

FARMAKOTERAPI

OBAT PADA SISTEM REPRODUKSI

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Pokok Bahasan

- **Obat Hormonal : Estrogen & Progesteron**
(KB, Gangguan Haid, Penunda menstruasi)
 - **Obat Ibu Hamil**
(obat teratogenik & obat yang aman untuk Ibu hamil, obat Ibu Melahirkan)
 - **Obat Ibu Menyusui**

Obat Hormonal Reproduksi

Estrogen & Progesteron

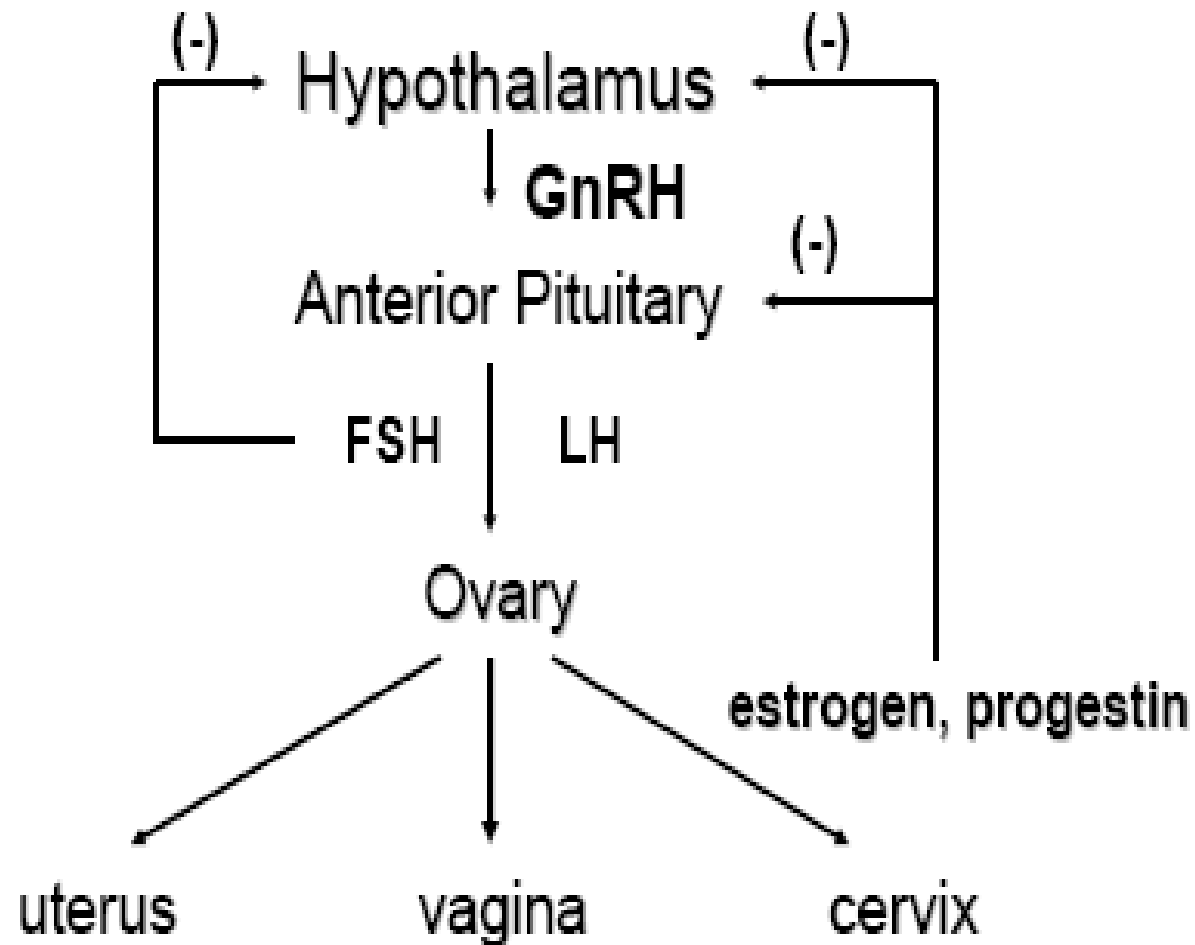


ESTROGEN

- Estrogen endogen : estradiol (terbanyak), estron, dan estriol.
 - ❖ Estradiol : disekresi o/ ovarium
 - ❖ Estrone : hsl konversi estradiol & androstenedion di perifer
 - ❖ Estriol : hsl metabolit dr estron
- Potensi estradiol > estron > estriol
- Tempat sintesa : ovarium (90%), hepar, korteks adrenal, lemak, plasenta, testis

Regulasi Sintesa Estrogen :

Hypothalamic-pituitary-ovarian axis



Efek Fisiologi Estrogen

■ Sistem Reproduksi

- pertumbuhan & perkembangan seks primer : tuba falopii, uterus, serviks, dan vagina
- sekret kelenjar serviks & vagina : lebih >, lebih cair, proliferasi kelenjar & pembuluh darah endometrium
- Pertumbuhan & perkembangan seks sekunder : mammae, penimbunan lemak, kulit halus, pertumbuhan rambut, hiperpigmentasi areola dan genetalia

Efek Fisiologi Estrogen

■ **Metabolisme :**

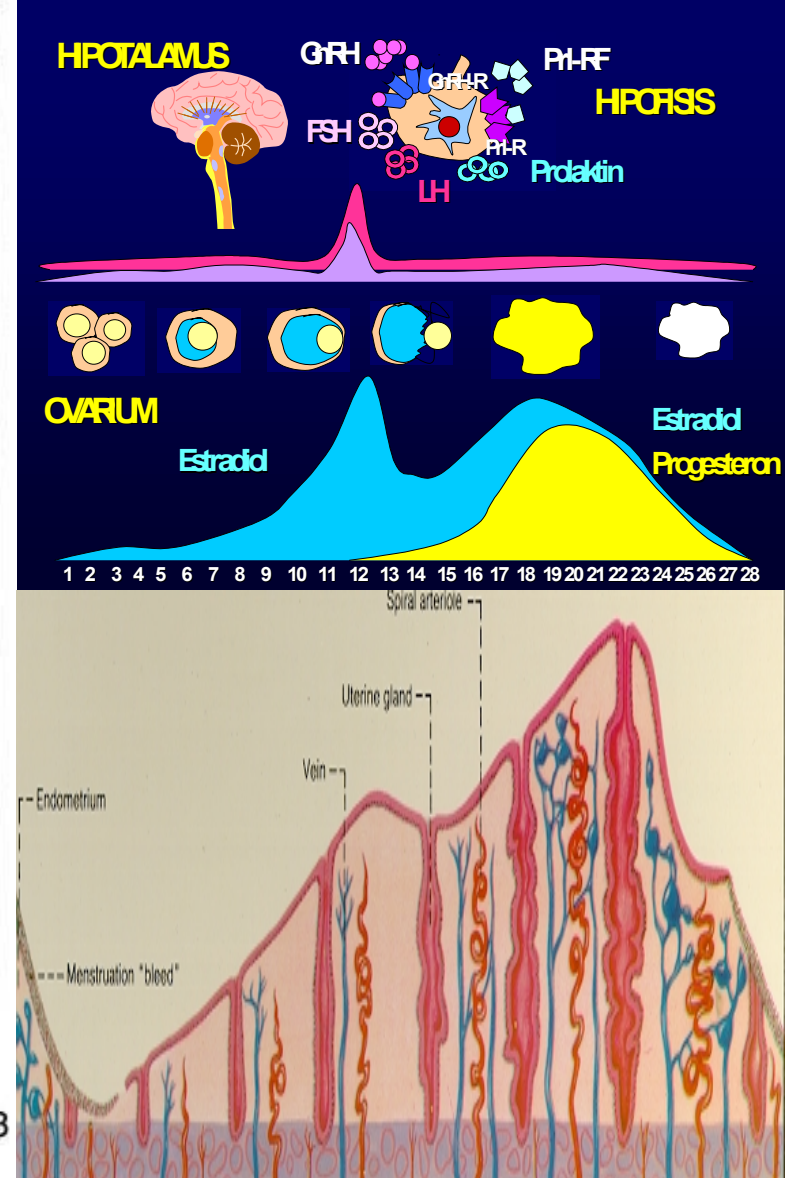
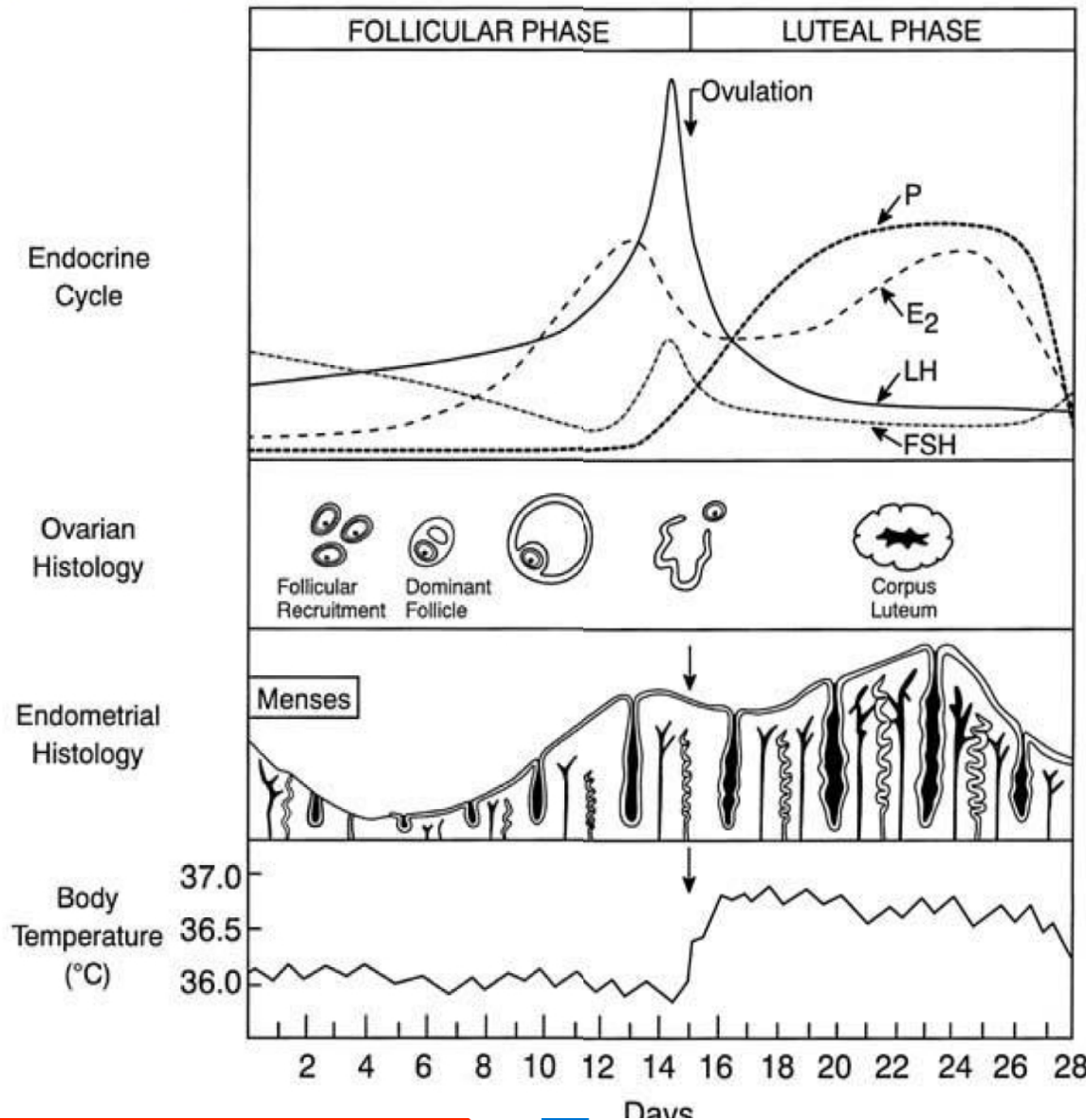
- ✓ Protein : anabolisme
- ✓ Lemak : HDL , LDL , TG , kolesterol total
- ✓ Tulang : menghambat proses resorpsi tulang
- ✓ endothel vaskuler : NO dan prostasiklin vasodilatasi
- ✓ Retensi air dan garam (mel. Angiotensin II) edema → rasa kencang pd mammae

■ **Siklus menstruasi**

FASE FOLIKULER

- FSH meningkat, Folikel berkembang dan sebagian mematangkan diri
- Estrogen meningkat → endometrium proliferasi
- Estrogen meningkat → umpan balik negatif, yaitu menekan FSH
- Folikel tetap berkembang meski FSH menurun
- Estrogen meningkat → umpan balik positif pada LH, yaitu lonjakan LH (LH surge) → ovulasi

Reproductive hormonal & endometrial patterns



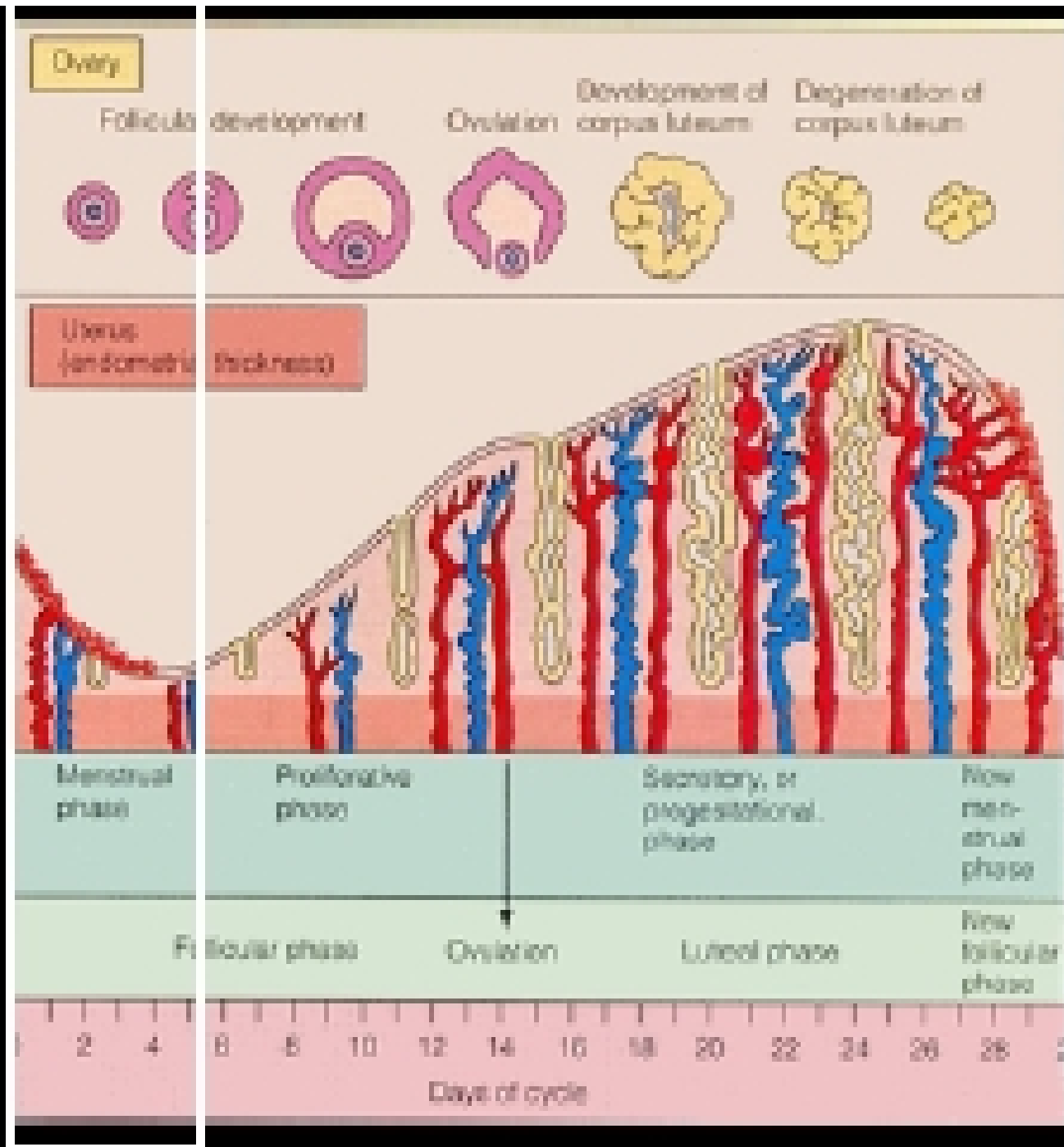
Menstrual phase

estrogens ↓,
progesterone ↓,
prostaglandins ↑

necrosis of the
endometrial lining

uterus
contractions.
(→ dysmenorrhea)

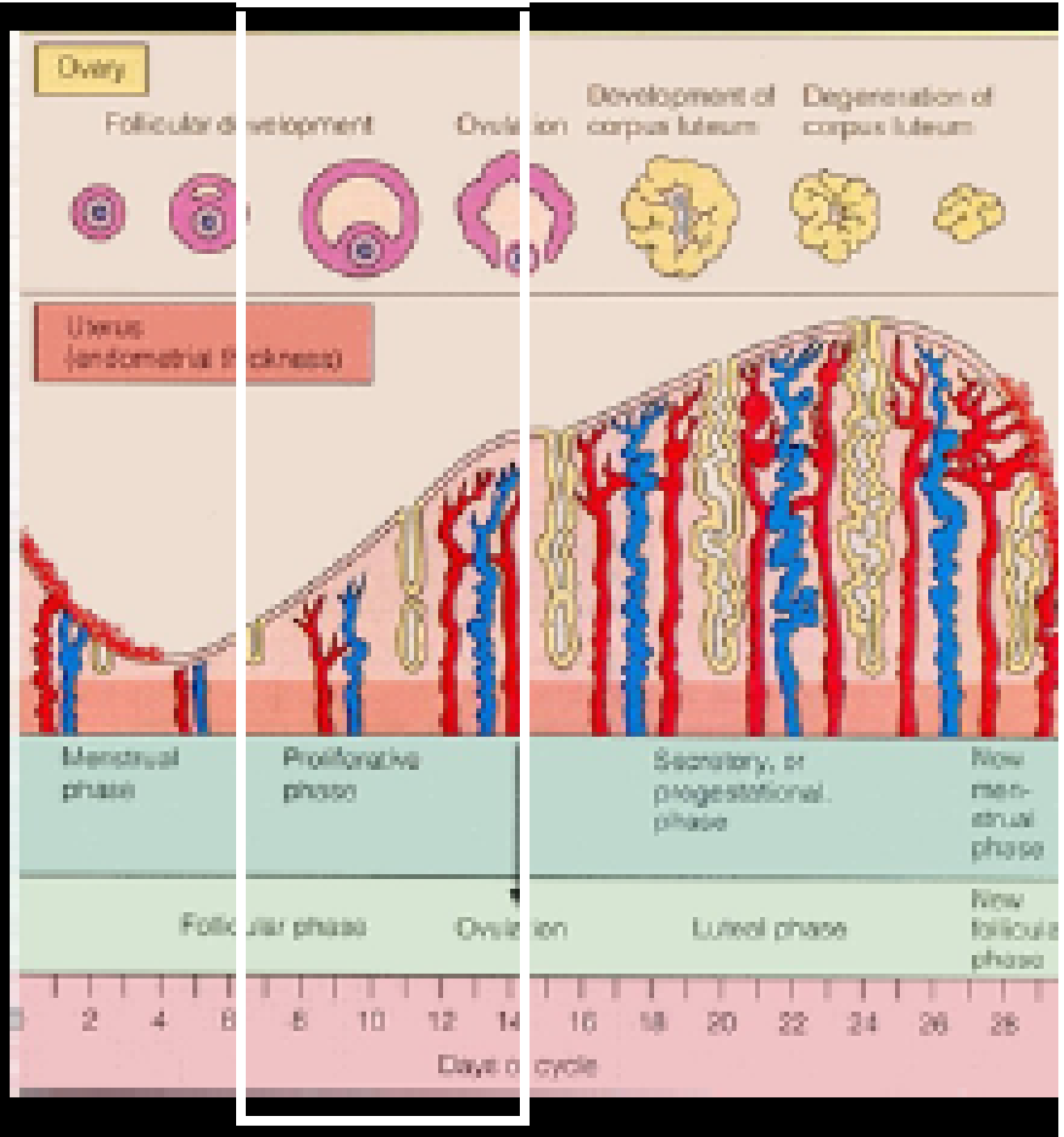
After 5 days:
arterioles constrict
again → bleeding
stops



Proliferative phase

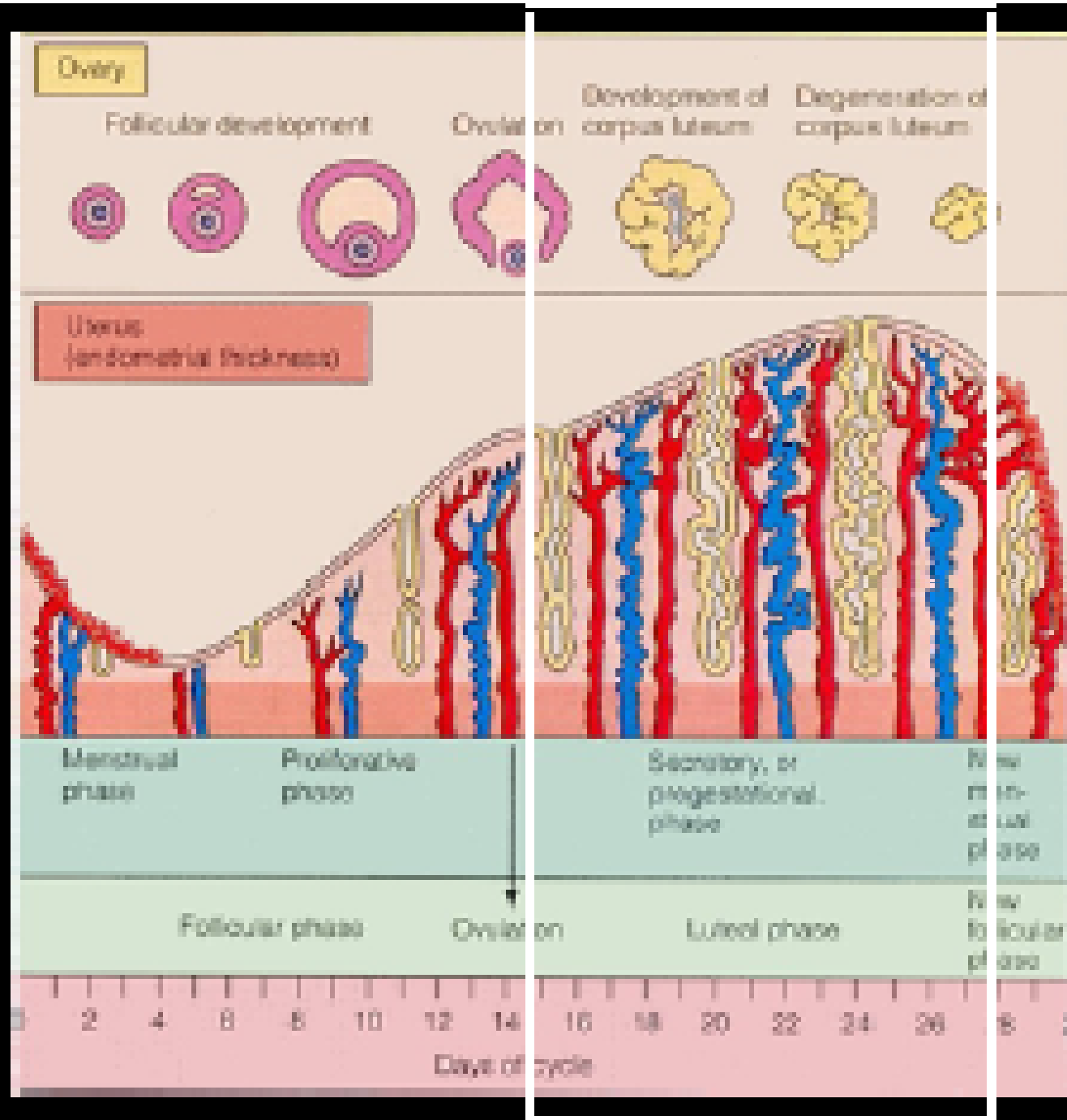
regeneration of
endometrial lining
in response to
estrogens:

- endometrium regenerates
- uterine glands enlarge → length ↑
→ become coiled
- blood vessels grow → arterioles become coiled → blood supply ↑
- progesterone receptors synthesized

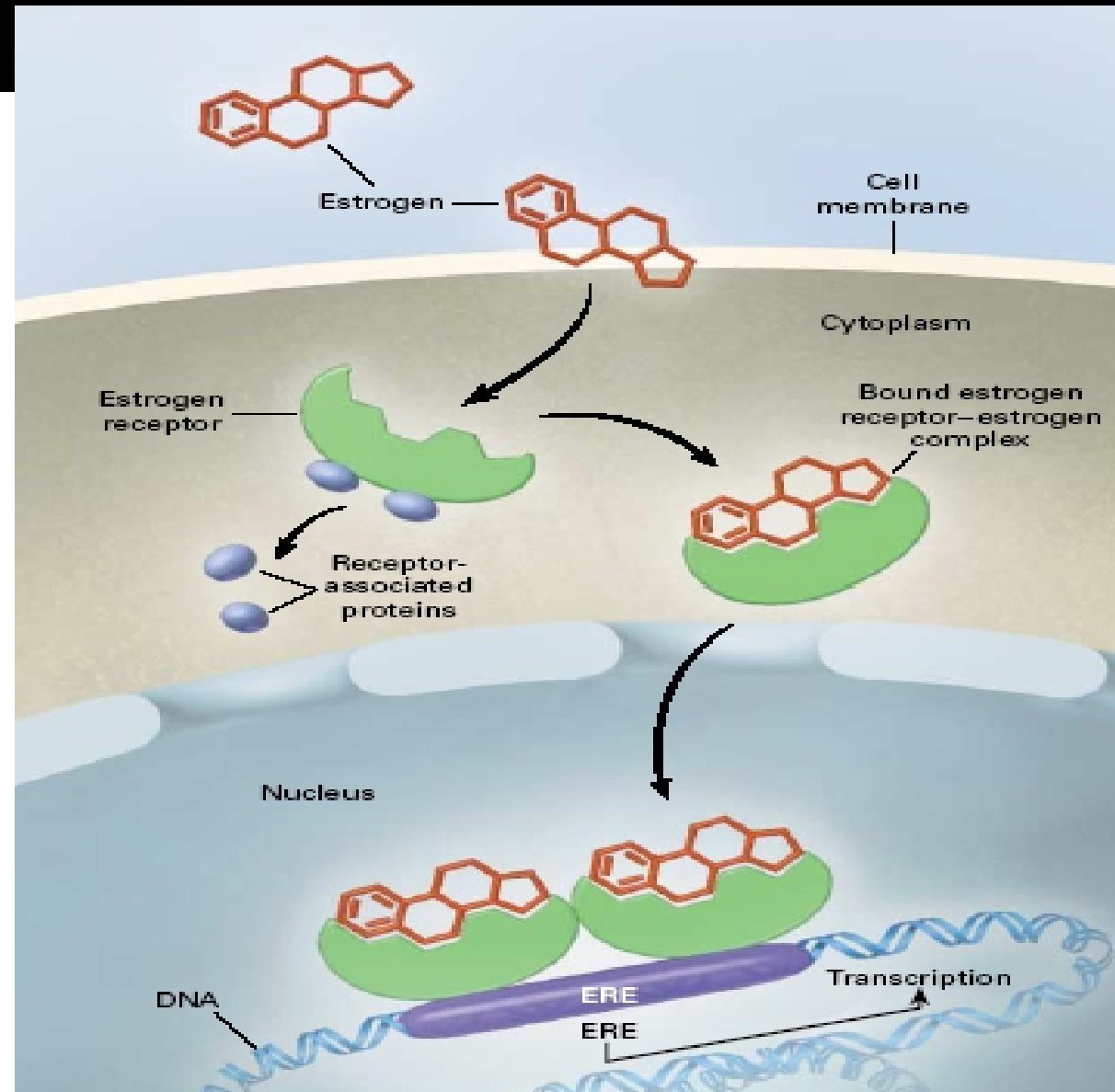


Secretory phase

In response to estrogens and (mainly) progesterone → changes in the endometrium to prepare for possible implantation of the blastocyst
Endometrium: Increase in vascularization glands become more coiled, secretory activity ↑↑ → large amounts of nutrients secreted (glycogen↑↑)



Mekanisme Kerja Estrogen



Farmakokinetik Estrogen

- **Absorpsi :**
 - Mudah diabsorpsi lewat sal. cerna, mukosa atau kulit bisa peroral, parenteral, trans dermal, topikal.
 - Tidak larut dalam air
 - Absorpsi cepat, metabolisme cepat masa kerja singkat
- **Distribusi :**
 - sebagian besar terikat kuat dg protein (SHBG)
 - mengalami sirkulasi enterohepatik
- **Metabolisme :** di hepar, estradiol → estron → estriol. Konjugasi dg asam sulfat atau glukoronat → konjugat sebagian alami enterohepatic cycle. (bakt usus → enz hidrolitik → ubah konjugat menj hormon bebas lg → diabsorpsi lg o/ usus → sirkulasi). Konjugat yg tdk alami enterohepatic cyc diekskresi lwt faeces
- **Ekskresi :** lewat ginjal dalam bentuk terkonjugasi dg asam sulfat atau glukoronat

Estrogen Sintetik

- Estrogen sintetik : **diethylstilbestrol, ethynil estradiol, mestranol**
- **metabolisme lebih lambat** sehingga mempunyai masa kerja lebih panjang dan potensinya lebih besar daripada estrogen alami.
- Larut dalam lemak sehingga dapat disimpan dalam jaringan lemak dan secara **lambat dilepaskan**.

Penggunaan Terapi Estrogen

- **Mengganti produksi estrogen yg kurang**
 - **hipogonadisme primer** (terapi pengganti pada wanita yang mengalami defisiensi estrogen.
 - Terapi hormonal pada **post-menopause** : osteoporosis, gangguan vasomotor, mencegah penyakit kardiovaskuler, vaginitis
- **Menekan produksi estrogen endogen (kontraseptif)**
 - sebagai **kontrasepsi oral** (kombinasi bersama progesterone).
 - sebagai **morning after pill** (DES atau ethinyl estradiol)
- **Mengatasi keadaan / penyakit yang dipengaruhi hormon estrogen**
 - **dismenorrhoe** yang berat (diberikan bersama dengan progesterone)
 - **karsinoma prostat** (DES)
 - **endometriosis** (estrogen & progesterone digunakan untuk mensupresi ovulasi secara jangka panjang sehingga menghasilkan endometrium yang atropi.

EFEK SAMPING TERAPI ESTROGEN

- Abnormal menstrual bleeding
- Retensi cairan
- Mual
- Peningkatan sintesa hormon-binding globulin oleh hepar
- Peningkatan kadar TG
- Peningkatan blood clotting
- Meningkt resiko Ca mammae & uterine

SERMs (Selective Estrogen Receptor Modulators)

- Yaitu senyawa yang mempunyai memiliki aktivitas estrogenik pada jaringan tertentu.
- **Tujuan** : menghasilkan obat yang
 - memberikan efek estrogenik pada jaringan tertentu dimana efek tersebut menguntungkan, mis : tulang, otak, hepar (*Raloksifen* parsial agonis pd tulang tp tdk menstimuli proliferasi endometrium Tx. osteoporosis)
 - tidak berefek atau berefek antagonis pada jaringan seperti mammae dan endometrium efek proliferasi hilang (*Tamoksifen, Toremifene*). Tamoksifen sitrat efek antagonis thd transkripsi gen ttt pada jar. mammae RE di sitoplasma hamb proliferasi sel yg dependent estrogen (Tx. Ca mammae)

ANTIESTROGEN

- Senyawa yang bersifat **antagonis murni** terhadap hampir semua jaringan
- Mekanisme kerja : **kompetitif antagonis thd reseptor estrogen (RE)**
- Mis : **klomifen, ICI 182,780**
 - ✓ Klomifen hambat feedback (-) pd pituitari FSH, LH ovulasi (Tx. Infertilitas)
 - ✓ ICI 182,780 mengikat RE dan , menekan transaktivasi, me degradasi RE tapi melindungi RE dari degradasi hamb proliferasi Ca mammae yang resisten thd tamoksifen.

PROGESTIN

- **Sintesa sekresi** di : ovarium (korpus luteum, fase luteal, stimulasi oleh LH), korteks adrenal, testis, plasenta
- **Efek Fisiologi :**
 - Fase sekresi endometrium, sekret kelenjar endoserviks lbh pekat & jml berkurang penetrasi sperma ke cervix lbh sulit.
 - Hamil (progestin): hambat kontraksi uterus, implantasi, cegah reaksi penolakan thd fetus, mempertahankan kehamilan, proliferasi kelenj asini
 - Menyebabkan withdrawl bleeding ketika kdr P tiba-tiba turun
 - Efek termogenik (suhu tubuh naik 10 F)
- **Farmakokinetik** : mirip estrogen

PROGESTIN SINTETIK

- a. **Derivat progesteron** : medroxyprogesteron acetate (parenteral)
- b. **Derivat testosteron** : norethindrone, norgestrel, ethynodiol diacetate, levonogestrel (peroral)
- Progestin terbaru (efek androgenik minimal) : desogestrel, norgestimate, gestodene
- Efek androgenik progestin : me HDL, me LDL, toleransi glukosa.
- Desogestrel (inaktif), metabolitnya aktif

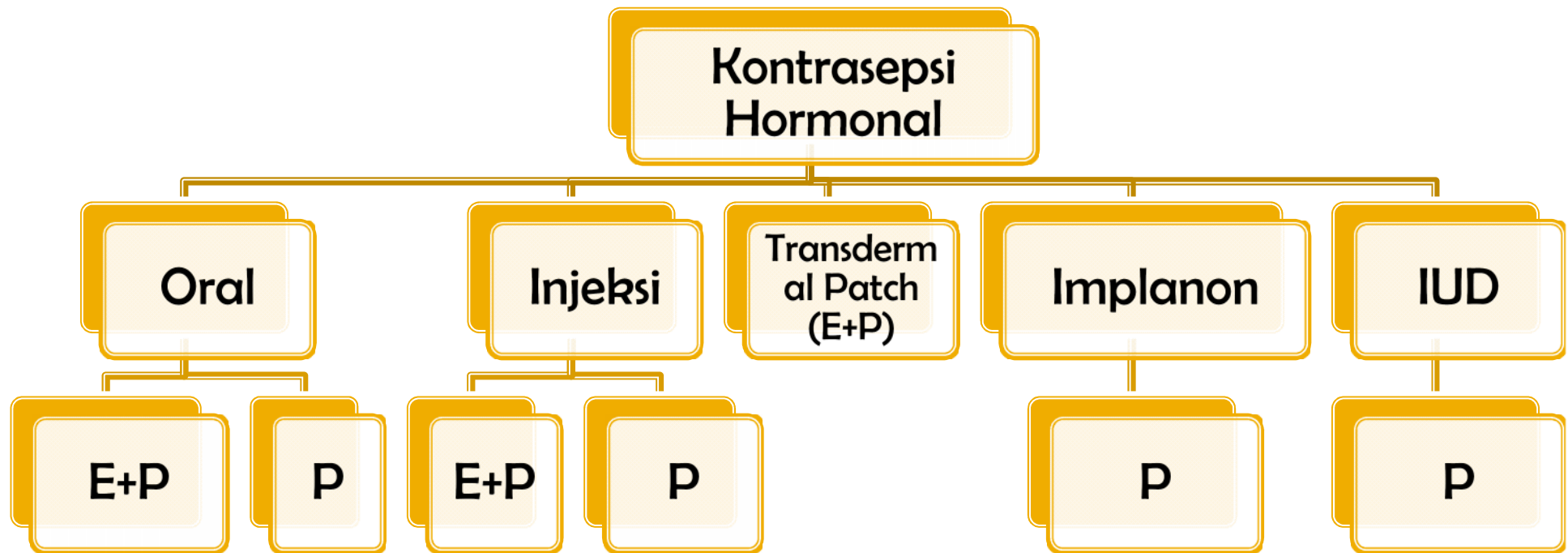
Penggunaan Progestin

- **Kontrasepsi**. Umumnya digunakan dalam bentuk kombinasi dengan estrogen. Progestin bekerja sebagai kontrasepsi dengan cara menurunkan kemungkinan terjadinya konsepsi dan implantasi melalui efeknya pada mucus cervical, uterus dan endometrium serta motilitas uterus. Pada dosis >>> (mis. **depot medroxyprogesterone**) progesterone juga menghambat pelepasan GnRH sehingga kontrasepsi menjadi lebih efektif.
- Mengontrol **perdarahan disfungsional** dari uterus (DUB).
- Terapi **endometriosis** (ectopic endometrial tissue) & **dysmenorrhea**
- **Mengatur haid**
- **Supresi laktasi pada post partum**

EFEK SAMPING PROGESTIN

- BB ↑
- Gangg toleransi glukosa(efek diabetogenik) → me ↑
kebut OAD/insulin
- HDL↓, LDL ↑ → resiko IMA
- Udem→ HT, sakit kepala
- Mual, muntah
- Eksaserbasi acne
- me ↑ fakt koagulasi VII, VIII, IX, X& XII, me ↓ fakt
antikoagulasi prot C, prot S & antitrombin III →
pembekuan drh >>> → resiko trombemboli

Kontasepsi Hormonal



KONTRASEPSI "PROGESTERON ONLY"

Mechanism of action

1-Main mechanism is alteration of Cx mucous

- volume of mucous
- viscosity
- alter its molecular structure
 - ➔ Little or no sperm penetration
 - ➔ Sperm motility is impaired ➔ fertilization

2- Ovulation is suppressed in 60% of the women

3-Endometrial changes ➔ implantation

ORAL PROGESTINS/ PROGESTIN ONLY PILL / MINIPILLS

- Package contains 28 tab
- Started on the 1st day of the menstrual cycle/ or any day if pregnancy excluded
- Must be used at the same time every day within 3 hrs
- A back up contraception must be used for 7 days
- Norethindrone 0.35 mg ➡ micronor
- Must be used continuously ➡ no pill-free interval
- Perfect use failure rate ➡ 0.5%
- Typical use failure rate ➡ 5-10% (It must be taken the same time every day)
- It can be used immediately postpartum with no effect on lactation

PROGESTIN ONLY PILL

Indications

- It can be used for any women seeking reliable, reversible, coitally independent method of contraception in the absence of contraindications
- Women with contraindication to estrogen
- Women > 35 Y who smoke
- Women having migraine headache with neurological symptoms
- Women who have unwanted side-effects of COCP
- Breast-feeding women

Absolute Contraindications

- Pregnancy
- Current breast cancer

Relative Contraindications

- Active viral hepatitis
- Liver tumors

PROGESTIN ONLY PILL

Non contraceptive benefits

- menstrual flow
- 10% amenorrhea
- dysmenorrhea, PMS

Side-effects

- Irregular bleeding
 - ➔ spotting -12% ➔ 1st month
 - 3% ➔ 18 months
 - ➔ 40 % continue to have regular cycles
- Hormonal side-effects
Headache, bloating, acne, breast tenderness

PROGESTIN ONLY PILL (POP)

Risks

- Not associated with any major morbidity
- No risk of VTE, stroke or MI

Myths & misconception

- POP hanya dapat digunakan oleh ibu yg menyusui
Fakta ➔ dapat digunakan o/ stp wanita yg menginginkan metode kontrasepsi yg reversibel
- POP bukanlah metode kontrasepsi yang efektif
Fakta ➔ Ketika digunakan sec benar & aman, efektif dengan tingkat kegagalan hanya 0,5%

POP TROUBLESHOOTING

1-Irregular bleeding

- A common side effect
- Pregnancy, infection & genital pathology must be ruled out

Rx options

- Non steroidal anti-inflammatory for 10 days
- Switching to COCP
- Adding a short course of estrogen
 - ➔ 0.625 mg conjugated equine estrogen (premarine) for 28 days
 - ➔ 1-2 mg micronized 17 β -estradiole—28 days
 - ➔ Transdermal 50-100 μ g 17 β -estradiole patch – 25 days
- Antiprogestinic agents ➔ mifepristone

POP TROUBLESHOOTING

2-Missed pill

- Minum segera begitu ingat, pil berikutnya diminum sesuai waktunya.
- Jika lupa > 3 jam ➡ gunakan back up kontrasepsi lain selama 48 jam
- Jika lupa 2 /lebih pil ➡ **minum** 2 pil / hari selama 2 hari + back up kontrasepsi lain selama 48 jam

3- Drug interactions ➡ anticonvulsants may effectiveness of POP

KONTRASEPSI KOMBINASI

Mechanism of action

- Supresi sekresi GnRH ➔ hambatan ovulasi (mekanisme utama)
- Atrofi endometrium ➔ implantasi terhambat
- Lendir Cx kental ➔ hambat transportasi sperma
- Kemungkinan berefek pada sekresi & peristaltik tuba fallopi ➔ mengganggu transportasi ovum & sperma

KONTRASEPSI ORAL KOMBINASI

- Estrogen ➔ 20-35µg/ day
 - Two types of estrogens are used:
 - ethinyl estradiole
 - mestranol. Mestranol is converted in the body to ethinyl estradiole
 - Used for 3 wks with one wk gap when menstruation occurs
- Several progestins of varying potency are used in the combined OCP

Types of progestins in C OCP

- Estrane ➔ Norethindrone, ethynodiol diacetate
- Gonane ➔ Levonorgestrel, desogestrel, norgestimate (gonans more potent)

Newer Progessteron ➔ desogestril & norgestimate have little or no androgenic activity

KONTRASEPSI ORAL KOMBINASI

Formulations

- Monophasic ➡ jumlah estrogen & progestin tetap
- Biphasic ➡ jumlah estrogen tetap, sedangkan progestin meningkat pd pertengahan siklus
- Trifasik ➡ jumlah estrogen mungkin tetap / variabel, sedangkan jumlah progestin meningkat dalam 3 fase

KONTRASEPSI ORAL KOMBINASI

Absolute contraindications

- < 6 Wk postpartum if breastfeeding
- Smoker \geq 15 cigarettes/day, > 35 Y of age
- HPT systolic \geq 160 mm Hg or diastolic \geq 100 mm Hg
- Current or past Hx of venous thromboembolism VTE
- Ischemic heart disease
- Hx of cerebrovascular accident
- Complicated valvular heart disease (pulmonary HPT, atrial fibrillation, subacute bacterial endocarditis)
- Migraine headache with focal neurological symptoms
- Current breast cancer
- Diabetes with retinopathy/ nephropathy/ neuropathy
- Severe liver cirrhosis
- Liver tumour (adenoma or hepatoma)

KONTRASEPSI ORAL KOMBINASI

Relative contraindications

- Smoker < 15 cigarettes /day >35 Y of age
- Adequately controlled HPT
- HPT systolic 140-159 mm Hg, diastolic 90-99 mm Hg
- Migraine headache > 35 Y of age
- Currently symptomatic gallbladder disease
- Mild liver cirrhosis
- Hx of C OCP related cholestasis
- Medications that might interfere with OCP metabolism

KONTRASEPSI ORAL KOMBINASI

Non-contraceptive benefits

- Cycle regulation
- menstrual flow → anemia
- bone mineral density
- dysmenorrhea
- peri-menopausal symptoms
- acne
- hirsutism
- ovarian ca 50% after 5 Y of use
- endometrial ca 50%
- risk of fibroids
- Possibly ovarian cysts
- Possibly benign breast disease
- Possibly colorectal ca
- incidence of salpingitis
- incidence or severity of premenstrual syndrome

SIDE-EFFECTS OF COMBINED OCP

Minor side-effects commonly occur during the 1st 3 cycles & may lead to unnecessary discontinuation

1. Irregular bleeding (breakthrough bleeding/spotting)

- 10-30% in the 1st month of use
- improves with time over 3 cycles
- amenorrhea 2-3% of the cycles

2. Breast tenderness & nausea

- Improve with time
- Less with lower estrogen dosage

SIDE-EFFECTS OF COMBINED OCP

3-Wt gain

- Placebo controlled trials have failed to show any association between wt gain & COCP

4-Mood changes

- Women report depression & mood changes
- Placebo controlled trials have failed to show any significantly increased risk of mood changes with COCP

RISKS OF COCP

1-Venous thromboembolism

- VTE 3-4 X higher in users than nonusers
- Absolute risk of VTE in COCP users –
1-1.5/10 000/year
- Risk of VTE is higher during the 1st year of use than subsequent years
- The risk is attributed to the estrogen component of the pill & decline with lower dosage

RISKS OF COCP

2- Myocardial infarction

- In the past with pills containing $>50\mu\text{g}$ ethinyl estradiol --- 3X in MI
- Recent studies with pills containing $< 50\mu\text{g}$ ethinyl estradiol ----- No significant risk

RISKS OF COCP

3-Stroke

- Some studies showed 2X risk of stroke
- Smoking & HPT risk of stroke

4-Gallbladder disease

- COCP secretion of cholic acid in bile ➔ incidence of gallstone formation
- No significant risk of gallstone formation in COCP users

5-Breast cancer

- Still controversial
- A large meta-analysis 1996 ➔ significant risk of breast ca in women currently taking the COCP (Relative Risk 1.24) & in the 1st 10 Y after discontinuing it

RISKS OF COCP

5-Breast cancer

- More recent study > 9000 women ➡➡ no significant in breast ca risk
 - ➡➡ No risk with different dosage of estrogen, longer periods of use, or with different progestin components
 - ➡➡ No risk in Pt with family Hx of breast ca
 - ➡➡ No risk in Pt who started using the pills at an earlier age
 - ➡➡ risk in Pt who carry BRCA1, BRCA2 genes

RISKS OF COCP

6-Cervical cancer

- One study ➔ risk of Cx ca in long term COCP users who are HPV positive
- A review of 28 studies of women with Cx ca ➔ risk of Cx ca with duration of COCP use
- Probably due to risk of HPV (a major risk factor for cx ca) that might be related to sexual behavior which differs in users & non users of COCP

MYTHS & MISCONCEPTION

- **Women on COCP should have periodic pill breaks**

Fact ➔ this would risk of unwanted pregnancies & cycle irregularities

- **COCP affects future fertility**

Fact ➔ fertility restored 1-3 M after stopping the pills

- **COCP must be stopped in all women >35 Y**

Fact ➔ Healthy non-smoking women can continue taking the pills until menopause

- **COCP causes acne**

Fact ➔ it improves acne due circulating free androgens

INITIATION

Patient assessment

- Anamnesis lengkap utk menyingkirkan kemungkinan KI
- No routine lab screening is required

Counselling

- Instructions on how to use the pills
 - ➔ mulai pada 5 hr pertama siklus
 - ➔ Quick start method ➔ bisa dimulai hr kebrp pun dr siklus ➔ tp perlu back up kontrasepsi lain selama 1 mgg pertama.

TROUBLESHOOTING

1-Breakthrough bleeding

- lanjutkan minum pil, biasanya membaik seiring berjalannya waktu (jangan langsung mengganti obat.
- jika perdarahan berlangsung > 3 bln (atau perdarahan tjd pada ibu yg sdh menggunakan obat tsb jangka panjang), singkirkan penyebab lain perdarahan:
 - tidak teratur minum pil
 - kehamilan
 - infeksi / pathologi pd rahim atau Cx
 - malabsorpsi / diare, muntah
 - ada interaksi dg obat lain

Management of breakthrough bleeding

- Oral estrogens: premarine 1.25 mg or estradiole -17 β /7 days
- Change the another preparation with different progestin

TROUBLESHOOTING

2-Missed pills

- minum pil segera setelah ingat (bisa 2pil dlm 1 hari)
- Jika lupa 2 pil berturut-turut dlm 2 mgg pertama ➡ minum 2 / hr selama 2 hari
- Jika lupa 2 pil berturut-turut dlm 3 mgg pertama ➡ tinggalkan sisa paket & mulailah dg paket yg baru + back up kontrasepsi lain slm 7 hari pertama pemakaian paket baru
- Jika lupa 3 pil berturut-turut ➡ ikuti langkah diatas
- Jika hubungan seksual terjadi setelah lupa minumpil ➡ gunakan kontrasepsi darurat

TROUBLESHOOTING

3-Amenorrhea

- Ini terjadi pada 2-3% dari pengguna COCP, tdk berbahaya ➔ tdk perlu diobati
- Jk hamil , segera stop
- Jika px tetap menginginkan mens ➔ Ganti obat
➔ Tambahkan estrogen oral selama 10 hari

4-chloasma

Penggelapan kulit wajah, Gunakan tabir surya untuk mencegah lebih gelap

- Mungkin tidak bisa benar-benar hilang
- Ganti preparat lain jk tdk membantu

TROUBLESHOOTING

5-Breast tenderness & galactorrhea

- Often resolves with continued use
- caffeine intake may help
- estrogen content
- Galactorrhea is rare ➡ if it happens ➡ check prolactin level

6-Nausea

- with time
- Taking the pill with food or bedtime
- estrogen content
- If it occurs in a long time user ➡ rule out pregnancy

7-Pregnancy

- Pills must be stopped immediately
- There is no risk of birth defects

INTERAKSI DENGAN OBAT LAIN

Obat yang bisa menurunkan efikasi kontrasepsi :

- ✓ Induksi metab :dilantin (fenitoin), primidone, karbamazepin, barbiturate, rifampisin, fenilbutazon, griseofulvin ,terbinafin
- ✓ Membunuh bakt usus: penisilin, tetra, kloramp, sulfonamid

Obat yg efikasinya dipengaruhi kontrasepsi oral :

asetaminofen(↓), antikoagulan(↑), hipoglikemia oral (↓), metil dopa , guanetidin, steroid(↑)

Obat yang mengalami potensiasi jika diberikan bersama kontrasepsi oral : antidepressant, benzodiazepine, beta bloker, kortikosteroid, teofilin, vitamin C

TRANSDERMAL CONTRACEPTIVE PATCH

- Delivers 150µg norgestimate & 20 µg Estradiole daily
- One patch is applied weekly for 3 wks followed by one patch-free-wk
- Women weighing more than 90 kg ➡ risk of pregnancy
- Mechanism of action similar to COCP
- Irregular bleeding in the 1st M of use is more 18% for the patch than COCP 11% / Amenorrhea is rare
- Breast symptoms are more 22% in the 1st 2 cycles of the patch use than COCP use
- Local skin reaction 20%

PROGESTIN IMPLANTS

- NORPLANT ➔ Levonorgestrel
- Implanon ➔ Etonogestrel
- Highly effective failure rate 0.1% / year
- 6 rods implanted under the skin ➔ effective for 5 years
- Women < 70 kg effective for 7 Y pearl index < 2
- Reversible contraception
- Mechanism of action
 - ➔ Suppression of ovulation
 - ➔ Endometrial atrophy
 - ➔ Rendering Cx mucous impermeable to sperms
- Prolonged irregular bleeding the major side effect

KONTRASEPSI PARENTERAL

A. Kombinasi E & P : IM

- 1bulan/x .

mis: cyclofem (25 mg depotmedroxyprogesterone acetate & 5 mg estradiol cypionate),

mesigyna (50 mg norethindrone enanthate dan 5 mg estradiol valerate)

B. P saja : IM,

- 2 bln /x

Mis NET-EN

- 3 bulan / x

mis : Depo Provera (depot-medroxyprogesterone acetat =DMPA)

Name	Active ingredients	Duration of effect	Common trade names
DMPA (progestogen-only)	150 mg medroxyprogesterone acetate in an aqueous microcrystalline suspension	90 days	Depo-Provera, Depo-Clinovir, others
NET-EN (progestogen-only)	200 mg norethisterone enanthate in an oily preparation	60 days	Noristerat, Norigest, Doryxas, and others
Mesigyna (combined)	50 mg norethisterone enanthate and 5 mg estradiol valerate	30 days	Mesigyna, Norigynon

GANGGUAN HAID

HIPERMENORAE = MENORAGIA			
HIPOMENORAE			
POLIMENORAE			
OLIGOMENORAE			
METORRAGIA = METROPATIA			
AMENORAE SEKUNDER			
AMENORAE PRIMER			
BREAK THROUGH BLEEDING (BTB)			
SPOTTING			

PENYEBAB GANGGUAN HAID

Secara umum dapat digolongkan menjadi :

- **Penyebab organik**

Pasca miomektomi, endometriosis, kongesti ovarium, gangguan hipofisis, gangguan gonad (sindroma Turner), gangguan tiroid, gangguan uterus / vagina

- **Penyebab umum**

Gangguan gizi, obesitas, psikosis

- **Penyebab endokrinologis**

Ketidakseimbangan hormonal (estrogen & progesteron)

TERAPI

- Terapi harus berdasarkan penyebabnya.
- Untuk ketidakseimbangan hormonal diperlukan terapi hormon :
 - estrogen atau progesteron
 - kombinasi estrogen dan progesteron

KONTRASEPSI DARURAT

- IUD / AKDR (T Cu₃₈₀A, Multiload, Nova-T).
dipasang 3-5 hr pascasanggama.
- Pil Kombinasi (Diberikan dlm 3 hr pascasanggama).
 - ✓ microgynon 50, ovral, neogynon, nordiol, eugynon.
 - ✓ Microgynon 30, nordett, mikrodiol.
- Progestin : Postinor
- Estrogen : Lynoral, Premarin, Progynova

OBAT PENUNDA MENSTRUASI

- Komposisi : Progestin, KB Kombinasi
- Contoh : norethisterone (Primolut N®), lynesterol (Endometril®)
- Pemakaian Progesteron: dimulai 7-10 hari sebelum hr I menstruasi yg akan dtg , diminum 2-3x1 tab dan dihentikan 3 hari sebelum waktu yang diinginkan utk haid. 2-3 hr stlh obat dihentikan withdrawl bleeding
- Efek samping : perdarahan terus menerus, spotting

OBAT YANG MEMPENGARUHI MOTILITAS UTERUS

**OBAT MENINGKATKAN KONTRAKSI
(UTEROTONIC AGENT)**

**OBAT MENURUNKAN KONTRAKSI
(TOCOLYTIC AGENT)**

Obat yang Me↑ Motilitas Uterus

- Digunakan u/
 - a. induksi persalinan
 - Oksitosin
 - Agonis Muskarinik, Agonis α -1 adrenergik (minor excitatory)
 - b. kontrol perdarahan post-partum
 - Oksitosin
 - 5-HT (ergot alkaloid :ergonovine, methylergonovine) →
vasokonstriksi, supresi laktasi
 - PGF_{2 α} (carboprost)
 - PGE₂ (dinoprostone)
 - c. aborsi
 - RU 486 (mifepristone) : progesteron antagonis
 - PGE₂ atau PGF_{2 α}

Tocolytic Agent

= anti-contraction medications = labour repressants

Tujuan :

- mencegah persalinan prematur
- memperlambat persalinan slm perjlnan
- sekaligus u/memberi kesempatan pemberian glukokortikoid 2x 24j u/ maturitas paru janin

Golongan obat Tokolitik :

- 2 Agonis (Terbutalin, Ritodrine)
- Ca antagonis (nifedipin)
- Antagonis R/ Oksitosin (Atosiban)
- NSAID (Indometasin, Sulindac)

TOCOLYTIC AGENT

Agent	Regime	Side effects		Contraindications
		Maternal	Fetal	
Nifedipine	<p>Initial dosage :- sublingual 10mg, repeat every 15 minutes until contractions cease total maximum dosage 40mg</p> <p>- Maintenance dosage: Oral 20mg start 6 hrs after the initial sublingual dose q8h for 2 days</p> <p>Titrate against response and side-effects</p> <p>Can increase dosage, firstly to 20mg q6h then up to 40 mg q6h on the first day</p>	<p>- Flushing or headache</p> <p>- Significant hypotension, maternal tachycardia,</p>	<p>Foetal tachycardia</p>	<p>Hypotension</p> <p>Preload-dependent cardiac lesions (e.g. aortic insufficiency)</p>

TOCOLYTIC AGENT

Agent	Regime	Side effects		Contraindications
		Maternal	Fetal	
Atosiban	Loading dose: - 6.75mg ivi over 1 minute - Then start high dose loading infusion: 75mg in 100ml. Infusion rate 24ml/hour (18mg/hour or 300mcg/min) for 3 hours - Then start low dose Maintenance infusion: (75mg/100ml) Infusion rate to 8ml/hour (6mg/hour or 100mcg/min) for 21 hours (Maximum duration: 45 hours)	- Nausea and vomiting - Dizziness and hot flushes - Tachycardia and hypotension - Hyperglycaemia - Injection site reaction		Allergy to Atosiban

TOCOLYTIC AGENT

Agent	Regime	Side effects		Contraindications
		Maternal	Fetal	
Indomethacin	50 to 100mg rectal suppository Then 15mg 4-6 hrs for 48 hours	GI upset (Nausea, heartburn) Drug rash, bleeding disorders	Transient constriction foetal ductus arteriosus, oligohydramnios	Asthma Drug allergy Renal, cardiac, hepatic impairment Peptic ulcer Thrombocytopenia
Sulindac	200mg po Q12H for 4 doses			
Ritodrine	Start IV infusion using syringe pump (150mg in 50ml 5%-dextrose) with 50ug/min or 1ml/hr Increment at 15 minute-interval by 50ug/min until uterine contractions are suppressed, or maximum dosage attained (350ug/min), or complications arise Maintain infusion rate for at least 6 hours after contractions have ceased, and up to 24 hours for steroid to	Tachycardia and hypotension Palpitation Shortness of breath chest discomfort Hypokalaemia Hyperglycaemia ECG changes (ST depression, prolonged QT interval), pulmonary edema	Foetal tachycardia Increased intraventricular haemorrhage	- Severe cardiac diseases and arrhythmia - Poorly controlled hyperthyroidism or taking beta-blocker for control of tachycardia - Poorly controlled diabetes mellitus

Terimakasih

