In the name of ALLAH

Pharmacotherapy of common problems in women

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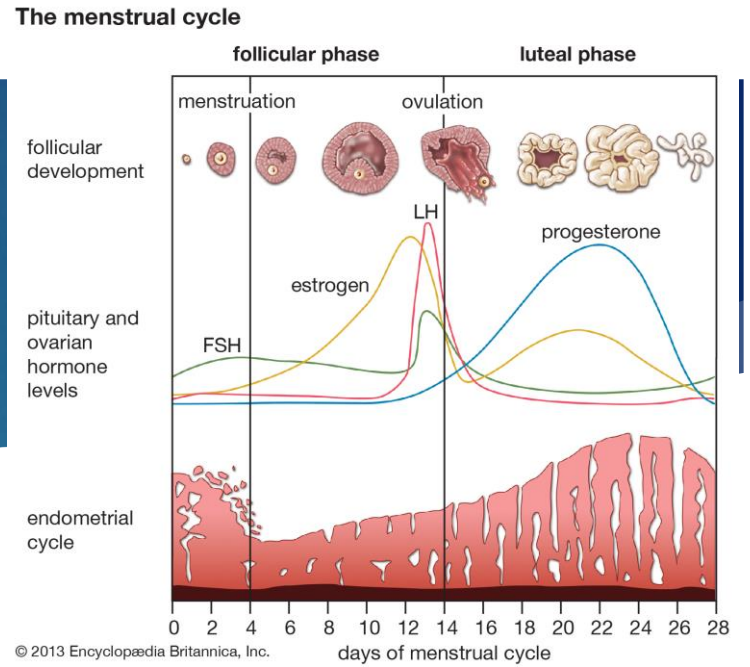
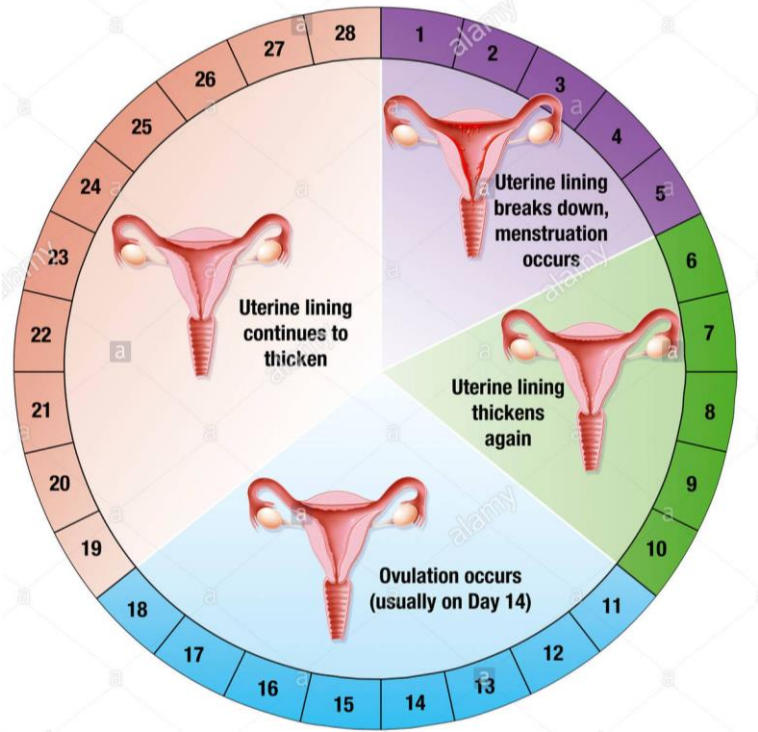
Normal menstrual cycle:

- Median age of menarche of **12.4 years**, and menarche by age 15

- Menstrual cycle interval between 21 and 45 days (mostly 24- 28 days)
- Menstrual **flow length 7 days or less**
- Menstrual product use between **3 to 6 pads or tampons per day**

- **A normal menstrual period usually lasts between 4.5 and 8 days, and cycle lengths range from 24 to 28 days**
- **And 5 -80 ml blood loss may occur in each cycle**
- **Ovulation is** required for the follicle (an estrogen-secreting body) to become a corpus luteum (a progesterone-secreting body)





AMENORRHEA

- Amenorrhea is defined as no menstrual bleeding in a 90-day period
- **Primary amenorrhea**: absence of menses by age 15 years in women who have never menstruated. (0.1% population)
- **Secondary amenorrhea** is the absence of menses for three cycles or for 6 months in a previously menstruating woman (3-4 % of population)

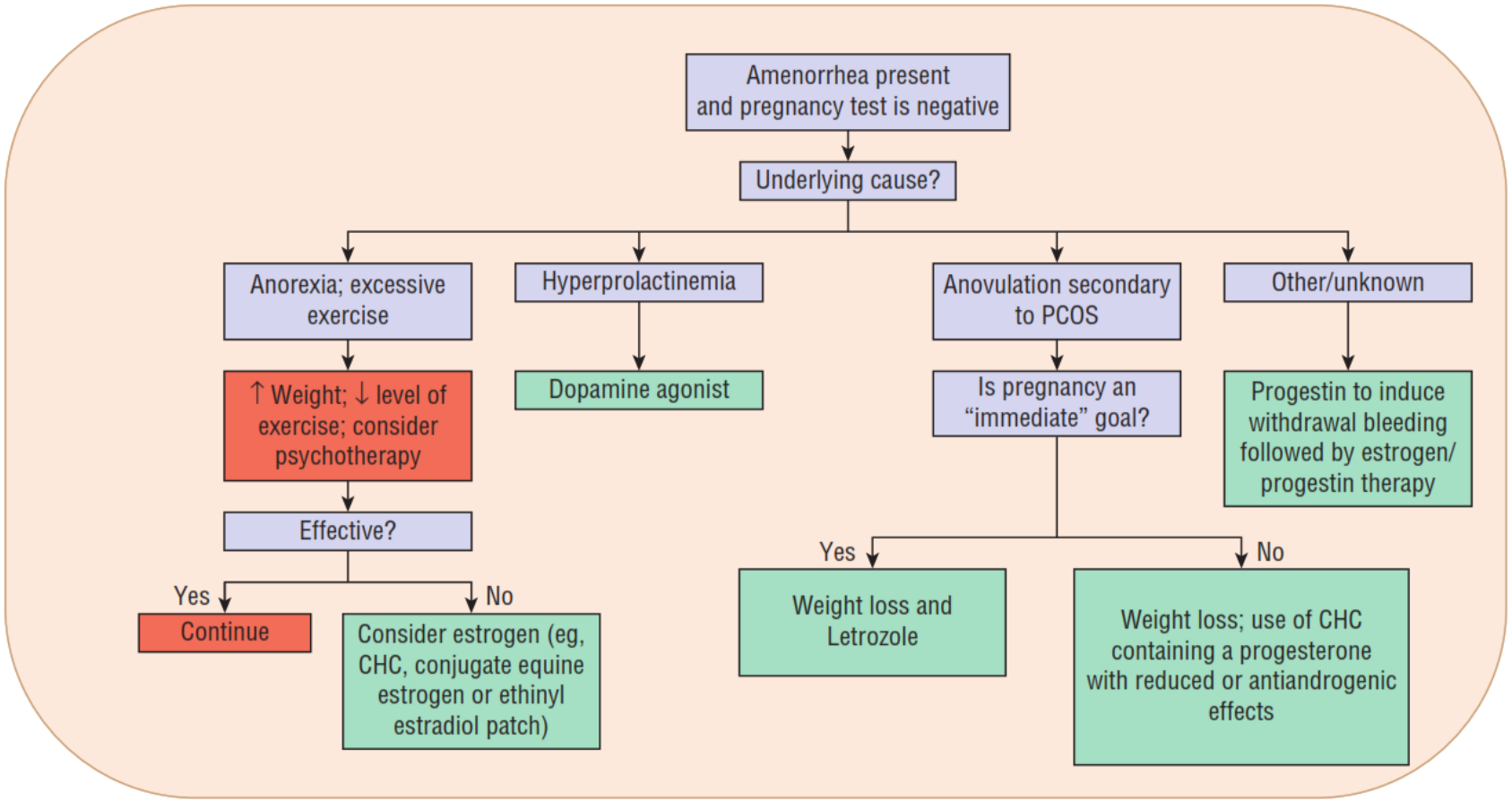
- Amenorrhea is not itself a diagnosis, **but a sign of a disorder.**

- **Causes:**

✓ **A urine pregnancy test should be done first!!!**

- **1.Anatomical causes**, including pregnancy and uterine structural abnormalities
- **2.Endocrine disturbances** leading to chronic anovulation (PCOS, Hyperprolactinemia), stress/ heavy physical activities
- **3.Ovarian insufficiency/failure**

Treatment (Algorithm)



Treatment

- **FHA:**
- Guideline recommend nutrition, psychological and physical activity modulation (first line)
- **Hormonal replacement therapy (alternative)**

- **3. Hyperprolactinemia** is the cause of amenorrhea, dopamine agonists such as bromocriptine (58%) and cabergoline (more effective>80%).

- **4.Progestins challenge:** induce withdrawal bleeding in women with secondary amenorrhea (within 7 days)
- Tab.Medroxyprogesterone (5-10 mg/d for 5-10 days or Amp progesterone 50-100 mg stat)

- Absence of withdrawal bleeding after a progestin challenge may **suggest outflow** tract obstruction or insufficient endometrial estrogen exposure

HEAVY MENSTRUAL BLEEDING (HMB)

- It is using instead of **menorrhagia**
- **Definition:** menstrual blood loss greater than 80 mL per cycle or menstrual bleeding lasting greater than 7 days per cycle
- HMB is one of the **most commonly =**18% to 30% of gynecologic visits.

Pathophysiology

- **HMB may be the result of one of several very diverse causes including** hematologic, hepatic, endocrine(PCOS , Hypothyroidism) , and/or uterine disorders

Abnormal Uterine Bleeding Associated with Ovulatory Dysfunction (AUB-O)		
Physiologic causes	Adolescence	Immaturity of the HPO axis: no LH surge
	Perimenopause	Declining ovarian function
Pathologic causes	Hyperandrogenic anovulation (PCOS)	Hyperandrogenism: high testosterone, high LH, hyperinsulinemia, and insulin resistance
	Hypothalamic dysfunction (physical or emotional stress, exercise, weight loss)	Suppression of pulsatile GnRH secretion and estrogen deficiency: low LH, low FSH
	Hyperprolactinemia (pituitary gland tumor, psychiatric medications)	High prolactin
	Hypothyroidism	High TSH
	Premature ovarian failure	High FSH
Heavy Menstrual Bleeding (HMB)		
Hematologic	von Willebrand disease	Factor VII defect causing impaired platelet adhesion and increased bleeding time
	Idiopathic thrombocytopenic purpura	Decrease in circulating platelets, can be acute or chronic
Hepatic	Cirrhosis	Decreased estrogen metabolism, underlying coagulopathy
Endocrine	Hypothyroidism	Alterations in the HPO axis
Uterine	Fibroids	Alteration of endometrium, changes in uterine contractility
	Adenomyosis	Alteration of endometrium, changes in uterine contractility
	Endometrial polyps	Alteration of endometrium
	Gynecologic cancers	Various dysplastic alterations of endometrium, uterus, cervix

Treatment

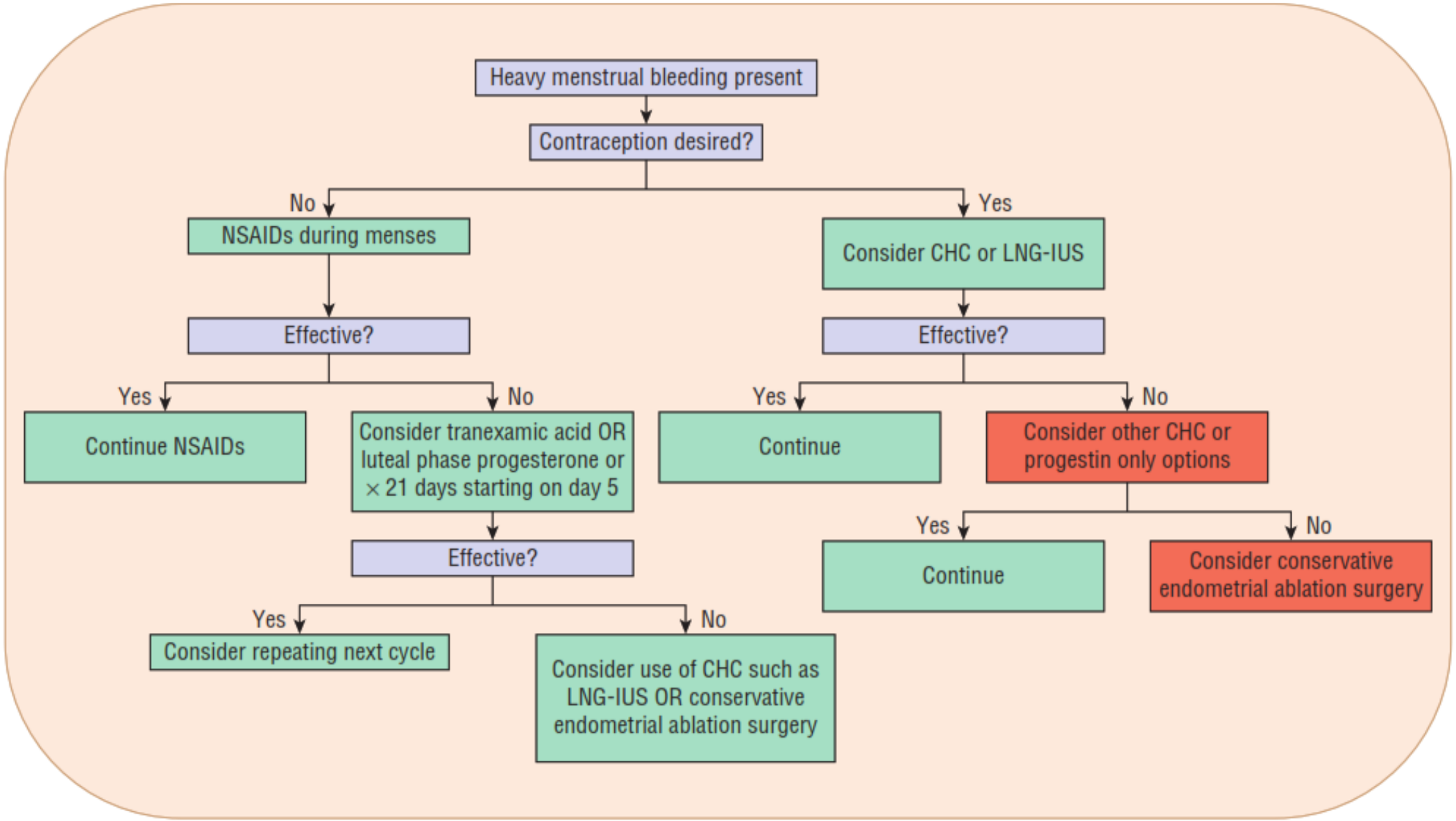
- **Resolve underlying diseases**

- **Structural lesions**
- **Submucosal fibroids** are a common cause of heavy menstrual bleeding (HMB) and can be treated with medical or surgical therapies.

- **Endometrial polyps** are a common cause of AUB and are typically easily removed with hysteroscopic polypectomy.
- **Adenomyosis is** a common cause of HMB and dysmenorrhea; while hysterectomy is the definitive treatment, medical or other surgical therapies may also be effective.

- **Surgery:** in selected cases which dose not respond to pharmacologic therapy

- **Acute phase : Estrogen** is the recommended treatment for managing acute severe bleeding episodes in women without suspected or known bleeding
- **Continuation** may be necessary to prevent future occurrences. Both estrogen-containing CHCs and progestin-only regimens can be used for maintenance therapy.


Heavy menstrual bleeding present
Contraception desired?
No
NSAIDs during menses
Effective?
Yes
Continue NSAIDs
No
Consider tranexamic acid OR luteal phase progesterone or × 21 days starting on day 5
Effective?
Yes
Consider repeating next cycle
No
Consider use of CHC such as LNG-IUS OR conservative endometrial ablation surgery
Yes
Consider CHC or LNG-IUS
Effective?
Yes
Continue
No
Consider other CHC or progestin only options
Yes
Continue
No
Consider conservative endometrial ablation surgery

Dysmenorrhea

- Defined as crampy pelvic pain occurring **with or just prior to menses**.
- **Epidemiology:** Up to 90% of adolescents report some pain with menstruation, and up e pain that is sufficiently severe and disabling to interfere with activities of daily life.

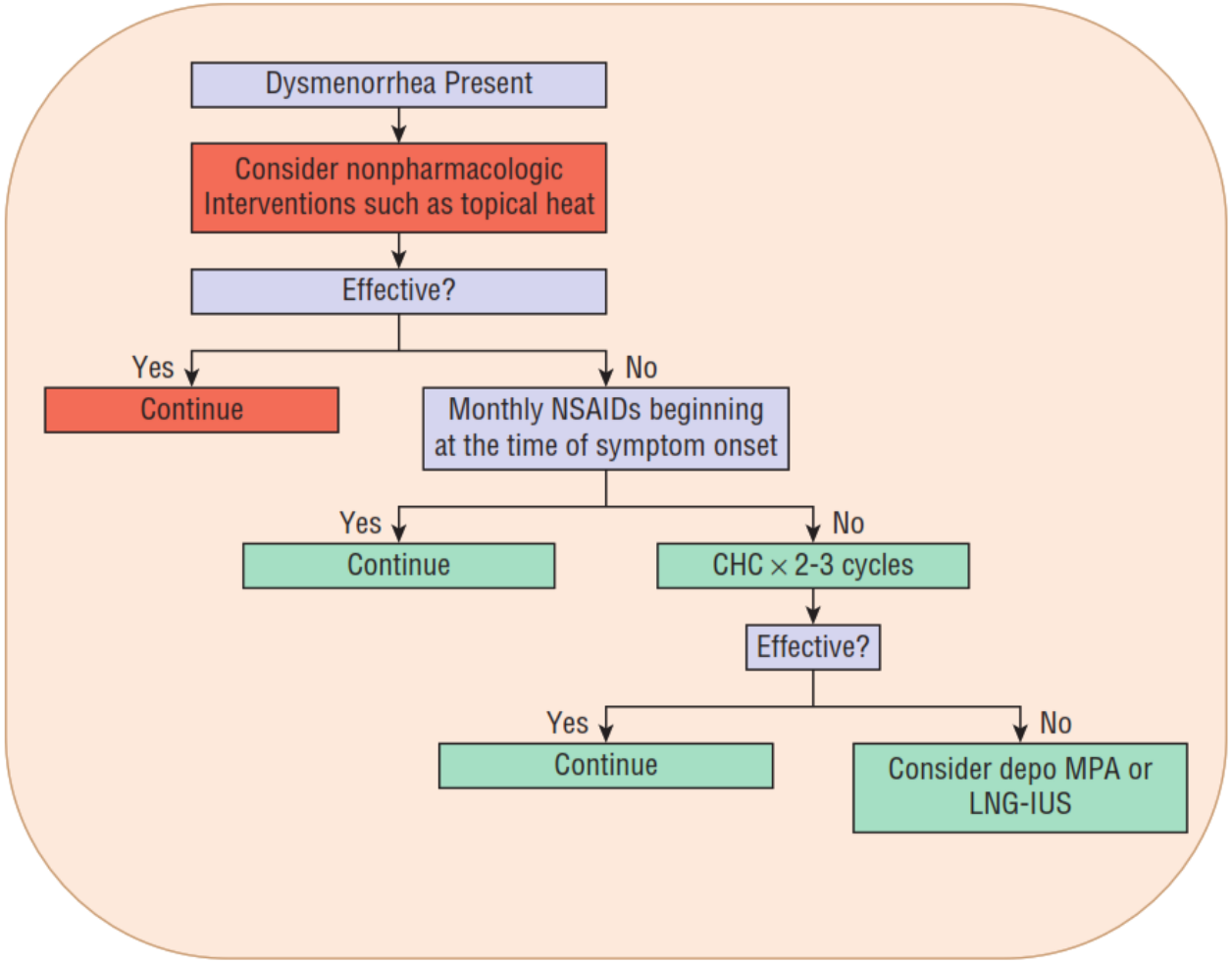
- **Primary dysmenorrhea** implies pain in the setting of normal pelvic anatomy and physiology: **90% it's normal**

- **Secondary dysmenorrhea** is associated with underlying pelvic pathology : 10%, more common in women>30yrs.

Treatment

- Initial treatment choice is influenced by whether or not the woman **desires pregnancy**

- **Non-pharmacologic:**
  - ✓ **Topical heat therapy,**
  - ✓ **Exercise, acupuncture**
  - ✓ **Low-fat vegetarian diet have been Shown to reduce dysmenorrhea intensity.**
  - ✓ **Supplements** (low evidence, can be tried): fish oil, vitamin B1, ginger, valerian, Magnesium and zinc sulfate



Pharmacologic therapy

- **1.NSAIDs are the initial treatment** of choice. These agents do not differ in efficacy with the most commonly used agents being naproxen and ibuprofen and mefenamic acid

- **80-85% of patients would be controlled by NSAIDs**
- All NSAIDS have a propensity for causing **GI distress and ulceration**;
- Their administration with food or milk minimizes these effects. Glass of water
- All NSAIDS should be dosed on an individual basis and are most effective if **started 1 to 2 days prior to the onset of menses and continued through the first 2 to 3 days** of menstrual bleeding.
- **Some data suggest that an oral loading dose** of naproxen sodium (550 mg) might improve pain control in dysmenorrhea

- **2. CHC:** alternative/ if NSAID is not effective or contraindicated/ first line if contraception is desired
  - **Reduce endometrial tissue proliferation which reduces endometrial-derived prostaglandin and leukotriene**.

- **Both cyclic and continuous** (may be more effective) regimens have been used successfully

- OCs relieve dysmenorrhea symptoms in **50% to 80% of patie**nts within **3 to 6 months after beginning** hormone therapy

PREMENSTRUAL SYNDROME(PMS) AND PREMENSTRUAL DYSPHORIC DISORDER(PMDD)

- Occurring in the last week of the menstrual cycle **that resolve** with menstrual flow

- **Diagnosis(PMS) :**
- at least one moderate-to-severe somatic or psychiatric symptom is present in the last week of the luteal phase (then resolve after bleeding) for at least 3 months

- **PREMENSTRUAL DYSPHORIC DISORDER (PMDD).**
- In PMDD, at least five symptoms are present/ more severe
- ✓ **In** both PMS or PMDD, there is no underlying diseases.

TABLE 96-5 Diagnostic Criteria for Premenstrual Syndrome

At least one of the following somatic or affective symptoms should be present during the 5 days before menses in the last three menstrual cycles

Somatic symptoms	Affective symptoms
Abdominal bloating	Angry outbursts
Breast swelling or tenderness	Anxiety
Headache	Depression
Muscle or joint pain	Difficulty in concentration, or confusion
Swelling of extremities	Irritability
Weight gain	Social withdrawal

Pharmacotherapy:

- **1.SSRI (first line)/ SNRI : effective esp for PMDD**
- **2.CHC:** second choice
- **3.GNRH agonist:** last choice (if previous ones are not effective)

- **SSRI:** data support the use of citalopram, escitalopram, fluoxetine,
- fluvoxamine, paroxetine, and sertraline
- **Luteal dose as effective as continuous dosing**
- **Dose:** start from day 14 or symptoms onset **until the next cycle or symptom resolution**

- **Abrupt discontinuation is OK! (no withdrawal symptoms)**

Pharmacotherapy:

- **CHC:** drospirenone + EE may be offered as an alternative esp for who desire contraception.
- Drospirenone has anti-androgenic effect (probably less psychiatric side effects)

- **Refractory:** GNRH analogue

PCOS

- **The polycystic ovary syndrome (PCOS)** is an important cause of androgen excess, menstrual irregularity, and cardiometabolic dysfunction in women.

- **Common problem in women**
- **Polycystic ovary syndrome (PCOS)** affects ~6% to 21%, or ~1 in 10, patients of reproductive age, making it the leading cause of anovulatory infertility and the most common endocrine abnormality for this age group

Diagnosis

- Polycystic ovary syndrome (PCOS) is characterized clinically by **oligomenorrhea and hyperandrogenism,** as well as the frequent presence of associated risk factors for cardiovascular disease, including obesity, glucose intolerance, dyslipidemia, and obstructive sleep apnea

- ✓ **Two out of three of the following** are required to make the diagnosis:
- **Oligomenorrhea, hyperandrogenism, and polycystic ovaries on ultrasound.**

- **Hyperandrogenism** may be diagnosed by either clinical (acne, hirsutism, or male-pattern hair loss) or biochemical (elevated serum androgen concentration [usually total testosterone]) criteria
- we suggest measuring serum **dehydroepiandrosterone sulfate (DHEAS**), as well as total testosterone to look for adrenal sources of hyperandrogenism

- **All of the patient may not have hyperandrogenism.**

Treatment

Goals:

- **Amelioration of hyperandrogenic features** (hirsutism, acne, scalp hair loss)
- **Management of underlying metabolic abnormalities** and reduction of risk factors for type 2 diabetes and cardiovascular disease
- **Prevention of endometrial hyperplasia** and carcinoma, which may occur as a result of chronic anovulation
- **Contraception** for those not pursuing pregnancy, as women with oligomenorrhea ovulate intermittently and unwanted pregnancy may occur

- **Ovulation induction** for those pursuing pregnancy

- **Weight loss**, which can restore ovulatory cycles and improve metabolic risk, is the first-line intervention for most women.

1.Menstrual dysfunction (for who do not want to get pregnant)

- **Endometrial protection**
- **The chronic anovulation** seen in PCOS is associated with an increased risk of endometrial hyperplasia and possibly endometrial cancer

- We suggest combined estrogen-progestin oral contraceptives (COCs) as first-line therapy for menstrual dysfunction and endometrial protection
- **Absence of pregnancy should be documented before COCs are begun.**

- **COC benefits:**
- ✓ Daily exposure to progestin, which antagonizes the endometrial proliferative effect of estrogen
- ✓ Contraception in those not pursuing pregnancy, as women with oligomenorrhea ovulate intermittently and unwanted pregnancy may occur
- ✓ **Cutaneous benefits** for hyperandrogenic manifestations (Acne, hirsutism)

1.Menstrual dysfunction (for who do not want to get pregnant)

- Alternative treatments :
- Medroxyprogesterone acetate (5 to 10 mg) or micronized progesterone 200 mg for **10 to 14 days every** one to two months.
- Mini pill can also be used.

- **Metformin** is a potential alternative to restore menstrual cyclicity as it restores ovulatory menses in approximately 30 to 50 percent of women with PCOS

2.Androgen excess (Hirsutism)

- **1.COC as first-line pharmacologic therapy** for most women
- **2.Antiandrogen** is then added after 3-6 months if the cosmetic response is suboptimal
- **Spironolactone (good option) 50-100 mg BD, cyproterone acetate, finasteride, flutamide (not recommended due to hepatotoxicity)**

- Spironolactone alone does not regularize menstrual cycles, and in fact, it is sometimes associated with menstrual irregularities
- **Finasteride:** has been used for female hirsutism, but its lack of specificity for type I 5a-reductase in the pilosebaceous unit and toxicity may make this a suboptimal treatment choice.

2.Androgen excess (Hirsutism)

- **3. Gonadotropin-releasing hormone (GnRH) agonists are also sometimes used to suppress ovarian androgen production**
- **4. Hirsutism can also be treated by removal of hair by mechanical means such as shaving, waxing, depilatories, electrolysis, or laser treatment.**

3. Androgen excess (Acne)

- Like normal population
- **Drugs such as tretinoin, benzoyl peroxide. Topical or oral AB and finally isotretinoin may be used based on disease severity.**

Hormonal therapy is recommended for PCOS patients (COC. Anti androgen therapy)

4.Metabolic abnormalities

- **Weight loss (even 5-10%)**, which can restore ovulatory cycles and improve metabolic risk, is the first-line intervention for most women.
- **Even pharmacotherapy intervention may be considered. (metformin/ GLP1 agonist)**

- **Weight loss results in insulin receptor sensitivity, a decrease in serum androgen concentrations and, in some instances, improvements in hirsutism**

Metabolic abnormalities

- Several drugs, including biguanides (metformin: more evidence) and thiazolidinediones (pioglitazone, rosiglitazone), can reduce insulin levels in women with PCOS.
- These drugs may also **reduce ovarian androgen production** (and serum free testosterone concentrations) and restore normal menstrual cyclicity
- **Statins (based on indication)** are effective for dyslipidemia in women with PCOS but do not appear to have other clinically important metabolic or endocrine effects.
- **The prevalence of nonalcoholic steatohepatitis (NASH)** appears to be increased in women with PCOS. Both weight loss and metformin use appear to improve metabolic and hepatic function in these women

5.WOMEN PURSUING PREGNANCY

- **Weight loss**
- **Metformin** (alone or in combination with clomiphene)
- For oligoovulatory women with PCOS undergoing ovulation induction, we now suggest letrozole (may be more effective) as first-line therapy over clomiphene citrate, regardless of the patient's BMI.
- **Metformin inhibits** hepatic glucose output, providing lower insulin concentrations and reducing androgen production in the ovary
- **Cabergoline:** in hyperprolactinemia
- **Gonadotropin therapy :**Another method to induce ovulation is administration of exogenous gonadotropins

- **IVF:** last action for pregnancy

Contraception

Introduction

- **Contraception is currently an issue worldwide.**
- Preventing unintended pregnancy is an important goal of contraceptive use, particularly in countries where population control is a goal.
- It is important **mentally, physically and economically**

Combined hormonal contraceptive (CHC)

Combined hormonal contraceptive (CHC) agents are a combination of estrogen and progestin.

Include a combination of estrogen and progestin (oral tablet, vaginal ring, and transdermal patch)

- **Other CHC benefits: acne, hirsutism, premenstrual syndrome (PMS**) and endometrial cancer; menstrual cycle regulation; and prevention of ovarian cancer and functional ovarian cysts.

- They may increase the risk of breast cancer

Oral Contraceptives

- **1.Ethinyl estradiol:** is the most commonly used estrogen in hormonal contraceptive products.

- **Most combined OCs**, transdermal patch, and vaginal ring contain estrogen at doses of 20 to 50 mcg of EE.
- **2.Progestin:** is a term used for a synthetic progesterone
  - **Androgenic activity** : levonorgestrel> desogestrel**>** drospirenone, cyproterone acetate (anti androgen)

Adverse Effects Associated with Type of Hormonal Activity

Estrogenic	Progestational	Androgenic
Bloating	Headache	Acne/oily skin
Nausea/vomiting	Breast pain/tenderness	Weight gain
Breast fullness	Hypertension	Hirsutism
Breakthrough bleeding		Fatigue
Irritability		Depression
Headache		
Hypertension		

Activity of Progestin Agents

Generation	Progestin	Estrogenic	Progestational	Androgenic
First	Norethindrone	++	++	++
	Ethynodiol diacetate	++	+++	+
	Norgestrel	–	+++	+++
	Norethindrone acetate	++	++	++
Second	Levonorgestrel	–	++++	++++
Third	Norgestimate	–	++	++
	Desogestrel	+/–	++++	++
Fourth	Drospirenone	–	+/–	–

Oral Contraceptives

- **Initiating an Oral Contraceptive** Oral contraceptives may be initiated by several different methods, including on the 1-5 days of bleeding during the menstrual cycle, after this time, a back up method for 7 days is necessary.

- With combination OCs, the types and doses of estrogen and progestin remain constant during the **21 to 24 days** that active tablets are taken.
- The next blister should be started (do not wait for bleeding)

- **Monophasic OCs contain** the same amounts of estrogen and progestin for 21 days, followed by 7-day placebo phase. / better choice due to less hormonal variation
- **Multiphasic pills** (biphasic, triphasic, or quadriphasic) contain variable amounts of estrogen and progestin for 21 days, also followed by a 7-day placebo phase.

- **Other Indications:** PCOS (feedback action, rise SHBG), Acne (specially antiandrogenic COC), Irregular cycles and heavy bleeding (reduce blood volume), Premenstrual syndrome (PMS), Dysmenorrhea (second line after NSAIDS)
- **They may decrease the risk of ovarian and endometrial cancer but may increase the risk of Breast cancer**

Initiation and caution

- All combined OCs are similarly effective in preventing pregnancy.
- The initial choice is based on the hormonal content and dose, *preferred formulation, and coexisting medical conditions.*
- **Contraindication must be excluded.**
- **In women without coexisting** medical conditions, an OC containing **35 mcg or less of EE** is recommended (less risk of VTE, stroke, or MI)
- **Women with oily skin, acne, or hirsutism** should be given low androgenic such as **drospirenone**

Category 4: Unacceptable health risk (method not to be used)

- Breastfeeding or non-breastfeeding <21 days postpartum
- Current breast cancer
- Severe (decompensated) cirrhosis
- Current deep venous thrombosis/pulmonary embolism
- History/higher risk of deep venous thrombosis/pulmonary embolism (not on anticoagulant therapy)
- History/higher risk of deep venous thrombosis/pulmonary embolism (established on anticoagulant therapy for 3 months or greater)
- Thrombogenic mutations
- Major surgery with prolonged immobilization
- Migraines with aura, any age
- Systolic blood pressure ≥160 mm Hg or diastolic ≥100 mm Hg
- Hypertension with vascular disease
- Current and history of ischemic heart disease
- Benign hepatocellular adenoma or malignant liver tumor
- Peripartum cardiomyopathy, moderately or severely impaired cardiac function; normal or mildly impaired cardiac function <6 months
- Smoking ≥15 cigarettes per day and age ≥35
- Complicated solid organ transplantation
- History of cerebrovascular accident
- SLE; positive or unknown antiphospholipid antibodies
- Complicated valvular heart disease

Initiation

- **Extended use:** instead of 21/7 regimen
- **With extended use of OCs, active combination tablets are taken continuously for 84 days or longer followed by 7 days of inactive pills or estrogen-only pills.**

- **Better choice if woman prefers/ PMS/anemia/ menorrhagia /endometriosis is present**
- **Monophasic pills are recommended because of the consistent hormone content throughout the cycle.**

Missed Doses of Oral Contraceptives

- **1.** For combined hormonal OCs, if one tablet is missed or late then take the tablet as soon as remembered. (2 tablet)
- **if she forgets to take one pill, she should take two pills on the day she remembers**

- **2. If she misses two pills** in a row in week 1 or 2 of her pack, she must take two pills on the day she remembers and two pills the next day
- If tablets were missed in **the last week or more than 2 tablets of hormonal tablets**, finish the remaining active tablets (tablets with hormone) and then omit the hormone-free interval and start a new pack of tablets.
- **3. If she misses more than 2 tablets???**
- **7 days back up is necessary for items 2 and 3**

1. ***Return of Fertility***

   The average delay in ovulation after discontinuing OCs is 1 to 2 weeks. Infants conceived in the first month after discontinuation of an OC had no greater chance of miscarriage or being born with a birth defect

Drug – Drug interactions

- Ethinyl estradiol is a substrate of cytochrome P-450 3A4
- **Anticonvulsants** such as carbamazepine, oxcarbazepine, phenytoin, phenobarbital, primidone, and topiramate are CYP3A4 inducers.
- Some prescribers suggest using **a 50-mcg EE COC** in patients taking interacting drugs, although others might recommend using an **alternative method of contraception** if drug interactions are an issue
- **COCs have been reported** to decrease serum levels of lamotrigine and can affect seizure control.
- **Rifampin, isoniazid, and griseofulvin**, backup contraception should be used while taking the medication and **for 4 weeks after** discontinuation of the antibiotics

Progestin-only contraceptives

Progestin-only contraceptives are alternative agents for women with

Contraindications to CHCs. Or estrogenic side effects (N,V/ headache)

- Oral tablet, depot and subcutaneous injection
- **Common side effects** include weight gain, acne, mood changes, and irregular menses.

Pregnancy and lactation

General Rules

- **Suggestions for Prescribing Medication in Pregnant Women**

  When possible:
- Use medication only if **absolutely indicated**.
- Avoid initiating therapy during the first trimester.
- Select a medication with a proven track record in human pregnancy.
- Use a single-agent.
- Use the lowest effective dose.
- Discourage the use of over-the counter drugs that might interact with prescription medications.
- Ref: https://www.perinatology.com/exposures/druglist.htm

FDA Pregnancy Categories

FDA Pregnancy Categories

Category	Description
A	Controlled studies of pregnant women show no risk in first trimester
B	Animal studies show no risk, or animals show risk unconfirmed in humans
C	Animal studies show risk, caution is advised, benefits may outweigh risks
D	Evidence of risk to human fetus, benefits may outweigh risks in serious conditions
X	Risk outweighs benefit

Adapted from Dwosh E, et al. *Int MS J*. 2003;10:52-59.

MedscapeCME

Introduction

- The intense fetal growth and development during pregnancy requires maternal physiologic adaptation and a change in nutritional needs
- **Energy intake** (also called caloric intake) is a key nutritional factor in determining birth weight. In the first trimester, pregnant people typically do not need to increase their caloric intake.

- In the second and third trimesters, most pregnant individuals will need to increase their caloric consumption to promote appropriate weight gain
- **An additional 340 and 450 kcal/day is suggested for the second and third trimesters.**
- **Protein:** 1.1 gr/kg/day
- **DHA:** 200 to 300 mg/day of DHA.

RDA in Pregnancy

In the second trimester, you will need an extra 340 calories per day, and in the third trimester, about 450 extra calories a day.

References:
UpToDate 2023
ACOG 2022

Recommended dietary allowances, or adequate intakes, and tolerable upper limits for adult pregnant people

	Nonpregnant/ nonlactating females	Pregnant (age 14 to 18 years)	Pregnant (age 19 to 30 years)	Pregnant (age 31 to 50 years)	Upper limit
Macronutrients					
Protein (as % of kcal)	10 to 30%	10 to 30%	10 to 35%	10 to 35%	
Protein	46 g	71 g	71 g	71 g	
Carbohydrate (as % kcal)	45 to 65%	45 to 65%	45 to 65%	45 to 65%	
Carbohydrate	130 g	175 g	175 g	175 g	
Fiber	25 to 28 g	25 to 34 g	28 to 36 g	25 to 34 g	
Added sugars (as % of kcal)	<10%	<10%	<10%	<10%	
Total fat (as % of kcal)	20 to 35%	25 to 35%	20 to 35%	20 to 35%	
Saturated fat (as % of kcal)	<10%	<10%	<10%	<10%	
18:3 Linolenic acid	1.1 g	1.4 g	1.4 g	1.4 g	
Minerals					
Calcium	1000 mg	1300 mg	1000 mg	1300 mg	2500 mg
Iron	18 mg	27 mg	27 mg	27 mg	45 mg
Magnesium	310 to 360 mg	400 mg	350 mg	360 mg	350* mg
Phosphorus	700 mg	1250 mg	700 mg	700 mg	4000 mg
Zinc	8 mg	12 mg	11 mg	11 mg	40 mg
Iodine	150 mcg	220 mcg	220 mcg	220 mcg	1110 mcg
Selenium	55 mcg	60 mcg	60 mcg	60 mcg	400 mcg
Vitamins					
Vitamin A	700 mcg RAE	750 mcg RAE	770 mcg RAE	770 mcg RAE	3000 mcg RAE
Vitamin D	600 international units	600 international units	600 international units	600 international units	4000 international units
Vitamin E	15 mg	15 mg	15 mg	15 mg	1000 mg
Vitamin K	90 mcg	75 mcg	90 mcg	90 mcg	ND
Vitamin C	75 mg	80 mg	85 mg	85 mg	2000 mg
Thiamin	1.1 mg	1.4 mg	1.4 mg	1.4 mg	ND
Riboflavin	1.1 mg	1.4 mg	1.4 mg	1.4 mg	ND
Niacin	14 mg	18 mg	18 mg	18 mg	35 mg
Vitamin B6	1.3 mg	1.9 mg	1.9 mg	1.9 mg	100 mg
Vitamin B12	2.4 mcg	2.6 mcg	2.6 mcg	2.6 mcg	ND
Choline	425 mg	450 mg	450 mg	450 mg	3500 mg
Folate	400 mcg DFE	600 mcg DFE	600 mcg DFE	600 mcg DFE	1000 mcg DFE

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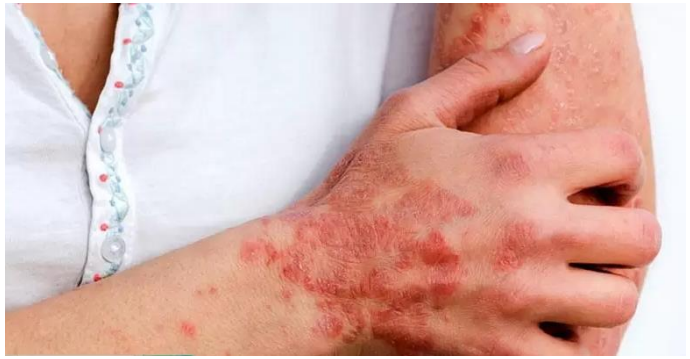
Multiple-micronutrient supplements
MMN for pregnancy

- **Prenatal vitamins are the standard approach**
- It is more important specially in **low income countries**
- **Candidate: include those carrying a multiple gestation, heavy smokers, adolescents, complete vegetarians (ie, vegans), substance abusers, and individuals who have had bariatric surgery or who have gastrointestinal conditions that cause malabsorption (eg, Crohn disease, bowel resection)**
- **Important ingredients:** Folic acid/ iron/ iodine/ vit D

World Health Organization (WHO) guidelines recommend use of MMNs in pregnant people receiving antenatal care in any healthcare facility or community-based setting, in the context of rigorous research . Because the evidence for this recommendation was mainly derived from low- and middle-income countries, they state that applicability to high-income countries or to populations not at risk of micronutrient (eg, adequate diet, food fortification programs) is unclear. The evidence was derived from trials using MMNs containing 13 to 15 micronutrients (including iron and folic acid) and the widely available United Nations International Multiple Micronutrient Antenatal Preparation (UNIMMAP), which contains 15 micronutrients (folic acid: 400 mcg, vitamin A: 800 mcg, vitamin D: 200 international units, vitamin E: 10 mg, vitamin B1: 1.4 mg, vitamin B6: 1.9 mg, vitamin B12: 2.6 mcg, niacin: 18 mg, vitamin C: 70 mg, zinc: 15 mg, iron: 30 mg, selenium: 65 mcg, copper: 2 mg, iodine: 150 mcg

Dermatology problems

- Such as dermatitis and psoriasis
- Topical corticosteroids
- They are safe
- Mild to moderate potency topical agents are preferable



Antibiotics

Drug	Effects	Drugs of choice
Tetracycline	• Bone damage • Malformation and permanent yellow discoloration of the primary teeth	• **Penicillin** group: ampicillin, amoxicillin, flucloxacillin, penicillin V, propicillin • Cephalosporins • Macrolides: erythromycin, azithromycin • Metronidazole • Nitrofurantoin
Aminoglycoside	• Ototoxicity (CN VIII toxicity) and hearing loss	
Trimethoprim/sulfonamide combinations	• Cardiovascular birth defects • Neonatal jaundice	
Chloramphenicol	• Gray baby syndrome: syndrome associated with chloramphenicol accumulation in the body, leading to ashen gray color of the skin, cardiovascular collapse, and abdominal distention	
Clarithromycin	• Embryotoxic	
Fluoroquinolones	• Bone and cartilage damage	

Antifungal

Antifungals

Drugs to avoid	Harmful effects	Recommended drugs
Ketoconazole, flucytosine, and griseofulvin	• Teratogenic and/or embryotoxic	• Topical: imidazoles • Vaginal: nystatin • Systemic: amphotericin B
Itraconazole, fluconazole (> 300 mg)		
Iodides	• Congenital goiter	

Antiviral

Antivirals

Drugs to avoid	Harmful effects	Recommended drugs
Efavirenz	• Fetal neural tube defects	• Acyclovir and valacyclovir for herpes • Oral oseltamivir and zanamivir for influenza • Zidovudine + lamivudine + nevirapine + atazanavir for HIV infection (see also HIV in Pregnancy)
Ribavirin	• Preterm birth • Significant teratogenic and/or embryocidal effects	
Interferon α		
Ribavirin and Interferon α combination		
Didanosine and stavudine combination	• Lactic acidosis and hepatic failure leading to death	
Nevirapine	• Potentially fatal hepatotoxicity	

Cardiovascular

Antihypertensives

Drugs to avoid	Harmful effects	Recommended drugs

Diuretics	• Reduction of placental perfusion, particularly in the third trimester.	• Methyldopa in arterial hypertension and hypertensive crisis
		• Beta blockers (particularly metoprolol and labetalol)
		  • Especially in the first and second trimesters
		  • Avoid during the third trimester
		• Dihydralazine in uncontrolled hypertension
		• Nifedipine

ACE inhibitors	• **First trimester**: cardiovascular and central nervous system malformations • **Second and third trimesters**: fetal kidney damage or death	
Angiotensin–receptor blockers	• Severe renal malformation • Oligohydramnios	
Atenolol	• Intrauterine growth retardation (IUGR) • ↓ Placental growth	

Cardiovascular

Anticoagulants

Drugs to avoid	Harmful effects	Recommended drugs

Warfarin
Phenprocoumon
	• Can pass through the placental barrier and may cause:
	  • Spontaneous abortion, stillbirth, or preterm death
	  • Cerebral hemorrhage leading to CNS abnormalities
	  • Bone deformities
		• **Heparin**: anticoagulant of choice
		• Aspirin (ASA)
		  • Low doses may be prescribed for high-risk preeclampsia.
		  • High doses should be especially avoided in the third trimester.

Non-vitamin K oral anticoagulants (apixaban, rivaroxaban, dabigatran)	• The data available does not suggest a high risk of embryopathy, but, because of significant data gaps, they are to be avoided in pregnancy.	

Hyperlipidemia

- Statins are contraindicated
- Cholestyramine may be used in hypercholesteremia

Analgesics

Drugs to avoid	Harmful effects	Recommended drugs
NSAIDs (in the second and third trimesters)	• Premature closure of the ductus arteriosus • Persistent pulmonary hypertension • Inhibits uterine contractility.	• Non-opioid analgesics • **Paracetamol**, especially in the third trimester

Neurologic Drugs

Antiepileptics

Drugs to avoid	Harmful effects	Recommended drugs

Phenytoin
Carbamazepine
	• Fetal hydantoin syndrome
	  • Characterized by **cleft palate, phalanx/fingernail hypoplasia, excessive hair growth**, and intrauterine growth restriction
	  • Due to impaired absorption of folate
	• Neural tube defects (carbamazepine only)
		• Individualized treatment based on seizure type and most tolerated drug

Valproate	• **Neural tube defects** (e.g., spina bifida)	

Depression and Anxiety

- **Sertraline and escitalopram have more evidence in depression**
- **Paroxetine is not recommended (SSRI and SNRI) can be considered**

Nausea and vomiting

Antiemetics during pregnancy

80% of pregnant women are affected by nausea and, potentially, vomiting, which may be treated with:

- Selected antihistamines:
  - **Doxylamine–pyridoxine (vitamin B_6) combination**
  - Meclizine
  - Dimenhydrinate: only in the first and second trimesters
- Metoclopramide, especially in the second trimester
- Ondansetron, promethazine, or prochlorperazine in patients with refractory nausea and vomiting despite other medical therapy

Ondansetron is not recommended in first trimester

Rheumatology medicines (Uptodate2022)

- **Compatible :** HCQ/Azathioprine/Sulfasalazine/ prednisolone (5-15mg/day)
- **Tumor necrosis factor (TNF)-alpha inhibitors, cyclosporine, tacrolimus, and intravenous immune globulin (IVIG)** are compatible with use during pregnancy.
- **Infants exposed to TNF inhibitors in utero should avoid live vaccines during the first six months of life**
- **We limit the use of high-dose glucocorticoids, cyclophosphamide (CYC), and rituximab only to women with life-threatening rheumatologic autoimmune disease in whom the benefits**
- **NSAIDs**: first trimester (low risk)/ second trimester (compatible)/third trimester (not recommended)

- **Leflunomide (LEF), methotrexate (MTX), and mycophenolate mofetil (MMF) should be avoided**

Others

Drugs to avoid	Harmful effects
Steroid therapy (especially as antiallergenics)	• Reduced birth weight • Increased risk of preeclampsia • Increased risk of oral and lip clefts
Oral antidiabetic agents	• Pre-eclampsia • Neonatal jaundice • Macrosomia • Neonatal hypoglycemia
Methotrexate	• Neural tube defects
Cholestyramine	• Fetal and maternal hemorrhage
Lithium	• Congenital heart defects (particularly Ebstein's anomaly)
Antineoplastic drugs (specifically antifolate metabolites and alkylating agents)	• Congenital malformation of digits; other malformations
Isotretinoin and excessive intake of vitamin A (> 8,000 IU vitamin A per day as retinol/retinyl esters)	• Multiple congenital malformations, including facial cleft and skeletal abnormalities
Misoprostol	• Abortions • Frontotemporal congenital malformations

Overview of the postpartum period: Disorders and complications

- **Postpartum Depression:** Selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs), psychotherapy, and in severe cases, electroconvulsive therapy (ECT).
- **Pain Management**: Nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and in some cases, opioids for severe pain, with caution due to their potential impact on breastfeeding infants.
- **Breastfeeding and Medication Compatibility**: Consideration of medications with a low transfer to breast milk, such as certain antibiotics, antifungals, and asthma medications, while avoiding medications with high transfer or potential adverse effects on the infant.
- **Contraception:** Non-hormonal methods such as barrier contraceptives, progestin-only contraceptives, or the non-hormonal copper intrauterine device (IUD) are often recommended during breastfeeding. For non-breastfeeding women, combined hormonal contraceptives can also be considered.
- **Management of Chronic Conditions:** Adjustments to medication regimens may be necessary to ensure the safety of medications during breastfeeding. For example, certain antihypertensive and antidiabetic medications may be preferred due to their safety profiles during breastfeeding.

Surgical site infection (SSI)

- Surgical site infection (SSI) is a common complication of childbirth, affecting approximately 2-15% of women who undergo cesarean delivery. SSIs can occur in the incision site, the uterus, or other areas of the abdomen.
- Cephazolin single dose is enough (up to 24 hours in some cases)

Pain management after delivery

Drug	Brand Name	Starting Dose	Usual Range	Special Population Dose	Other
Nonsteroidal anti-inflammatory drugs (NSAIDs)					
Aspirin, plain, buffered, or enteric-coated	Bayer, Ecotrin, Bufferin	325 mg three times a day	325-650 mg four times a day		Doses of 3,600 mg/day are needed for anti-inflammatory activity
Celecoxib	Celebrex	100 mg daily	100 mg twice daily or 200 mg daily		
Diclofenac XR Diclofenac IR	Voltaren-XR Cataflam	100 mg daily 50 mg twice a day	100-200 mg daily 50-75 mg twice a day		
Diflunisal	Dolobid	250 mg twice a day	500-750 mg twice a day		
Etodolac	Lodine	300 mg twice a day	400-500 mg twice a day		
Fenoprofen	Nalfon	400 mg three times a day	400-600 mg three to four times a day		
Flurbiprofen	Ansaid	100 mg twice a day	200-300 mg/day two to four divided doses		
Ibuprofen	Motrin, Advil	200 mg three times a day	1,200-3,200 mg/day in three to four divided doses		Available OTC and Rx
Indomethacin Indomethacin SR	Indocin Indocin SR	25 mg twice a day 75 mg SR once daily	Titrate dose by 25-50 mg/day until pain controlled or maximum dose of 50 mg three times a day Can titrate to 75 mg SR twice daily if needed		
Ketoprofen	Orudis	50 mg three times a day	50-75 mg three to four times a day		
Meclofenamate	Meclomen	50 mg three times a day	50-100 mg three to four times a day		
Mefenamic acid	Ponstel	250 mg three times a day	250 mg four times a day		
Meloxicam	Mobic	7.5 mg daily	15 mg daily		
Nabumetone	Relafen	500 mg daily	500-1,000 mg one to two times a day		
Naproxen	Naprosyn	250 mg twice a day	500 mg twice a day		
Naproxen sodium Naproxen sodium DR	Anaprox, Aleve Naprelan	220 mg twice a day	220–550 mg twice a day 375-750 mg twice a day		Available OTC and Rx
Oxaprozin	Daypro	600 mg daily	600-1,200 mg daily		
Piroxicam	Feldene	10 mg daily	20 mg daily		
Salsalate	Disalcid	500 mg twice a day	500-1,000 mg two to three times a day		


Thank
you!