs treating ED (TRANSURETHRAL)

Drug	Key Point	C.I
Alprostadil	M.O.A.: binds to <u>PGE1</u> Receptors and convert ATP into <u>cAMP</u> → vasodilatation	

## Drugs treating ED (INTRACAVERNOUS INJ.)

### These 3 are combined in severe cases

Drug	Key Point	C.I
Alprostadil	ADRs: bleeding at injection site, cavernosal fibrosis, priapism	
papaverine	A direct acting smooth muscle relaxant	
Phentolamine	$\alpha$ 1 blocker	

## Treatment of priapism

Phenylephrine	M.O.A.: $\alpha$ 1 agonist	
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# Drugs of Reproductive Block

## Oral and Other Forms of Contraception

### Combined pills (combined oral contraceptives)

Drug	Key Point	C.I
<b>Estrogen</b> (ethinyl estradiol, mestranol)	<b>M.O.A.:</b> <u>inhibit ovulation</u> by suppressing the release of Gns (FSH & LH). <u>Inhibit implantation</u> by causing abnormal cont. of fallopian tubes & uterine musculature. <u>Increase</u> viscosity of mucus.	1. Thrombophlebitis / thromboembolic disores 2. Vaginal bleeding 3. Pregnancy (or suspected) 4. Breast cancer or estrogen-dependant neoplasms
<b>Progestins</b>	<b>Methods of administration:</b> <u>Monthly pills</u> taken for 21 days (day 5 - day 26) <u>Seasonal pills:</u> taken continuously for 84 days, it Lessens menstrual periods to 4 times a year, useful in those who have premenstrual or menstrual disorders, and in perimenopausal women with vasomotor symptoms. <b>ADRs:</b> <u>Estrogen related:</u> impaired glucose tolerance (hyperglycemia), increase incidence of breast, vaginal and cervical cancer, CVS (thromboembolism, hypertension). <u>Progestin related:</u> depression of mood, menstrual irregularities, weight gain, hirsutism, masculinization ( <b>norethindrone</b> ).	

### Combined pills (COC) interactions

Drug	Key Point
<b>Ampicillin</b>	<b>Cause contraceptive failure</b> → Interferes with normal GI flora <small>Ampicillin is an antibiotic so it interferes with bacteria (normal flora)</small>
<b>Phenytoin, phenobarbitone, rifampin</b>	<b>Cause contraceptive failure</b> → decrease its catabolism
<b>Acetaminophen, erythromycin</b>	<b>Increase COC toxicity</b> → decrease metabolism of COC → toxicity
<b>Warfarin, cyclosporine, theophylline</b>	<b>Medications altered in clearance of combined oral contraceptive which increase their toxicity</b>

### Mini pills, Progestin only pills (POP)

Drug	Key Point
<b>Norethindrone, desogestrel, medroxyprogesterone</b>	<b>M.O.A.:</b> increase cervical mucus, so no sperm penetration & therefore no fertilization. <b>Uses:</b> alternative when estrogen is contraindicated (e.g. breastfeeding, hypertension, cancer, smokers over 35 y.o). <b>P.K:</b> I.M injection

# Oral and Other Forms of Contraception cont.

## Post Coital Contraception

Contraception on instantaneous demand, 2ndary to unprotected sexual intercourse

Drug	Key Point	Method of administration
Ethinyl estradiol + Levonorgestrel	<b>Indications:</b> - torn, leaking condom. - missed pills - exposure to teratogen e.g. live vaccine - rape  <b>Efficacy from highest to lowest:</b> Mifepristone ± Misoprostol: > Ethinyl estradiol > Ethinyl estradiol + Levonorgestrel > levonorgestrel	2 tablets twice with 12 hrs in between
High-dose only of Ethinyl estradiol		Twice daily for 5 days
High dose only of levonorgestrel		Twice daily for 5 days
Mifepristone ± Misoprostol		<a href="#">A single dose</a>

# Drugs in Ovulation Induction

Drug	Key Point	C.I
<b>Antiestrogens (SERMs)</b>		<b>SAQ</b>
<b>Clomiphene</b>	<p><b>M.O.A:</b> Compete with estrogen on the hypothalamus and anterior pituitary gland; reduce negative feedback of endogenous estrogen&gt;&gt; high GnRH&gt;&gt; production of FSH &amp; LH&gt;&gt; OVULATION</p> <p><b>indication:</b> female infertility; due to anovulation or oligoovulation with normal pituitary and no ovarian failure (<b>Normogonadotropic</b>)</p> <p><b>Method:</b> given 50 mg/d for 5 days from 5th day of the cycle to the 10th day, <u>No response?</u> 100 mg for 5 days again from 5th to 10th day</p> <p><b>ADRs:</b> Hyperstimulation of the ovaries &amp; <b>high incidence of multiple birth</b>, hot flushes &amp; skin rashes.</p>	-
<b>Tamoxifen (Non Steroidal)</b>	<ul style="list-style-type: none"> <li>- Good alternative to clomiphene in women with PCOS and clomiphene-resistant cases</li> <li>- Used in palliative treatment of estrogen receptor- positive breast cancer.</li> </ul>	-
<b>GnRH-agonists</b>		
<b>Leuprorelin</b>	<p><b>Uses:</b> Induction of ovulation in patients with <b>hypothalamic amenorrhea (GnRH deficient)</b></p> <ul style="list-style-type: none"> <li>- Given <b>S.C.</b> in a <b>pulsatile</b> (drip) to stimulate gonadotropin release start from <b>day 2-3</b> of cycle up to <b>day 10</b>.</li> <li>- <b>Given continuously, when gonadal suppression is desirable</b> e.g. precocious puberty and advanced breast cancer in women and prostatic cancer in men.</li> </ul> <p><b>ADRs:</b> Hypoestrogenism (long term use), Rarely ovarian hyperstimulation (ovaries swell &amp; enlarge), Osteoporosis, decreases Libido</p>	-
<b>Goserelin</b>		
<b>Gonadotropins</b>		
<b>HMGs (menotropin)</b>	<p><b>hMG:</b> Extracted from postmenopausal urine (contains LH &amp; FSH)</p> <p><b>hCG:</b> Extracted from urine of <b>pregnant</b> women (contains mainly LH)</p> <p><b>Indication:</b> Stimulation &amp; induction of ovulation in infertility 2ndry to gonadotropin deficiency (<b>pituitary insufficiency</b>)</p> <p><b>Administration:</b> hMG is given I.M starting at day 2-3 of cycle for 10 days, followed by hCG on (10th - 12th day) for OVUM RETRIEVAL .</p> <p><b>ADRs:</b></p> <ul style="list-style-type: none"> <li>- <b>FSH containing preparations:</b> Fever, Ovarian enlargement (hyper stimulation), Multiple Pregnancy (<b>true, but it's higher in clomiphene</b>)</li> <li>- <b>LH containing preparations:</b> Headache &amp; edema</li> </ul>	-
<b>HCGs (pregnyl)</b>		
<b>D<sub>2</sub> Receptors Agonists</b>		<b>SAQ</b>
<b>Bromocriptine</b>	<p><b>M.O.A:</b> D<sub>2</sub> Receptors Agonists binds to dopamine receptors in the anterior pituitary gland &amp; inhibits prolactin secretion.</p> <p><b>indication:</b> <b>Female infertility 2ndry to hyperprolactinemia.</b></p> <p><b>ADRs:</b> GIT disturbances; nausea, vomiting, constipation, Headache dizziness &amp; orthostatic hypotension, Dry mouth &amp; nasal congestion, Insomnia</p>	-

## Rx of Polycystic Ovarian Syndrome

(Most common cause of infertility, Insulin resistance may play a role)

**:Metformin**

Rx: medical prescription

Relin >> releasin >> Gn releasing hormone. No? Ok...

# Drugs of Reproductive Block

## Oxytocics & Tocolytics

Drug	Key Point	C.I
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### Drugs Producing Uterine Contraction

#### Oxytocics

<p><b>OXYTOCIN</b> (Syntocinon)</p>	<p><b>MOA:</b> The interaction of endogenous or administered oxytocin, with myometrial cell membrane receptor promotes the influx of <math>Ca^{++}</math> from extracellular fluid and from S.R. into the cell, this increase in cytoplasmic calcium, stimulates uterine contraction.</p> <p><b>Administration:</b> given IV or nasal spray</p> <p><b>Indication:</b> Induction &amp; augmentation of labor, Postpartum uterine hemorrhage, Impaired milk ejection (nasal spray)</p> <p><b>Side effects:</b> Maternal death due to hypertension, Uterine rupture, Fetal death (ischemia), Water intoxication</p> <p><b>Precautions:</b> previous c-section</p>	<ul style="list-style-type: none"> <li>-Hypersensitivity</li> <li>-Prematurity</li> <li>-Abnormal fetal position</li> <li>-Evidence of fetal distress</li> <li>-Cephalopelvic disproportion</li> <li>-Incompletely dilated cervix</li> </ul>
<p><b>Natural:</b> Ergometrine (Ergonovine) <b>Synthetic:</b> Methyl ergometrine (Methyletergonovine)</p>	<p><b>MOA:</b> induce TETANIC CONTRACTION of uterus without relaxation in between, it causes contractions of both fundus and cervical</p> <p><b>Administration:</b> given I.M (the only one of this lecture).</p> <p><b>USE:</b> Postpartum hemorrhage (3rd stage of labor)</p> <p><b>Side effects:</b> Hypertension Vasoconstriction of peripheral blood vessels, Gangrene</p>	<ul style="list-style-type: none"> <li>-Induction of labour 1st and 2nd stage of labor</li> <li>-vascular disease</li> <li>Severe -hepatic and renal impairment</li> <li>-Severe hypertension</li> </ul>
<p>1)PGE2 Dinoprostone 2)PGF2<math>\alpha</math>- Dinoprost, Carboprost 3)Misoprostol (synthetic PGE1)</p>	<p><b>MOA:</b> Contraction throughout pregnancy, soften the cervix</p> <p><b>Uses:</b> Induction of abortion (pathological), Induction of labor (fetal death in utero), Postpartum hemorrhage</p> <p><b>side effects:</b> Bronchospasm (PGF2<math>\alpha</math>) /Flushing (PGE2)</p>	<ul style="list-style-type: none"> <li>-Mechanical obstruction of delivery</li> <li>-Fetal distress</li> <li>-Predisposition to uterine rupture</li> </ul>

### Drugs Producing Uterine Relaxation

#### Tocolytics

Relax the uterus and arrest threatened abortion or delay premature labor.

<p><b>Ritodrine</b> (<math>\beta_2</math> - adrenoceptor agonists)</p>	<p><b>MOA:</b> Bind to <math>\beta_2</math>-adrenoceptors <math>\rightarrow</math> activate enzyme (Adenylate cyclase) <math>\rightarrow</math> increase cAMP level reducing intracellular calcium level.</p> <p><b>Side effects:</b> Hypotension /Hyperglycemia /Hypokalemia / tachycardia</p>
<p><b>Nifedipine</b> (calcium channel blockers)</p>	<p><b>MOA:</b> Markedly inhibits the amplitude of spontaneous and oxytocin-induced contractions</p> <p><b>side effects:</b> Flushing /Constipation/Ankle edema / hypotension / tachycardia</p>
<p><b>Atosiban</b></p>	<p>Compete with oxytocin at its receptors on the uterus. Given IV</p>



# Drugs of Reproductive Block

## Teratogens & Drugs of Abuse

**Teratogenesis** :Occurrence of congenital defects of the fetus.

Drug (Teratogen)	Teratogenic effect
Thalidomide	Phocomelia
Phenytoin	-Fetal Hydantoin Syndrome <u>-Oral Clefts (cleft lip and palate)</u>
Valproic acid	-Neural tube defect (spina bifida)
Antibiotics (Tetracycline)	-Altered growth of teeth and bones -Permanent teeth staining
Anticoagulants (Warfarin)	-Hypoplasia of nasal bridge -CNS malformation
Corticosteroids	<u>Cleft lip and Palate</u>
Hormones: Estrogens Androgens Diethylstilbestrol	Serious genital malformation
Lithium	Ebstein's anomaly: Cardiovascular anomalies mainly valvular heart defect
ACE inhibitor: Captopril Enalapril	-disrupt the fetal renin-angiotensin system -Fetal hypotension, Hypoperfusion → Growth retardation

## Drugs of Abuse in Pregnancy

Alcohol	-Contraindicated during <b>all trimesters</b> of pregnancy - <b>Cause Fetal Alcohol Syndrome (FAS)</b> : Microcephaly , Low birth weight , <b>CNS abnormalities</b> (attention deficits, intellectual disability, mental retardation)
Cocaine	-Inhibits reuptake of sympathomimetics -It decreases blood flow to uterus and fetal oxygenation (hypoxia) <u>-increases uterine contractility (Abruptio placentae)</u> <b>Characteristics</b> : microcephaly, growth and mental retardation, abruptio placentae
Tobacco	No evidence it causes birth defects <b>BUT</b> , Tobacco can increase risk of: Low blood flow to placenta , Fetal hypoxia ,Retarded fetal growth ,Low birth weight, Increased spontaneous abortion → preterm labor (perinatal mortality)

Cocaine and tobacco have more of a peripheral effect

# Teratogens & Drugs of Abuse cont.

## Adverse Effects of Drugs During Second and Third Trimesters:

Drug	Adverse effect
<b>Antibiotics (Tetracycline)</b>	-Impaired teeth & bone development -Yellow-brown discoloration of teeth Same as 1st trimester
<b>Aminoglycosides</b> (streptomycin, kanamycin)	-Ototoxicity "8th cranial nerve damage"
<b>Chloramphenicol</b>	-Gray baby syndrome
<b>Corticosteroids</b>	-Adrenal atrophy - growth retardation Different from 1st trimester
<b>Propranolol</b>	-Bradycardia, neonatal hypoglycemia, placental insufficiency, reduced uterine blood flow → fetal distress
<b>NSAIDs</b> aspirin-indomethacin	-Prostaglandin synthesis inhibitors: -Constriction of ductus arteriosus (close prematurely) -Pulmonary hypertension in newborns -Increase in gestation time -If taken near delivery: prolong labor, neonatal bleeding, risk of postpartum hemorrhage
<b>Benzodiazepines</b> Diazepam	Chronic use → neonatal dependence and withdrawal symptoms
<b>ACE inhibitor:</b>	-Renal damage
<b>CNS depressant</b> e.g. diazepam, morphine	-Interference with suckling -Respiratory depression -Reduced blood flow → fetal distress
<b>Sulfonamides</b>	Can displace bilirubin from albumin (neonatal hyperbilirubinemia, jaundice)

## Drugs in Pregnancy

Class	Probably Safe	C.I
<b>Hypertension</b>	-α- methyl dopa -Labetalol	-ACE inhibitors -Angiotensin II receptor blockers -Thiazide diuretics -Propranolol -Calcium channel injection blockers in mild hypertension
	<b>Emergency :Hydralazine ,Labetalol</b>	
<b>Coagulation Disorders</b>	<b>Heparin</b> <b>Protamine sulphate</b> As antidote for neutralization	<b>Warfarin</b> is contraindicated in ALL trimesters - Cross placenta membrane - 1st trimester: teratogenicity - <u>2nd &amp; 3rd: risk of bleeding</u>

# Teratogens & Drugs of Abuse cont.

## Drugs in Pregnancy cont.

Class	Probably Safe	C.I
<b>Antibiotics</b>	<p><b>-Penicillins</b> (ampicillin, amoxicillin)</p> <p><b>-Cephalosporins</b></p> <p><b>-Macrolides</b> (erythromycin, azithromycin) <u>as alternative in penicillin sensitivity.</u></p>	<p><b>-Aminoglycosides:</b> ototoxicity</p> <p><b>-Tetracyclines:</b> teeth and bone deformity</p> <p><b>-Sulfonamides:</b> neonatal jaundice-kernicterus</p> <p><b>-Chloramphenicol:</b> gray baby syndrome</p> <p><b>-Quinolones as ciprofloxacin:</b> bone and cartilage damage (arthropathy)</p>
<b>Antithyroid</b>	<b>-Propylthiouracil</b>	<p><b>-Methylthiouracil</b> (Methimazole)</p> <p><b>-Carbimazole</b></p> <p><b>-Radioactive Iodine</b> (I131)</p> <p>(Risk of congenital goiter and hypothyroidism)</p>
<b>Antidiabetics</b>	<b>Insulin</b>	avoids oral antidiabetics
<b>Analgesics</b>	<b>Acetaminophen</b>	-
<b>Anticonvulsants</b>	<b>Folic acid</b> supplementation prevents neural tube defects in women receiving <b>AEDs</b>	<p>-All <b>antiepileptics</b> have potential to cause malformations</p> <p><b>-Avoid valproic acid</b> (highly teratogenic)</p>

1. A woman on warfarin is trying to get pregnant what would you do?  
 ✓ Switch **warfarin** to **heparin**

# Drugs of Reproductive Block

## Hormone Replacement Therapy

Drug

Key Point

C.I

### Hormone replacement therapy

-Given for short term: never exceed 5 years to control menopausal symptoms without allowing ample time for malignant transition that might be induced by **estrogen**.

**Estrogen:**  
-Estradiol  
-Conjugated estrogens  
-Esterified estrogens

**M.O.A:** binds with its receptors; ER $\alpha$  (female hormonal functions) in endometrium, breast, ovaries and **hypothalamus** & ER $\beta$  (other hormonal functions) bone, **heart**, lungs.. etc.  
-Not given **unless** presence of symptoms; alone **only** after hysterectomy, or combined with progestin as HRT (**never exceed 5 yrs administration**).  
-**Uses: 1- In Menopause:** Improves urethral & urinary symptoms, Improves vaginal dryness, **improves cognitive function**, Increases bone density & Progestins act synergistic by blocking corticosteroid induced bone resorption (Decrease incidence of hip fracture) , Protects CVS **BUT HRT increases CVs problems (long term)** & Improves insulin resistance. 2- Contraception. 3- primary ovarian failure. 4- Amenorrhea & Hirsutism caused by excess androgens.  
-**ADRs: Irregular vaginal bleeding, Breast tenderness**, Vaginal discharge, Fluid retention, Spotting or darkening of skin.

-Undiagnosed vaginal bleeding.  
-Severe liver disease.  
-Thromboembolic manifestations.  
-Cancer.  
**Drug interdictions:**  
If given with  
1-SERMs  $\rightarrow$  additive side effects for both drugs.  
2-Aromatase inhibitors  $\rightarrow$  decrease efficacy.  
3-Corticosteroids increase side effects.

**Progestins**

-Synthetic progestins that have effects similar to progesterone but are **not degraded by GIT**.  
-**Uses: 1**  
- **In Menopause:** given in **combination with estrogen (Protects against possibility of estrogen induced endometrial cancer)**, Progesterone (**natural**) protects against breast cancer, Counteract osteoporosis, directly +ve osteoblasts. 2-Contraception (estradiol + progesterone ). 3-Dysmenorrhea. 4-Menopausal symptoms.  
-**How Progestins protect against possibility of estrogen induced endometrial cancer?** Estrogen promotes cell growth, if unopposed endometrial cell lining can show (atypical hyperplasia), progesterone then matures endometrial lining (become differentiated) and promotes apoptosis (natural death of cells) of atypical cells.  
-**Progesterone (natural)** protects against breast cancer development by anti-inflammatory & apoptosis mechanisms, but this effect is not as clear with synthetic progestins.  
-**Administration: IU; as Levonorgestrel or Progestasert.**  
-**ADRs: Hirsutism , masculinization (Not with new preparations)**, Mood changes, abdominal pain or bloating & Headache.

**SERMs:**  
Tamoxifen  
Raloxifene

-An **ideal SERM** use as HRT should be **agonistic** in brain, bone, CV system, vagina & urinary system **but antagonistic in breast & uterus**.  
-**Not ideal: 1-Tamoxifen: antagonist in breast and partial agonist in bone and endometrium. 2-Raloxifene: antagonist in breast and uterus and agonist in bone.**  
-**Tamoxifen:** increases risk of venous thrombosis, precipitate vaginal atrophy & **hot flushes**.  
-**Raloxifene: no effect on hot flushes (very effective preventing vertebral bone fracture** & CVs problems less compared to Estrogen) for osteoporosis use of bisphosphonate is better than SERMs.  
\* raloxifene is better than tamoxifen.

# Hormone Replacement Therapy cont.

Drug	Key Point	C.I
<b>Phytoestrogens</b>	<p>-<b>MOA:</b> 1-mimic action of estrogen on ER-<math>\beta</math> →alleviate symptoms related to hot flushes, mood swings, cognitive functions &amp; possess CVS protective actions.                      2-block actions mediated by ER<math>\alpha</math> in some target tissues lead to lower risks of developing endometrial &amp; breast cancer.</p> <p>-<b>Avoid in estrogen dependent breast cancer.</b></p>	-
<p><b>Androgens:</b>                      Testosterone                      Tibolone</p>	<p>-Testosterone is responsible for sexual arousal in females.                      -<b>Uses of Testosterone:</b> 1-sole therapy to menopausal women in whom their menopausal symptoms are <b>focused on lack of sexual arousal.</b> 2-adjutant to combined estrogen &amp; progesterin if all other menopausal symptom exist.</p>	-
<b>Non-hormonal agents (used in management of menopausal symptoms)</b>		
<b>Fluoxetine (SSRI)</b>	- <b>Uses:</b> reduces vasomotor symptoms.	
<b>Clonidine</b>	<p>-<b>MOA:</b> centrally acting antihypertensive, alpha 2 agonist.                      -<b>Uses:</b> helps vasomotor symptoms.</p>	
<b>Gabapentin (anticonvulsant)</b>	- <b>Uses:</b> reduces severity and frequency of hot flushes.	
<b>Physical activity:</b> exercise, smoking cessation and relaxation of mind will improve symptoms of menopause (e.g. hot flushes)		

# Drugs of Reproductive Block

## Drugs Affecting Breast Milk and Lactation

### Drugs & Lactation

#### 1. Drugs contraindicated during lactation

Drug	C.I
<b>Anticancer drugs</b> (doxorubicin, cyclophosphamide, methotrexate)	Cytotoxicity & neutropenia
<b>Alcohol &amp; Lithium</b>	They have high milk to plasma rate.
<b>Chloramphenicol</b>	Bone marrow suppression
<b>Potassium iodide</b>	Thyroid effect
<b>Ergotamine</b>	Convulsions in infants
<b>Tobacco smoke</b>	<ul style="list-style-type: none"> <li>○ restlessness for the baby</li> <li>○ decreased milk production</li> <li>○ increase respiratory and ear infections.</li> </ul>

#### Other drugs:

**Radiopharmaceuticals** (radioactive iodine), **CNS acting drugs** (amphetamine, heroin, cocaine), **Immunosuppressants** (cyclosporine), **Atenolol**.

#### 2. Drugs that can suppress lactation

Drug	Key Point
<b>Levodopa</b>	M.O.A.: dopamine precursor
<b>Bromocriptine</b>	M.O.A.: dopamine agonist

#### Other drugs:

estrogen, oral contraceptives that contain high-dose of estrogen and progestin, androgens, thiazide diuretics

#### 3. Drugs that can augment lactation

Dopamine antagonists: they stimulate prolactin secretion → galactorrhea

Drug	Metoclopramide	Domperidone	Haloperidol	Methyldopa	Theophylline
<b>Key Point</b>	antiemetic	antiemetic	antipsychotic	antihypertensive	used in asthma

### Antibiotics

Drug	Key Point
<b>Penicillins</b> (Ampicillin, amoxicillin)	<ul style="list-style-type: none"> <li>✓ No significant adverse effect</li> </ul> <b>ADRs:</b> allergic reactions, diarrhea

<b>Cephalosporins</b>	✓ No significant adverse effect <b>ADRs:</b> Alterations to infant bowel flora
<b>Macrolides</b> (erythromycin, clarithromycin)	
<b>Quinolones</b>	X <b>Should be avoided</b> <b>ADRs:</b> Theoretical risk of arthropathies
<b>Chloramphenicol</b>	X <b>Should be avoided</b> <b>ADRs:</b> Gray baby” syndrome
<b>Tetracyclines</b>	Absorption by the baby is probably prevented by chelation with milk calcium. X <b>Avoid</b> due to possible risk of <b>teeth discoloration</b> .
<b>Sulfonamides</b> (co-trimoxazole)	<b>ADRs:</b> hyperbilirubinemia → <b>neonatal jaundice</b> X <b>Should be avoided</b> in premature infants or infants with G6PD deficiency

Group	Drugs that can be used	Drugs that cannot be used
<b>Sedatives / Hypnotics</b>	- Single use of <b>benzodiazepines</b> , diazepam, lorazepam	- Prolonged use of <b>benzodiazepines</b> , diazepam, lorazepam. - <b>Barbiturates</b> (phenobarbitone)
<b>Antidiabetics</b>	- <b>Insulin</b> - <b>Oral antidiabetics (NOT in pregnancy)</b>	- <b>Metformin</b> [avoid due to lactic acidosis]
<b>Analgesics</b>	- Paracetamol - Ibuprofen	- <b>Aspirin</b> [ <b>reye’s syndrome</b> ]
<b>Antithyroids</b>	- Propylthiouracil	- potassium iodide - carbimazole, methimazole
<b>Anticoagulant</b>	- Heparin - <b>Warfarin</b>	-
<b>Anticonvulsants</b>	- <u>carbamazepine</u> - phenytoin	- Lamotrigine - valproic acid
<b>Antihistamines</b>	- non-sedating (loratadine)	- sedating
<b>Oral Contraceptives</b>	- progestin only pills - <u>mini pills</u>	- <b>Estrogen</b>
<b>Antidepressants</b>	- Paroxetine	-
<b>Antiasthmatics</b>	- Inhaled corticosteroids - prednisone	-

# Drugs of Reproductive Block

## Treatment of Sexually Transmitted Disease

Drug	Key Point	C.I
<b>TREATMENT OF SYPHILIS</b>		
<b>Penicillins (<math>\beta</math>-Lactam Antibiotics):</b> -Benzylpenicillin -Procaine -penicillinG -Benzathine -penicillinG	- <b>MOA:</b> Inhibits bacterial cell wall synthesis (Bactericidal). - <b>Use:</b> 1st choice in treating syphilis, Benzathine penicillin: <u>I.M</u> , the best one given due to its long action ( given once every 3- 4 weeks) - <b>ADRS:</b> Hypersensitivity, Convulsions, Super infections.	-renal failure/disease
<b>Tetracyclines</b> (Doxycycline)	- <b>MOA:</b> Inhibit bacterial protein synthesis by reversibly binding to <u>30S</u> bacterial ribosomal subunits (Bacteriostatic). - <b>ADRS:</b> Brown discoloration of teeth in children, Deformity or growth inhibition of bones in children, Hepatic toxicity, phototoxicity.	-Pregnancy. -Breastfeeding. -Children (below 10yrs.).
<b>Cephalosporins</b> (Cefixime, Ceftriaxone)	- <b>MOA:</b> Inhibit bacterial cell wall synthesis (Bactericidal) - <b>Cefixime</b> : more effective against gram negative bacteria. - <b>P.K</b> : <u>ceftriaxone is eliminated via biliary excretion.</u> - <b>ADRS</b> : Hypersensitivity reactions, Thrombophlebitis, Superinfections, Diarrhea.	-
<b>Macrolides</b> (Azithromycin)	- <b>MOA:</b> inhibits bacterial protein synthesis by binding to bacterial <u>50S</u> ribosomal subunits. - <b>P.K</b> : <u>Acid stable</u> , should be given 1 hour before or 2 hours after meals, <u>No effect on cytochrome P450</u> , penetrates most tissues except CSF	-

### WHO guideline for the Treatment of Syphilis:

**Pregnant** :• Benzathine penicillin G or Procaine penicillin G, Erythromycin or Ceftriaxone or Azithromycin

**late stages**:• Benzathine penicillin G or Procaine penicillin G, Doxycycline (If penicillin is not allowed due to allergy)

**congenital syphilis (infant)**: Aqueous benzylpenicillin i.v or procaine penicillin i.m

## Uncomplicated gonorrheal infections

<b>Cephalosporins</b>	<b>Use:</b> 1st line treatment Typically given in combination with a single dose of azithromycin or doxycycline.	-
<b>Fluoroquinolones</b> (Ciprofloxacin)	- <b>MOA:</b> Inhibit DNA synthesis by inhibiting DNA gyrase enzyme required for DNA supercoiling (Bactericidal). - <b>ADRS:</b> arthropathy, phototoxicity.	-Pregnancy -nursing mothers, -children under 18 years.
<b>Spectinomycin</b>	- <b>MOA:</b> Inhibits protein synthesis by binding to <u>30S</u> ribosomal subunits. - <b>Use:</b> gonorrheal infection with resistance to Cephalosporins + Fluoroquinolones. Given <u>I.M</u> - <b>ADRS:</b> Nephrotoxicity (not common).	-



# Treatment of Sexually Transmitted Disease cont.

Drug	Key Point	C.I
<b>Complicated gonorrhoeal infections (conjunctivitis in newborn)</b>		
<b>Silver nitrate</b>	-It has germicidal effects. - <b>Use</b> :With conjunctivitis in newborn Put into conjunctival sac once immediately after birth (no later than 1 h after birth)	-
<b>Erythromycin</b>	-prevention of corneal & conjunctival infections. - <b>Use</b> : With conjunctivitis in newborn, put into conjunctival sac once immediately after birth (no later than 1 h after birth)	-