Male infertility Drugs

Drug	Type	MOA	Administration	Side Effect	Contraindications
1.Non-hormonal: **a.Testesterone**	**Derived from Testosterone:** Esters proprionate, enanthate, cypionate or derivatives as Fluoxymesterone, Methyltestosterone, Danazol. **Derived from DHT (synthetic)**: **Mesterolone** (is not hepatotoxic). **Interactions:** With corticosteroids → leads to oedema (effect of testosterone & cortisol). With warfarin → bleeding. With insulin or oral hypoglycemic → hypoglycemia. With propranolol → ↓it's efficacy	Binds to Sex Hormone Binding Globulin [SHBG]: t1/2 = 10 –20 min (short). Inactivated in the liver. 90% of metabolites excreted in urine. Synthetic androgens: less rapidly metabolized & some are excreted unchanged in urine. **Mesterolone**: Used for the treatment of secondary hypogonadism & ↓ lvls of testosterone more safely. Cause: Not hepatotoxic. Not aromatized into estrogens → no –ve of GnRHs → encourages natural testosterone production & ↓its binding to SHBG →spermatogenesis is enhanced.	**1. Testosterone :** a. Ineffective orally. b. Given : I.M or S.C. c. Also skin patches & gels. **2. Synthetic** androgens **a. Derived from Testosterone** i. Esters; proprionate, enanthate, cypionate: I.M every 2-3 weeks ii. Or derivatives as Fluoxymesterone, Methyltestosterone, Danazol: **Orally** , daily **b. Derived from DHT:** Mesterolone (is not hepatotoxic), **Orally** , daily.	I. Behavioral changes a. physiologic dependence b. aggressiveness c. psychotic symptoms 2. Azoospermia (sperms are absent in the ejaculate) & 2ndry GnRH suppression (if taken > 6wks). a. This happens because of chronic use of testosterone without proper admission , the constant release will suppress the release of LH/FSH permanently 3. Alteration in serum lipid profile: ↓HDL & ↑LDL. 4. Salt & water retention → ↑ weight. 5. Hepatic dysfunction; a. ↑AST levels,↑alkaline phosphatase, b. ↑bilirubin & cholestatic jaundice. 6. Masculinization. 7. Acne. 8. Polycythemia.	Male patients with cancer of breast or prostate (androgens are a mediator of prostatic cancer). Severe renal & cardiac disease predispose to edema. Because testosterone has sodium & water retention effects it could ↑ the load on the heart & alter the rennin angiotensin system in the kidney. Psychiatric disorders. Hypercoagulable states. Polycythemia. Pregnant women.
b.GnRH	Used in hypothalamic dysfunction: Given as Pulsatile GnRH therapy (4-8 ug subcut every 2 hours) using a portable pump. Exogenous excess of GnRH→ down-regulation of pituitary GnRH receptors & ↓ LH responsiveness. When used for long periods it causes desensitization of the receptors.	**Side effect:** Headache, depression, generalized weakness, pain & gynecomastia. osteoporosis, neurological symptoms.	**c.Gonadotropines**	Used in secondary hypogonadism to increase spermatogenesis. GnHs replacement must be combined; hCG (3 x 2000 U/w. IM.→2 ms.) followed by hCG + hMG (3x 75 to 3 x 150 U /w. IM. →6 -12 ms).	ADRs; Headache, local swelling (injection site), nausea, flushing, depression, gynecomastia, precocious puberty, anaphylactic shock.

d.Anti-Estrogens	1. SERM's: a. Tamoxifen b. Clomiphene 2. Aromatase inhibitors: a. Anastrozole b. They block the conversion of testosterone to estrogen in the hypothalamus.	Used in: inducing spermatogenesis in oligozoospermia. Given daily for a period of 1-6 months. Best to improve sperm count & motility with good pregnancy rates.	**2.Non-Hormonal therapy**	1. Antioxidants: protect sperm from oxidative damage. 2. Kallikrien: Has proteolytic activity, cleaving kininogen to kinins → important for sperm motility **(improve asthenospermia).** 3. Folic acid : Plays a role in RNA and DNA synthesis during spermatogenesis & has antioxidant properties. 4. Zinc: Plays an important role in testicular development, spermatogenesis & sperm motility. 5. L-CARNITINE: Is highly concentrated in the epididymis & are important for sperm metabolism & maturation.	Mesterolone & Aromatase inhibitors Have less chance of feminization than.