A FOGSI President's Initiative

TOG 7th CONCLAVE
SOUTH ASIAN MEETING

By Dr. Nandita Palshetkar

# TOG-7
# ALGORITHMS

FEDERATION OF OBSTETRIC AND GYNAECOLOGICAL SOCIETIES OF INDIA
FOGSI
TM

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Safer • Stronger • Smarter

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IN THREATENED MISCARRIAGE &
RECURRENT PREGNANCY LOSS

# TRUST THE EVIDENCE

DOSAGE IN **TM**

**40 mg** **STAT** followed by 20/30 mg per day until symptoms remit*

IF IT'S ***ORALLY*** EFFECTIVE, IT'S†

**Duphaston®**

*Dydrogesterone Tablet IP 10 mg*

BACKED BY ***EVIDENCE***

DOSAGE IN **RPL**

**10 mg** **twice daily** until 20th week of pregnancy*

‡§ WORLD No. 1 PROGESTOGEN

§ 300 PUBLISHED STUDIES

#^ EXPOSURE IN 2 CR. PREGNANCIES

Duphaston® 60 YEARS§ OF DELIVERING INFINITE JOY

Pictures are for representation purpose only and not of actual patients.

**TM:** Threatened miscarriage. **RPL:** Recurrent pregnancy loss.

† Schindler AE. Progestational effects of dydrogesterone in vitro, in vivo and on human endometrium. Maturitas. 2009;65 (1):S3–S11. * Prescribing information of Duphaston®. Version: 6.0, dated 27th June, 2018. ‡ Internal calculations based on Quintiles IMS database, IMS Health Analytics Link MAT03 2017. § Data on file. #In utero exposure of fetuses.^ Mirza F, et al. Dydrogesterone use in early pregnancy. Gynecol Endocrino. 2016;32(2):97-106.

**Abbreviated Prescribing Information: Dydrogesterone Tablets IP Duphaston®. LABEL CLAIM:** Each film coated tablet contains: Dydrogesterone IP 10 mg, Excipients q.s. Colour: Titanium dioxide IP. INDICATION: Progesterone deficiencies: Treatment of dysmenorrhoea; Treatment of endometriosis; Treatment of secondary amenorrhoea; Treatment of irregular cycles; Treatment of dysfunctional uterine bleeding; Treatment of pre-menstrual syndrome; Treatment of threatened miscarriage; Treatment of habitual miscarriage; Treatment of infertility due to luteal insufficiency; Luteal support as part of an Assisted Reproductive Technology (ART) treatment and Hormone replacement therapy. DOSAGE AND ADMINISTRATION: Dysmenorrhoea: 10 or 20 mg dydrogesterone per day from day 5 to day 25 of the menstrual cycle. Endometriosis: 10 to 30 mg dydrogesterone per day from day 5 to day 25 of the cycle or continuously. Dysfunctional uterine bleeding: When treatment is started to arrest a bleeding episode, 20 or 30 mg dydrogesterone per day is to be given for up to 10 days. Secondary amenorrhoea: 10 or 20 mg dydrogesterone per day, to be given daily for 14 days during the second half of the theoretical menstrual cycle to produce an optimum secretory transformation of an endometrium that has been adequately primed with either endogenous or exogenous estrogen. Pre-menstrual syndrome: 10 mg dydrogesterone twice daily starting with the second half of the menstrual cycle until the first day of the next cycle. The starting day and the number of treatment days will depend on the individual cycle length. Irregular cycles: 10 or 20 mg dydrogesterone per day starting with the second half of the menstrual cycle until the first day of the next cycle. The starting day and the number of treatment days will depend on the individual cycle length. Threatened miscarriage: An initial dose of up to 40 mg dydrogesterone may be given followed by 20 or 30mg per day until symptoms remit. Habitual miscarriage: 10 mg dydrogesterone twice daily until the twentieth week of pregnancy. Infertility due to luteal insufficiency: 10 or 20 mg dydrogesterone daily starting with the second half of the menstrual cycle until the first day of the next cycle. Treatment should be maintained for at least three consecutive cycles. Luteal support as part of an Assisted Reproductive Technology (ART) treatment: 10 mg Dydrogesterone three times a day (30 mg daily) starting at the day of oocyte retrieval and continuing for 10 weeks if pregnancy is confirmed. Hormone replacement therapy: Continuous sequential therapy: An estrogen is dosed continuously and one tablet of 10mg dydrogesterone is added for the last 14 days of every 28-day cycle, in a sequential manner. Cyclic therapy: When an estrogen is dosed cyclically with a treatment-free interval, usually 21 days on and 7 days off. One tablet of 10 mg dydrogesterone is added for the last 12 -14 days of estrogen therapy. **CONTRAINDICATIONS:** Known hypersensitivity to the active substance or to any of the excipients. Known or suspected progestogen dependent neoplasms (e.g. meningioma). Undiagnosed vaginal bleeding. Treatment for luteal support as part of an Assisted Reproductive Technology (ART) treatment should be discontinued upon diagnosis of abortion /miscarriage. Contraindications for the use of estrogens when used in combination with dydrogesterone. **WARNINGS & PRECAUTIONS:** Before initiating dydrogesterone treatment for abnormal bleeding the etiology for the bleeding should be clarified. Breakthrough bleeding and spotting may occur during the first months of treatment. If breakthrough bleeding or spotting appears after some time on therapy, or continues after treatment has been discontinued, the reason should be investigated, which may include endometrial biopsy to exclude endometrial malignancy. If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with dydrogesterone and ceasing the treatment should be considered: Porphyria, Depression and Abnormal liver function values caused by acute or ehronic liver disease. **PREGNANCY & LACTATION:** It is estimated that more than 10 million pregnancies have been exposed to dydrogesterone. So far there were no indications of a harmful effect of dydrogesterone use during pregnancy. Dydrogesterone can be used during pregnancy if clearly indicated. Breastfeeding: No data exist on excretion of dydrogesterone in mother's milk. Experience with other progestogens indicate that progestogens and the metabolites pass to mother's milk in small quantities. Whether there is a risk to the child is not known. Therefore, dydrogesterone should not be used during the lactation period. Fertility: There is no evidence that dydrogesterone decreases fertility at therapeutic dose. **ADVERSE REACTIONS:** The most commonly reported adverse drug reactions of patients treated with dydrogesterone in clinical trials of indications without estrogen treatment are migraines/headache, nausea, menstrual disorders and breast pain/tenderness. Undesirable effects in adolescent population: Based on spontaneous reports and limited clinical trial data, the adverse reaction profile in adolescents is expected to be similar to that seen in adults. Undesirable effects that are associated with an estrogen-progestogen treatment (see also 'Warnings and Precautions' and the product information of the estrogen preparation): Breast cancer, endometrial hyperplasia, endometrial carcinoma, ovarian cancer; Venous thromboembolism; Myocardial infarction, coronary artery disease, ischemic stroke. Issued on: Date (27/06/2018). Source: Prepared based on full prescribing information (version 6) dated 27/Jun/2018. ® Registered Trademark of the Abbott Products Operations AG.

For full prescribing information, please contact: Abbott India Limited, Floor 16, Godrej BKC, Plot C-68, 'G' Block, Bandra-Kurla Complex, Near MCA Club, Bandra East, Mumbai-400 051. www.abbott.co.in



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By Dr. Nandita Palshetkar

***Dear FOGSIANs,***

*In this era of evidence-based medicine, Gynaecologists often must make decisions where neither evidence nor consensus exists. Fortunately, there is a growing body of evidence to assist in managing various conditions related to Obstetrics & Gynaecology. With the TOG-7 case-based algorithms, the idea is to regularly create evidence and consensus based practical approach to the diagnosis and management of indications, thereby ensuring a higher quality of care to patients.*

*FOGSI & TOG-7 intends to bring the bring the key opinion leaders in Obstetrics and Gynecology together from across the country and get them to discuss, deliberate, and create easy point of reference for better clinical practice.*

*Hope you all will maximise from the TOG-7 case based algorithm and pass on further for the betterment of the community and the STREE in all. Our sincere gratitude to Abbott India ltd. for their educational grant towards the TOG-7 case based algorithms.*

*I would also like to thank the delegates from Nepal and Sri Lanka for their valuable contribution in this event.*

**Best wishes!**

Dr. Nandita Palshetkar

MD, FCPS, FICOG
President 2019 - Federation of Obstetrics & Gynecological Societies of India (FOGSI)

# ADOLESCENT PCOS

**FOGSI President** : Dr. Nandita Palshetkar

**Moderators** : Dr. Sanjeeva Reddy

Dr. Pratik Tambe

**Panelists** : Dr. Aswath Kumar

Dr. Seema Pandey

Dr. Abhijeet Kamat

Dr. Monica Doshi

Dr. Sheetal Sawankar

Dr. Kedar Padte


**From left to right:** Dr. Ashwath Kumar, Dr. Abhijeet Kamat, Dr. Sheetal Sawankar, Dr. Sanjeeva Reddy, Dr.Pratik Tambe, Dr. Seema Pandey, Dr. Monika Doshi, Dr. Kedar Padte

# CASE 1

## CASE PRESENTATION

*A 15-year-old girl presented for evaluation of obesity and amenorrhoea. The patient started a marked weight gain from 8 years of age. Over the next 7 years, her weight increased from the 10$^{th}$ to 70$^{th}$ centile by the time of presentation. Menarche occurred at the age of 14, but she soon thereafter she developed secondary amenorrhea.*

## Examination and investigations

### Family history

- Her parents were of normal weight, and they both had hypertension, hypercholesterolemia, and impaired glucose tolerance. Her mother had gestational diabetes mellitus during her pregnancies.

### Vital signs

- The patient was obese; her height was 160.8 cm; weight 83.0 kg (71 centile), body mass index (BMI) 32.1 kg/m$^2$, waist circumference 85 cm, and blood pressure 135/84.
- The patient was hirsute (Ferriman-Gallwey score 12) and had mild acne. She had no acanthosis nigricans.

### Laboratory tests

- Elevated Serum testosterone and luteinizing hormone levels.
- Normal follicle-stimulating hormone, estradiol, and 17-OH progesterone levels.
- Normal serum thyroid-stimulating hormone, free thyroxine, prolactin, and 24-h free urinary cortisol.

### Physical examination

- Slightly elevated fasting blood glucose with an abnormal increase during an oral glucose tolerance test (OGTT).
- Abnormal lipid profile; elevated total cholesterol, low density lipoprotein (LDL)-cholesterol, triglycerides levels, and low high density lipoprotein (HDL)-cholesterol.

### Radiographic evaluation

- Transrectal pelvic ultrasound showed bilateral polycystic ovaries (Figure 1).

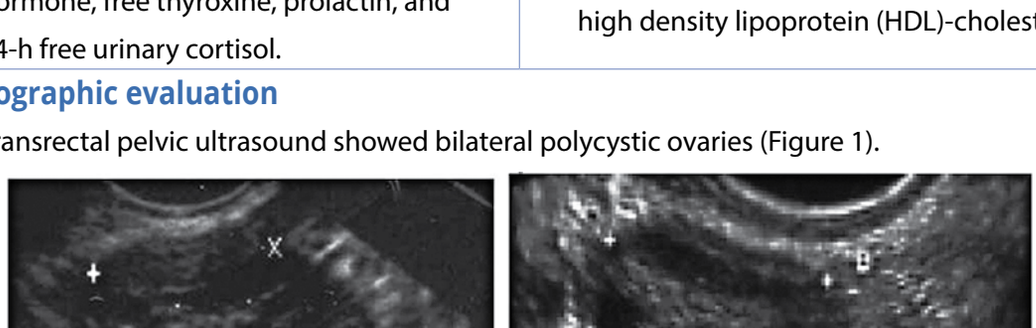


**Figure 1. Polycystic appearance of the patient's right (left panel) and left (right panel) ovaries by ultrasonographic examination**

## Diagnosis

**Secondary amenorrhea with hirsutism and an elevated testosterone level, together with the appearance of polycystic ovaries on ultrasound established the diagnosis of PCOS**

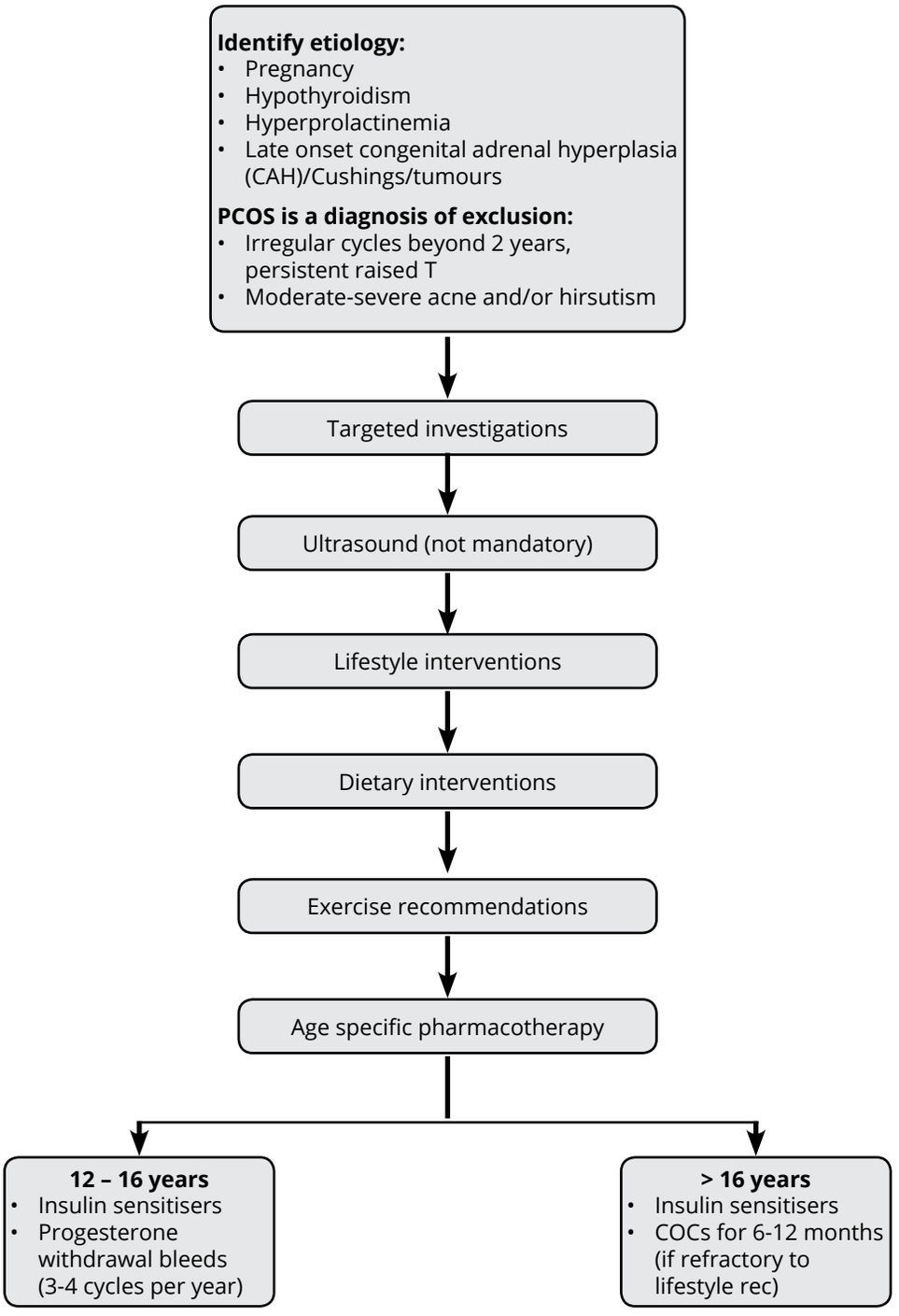
### Intervention

- Lifestyle modifications such as to reduce weight and increase physical activity was suggested.
- D-chiro-Inositol 27.6 mg + Folic acid 100 mcg + Myo-inositol 1100 mg was prescribed to improve insulin sensitivity.
- Dydrogesterone was suggested at days 15–24 of the menstrual cycle to induce menses.

### Follow-up after 6 months

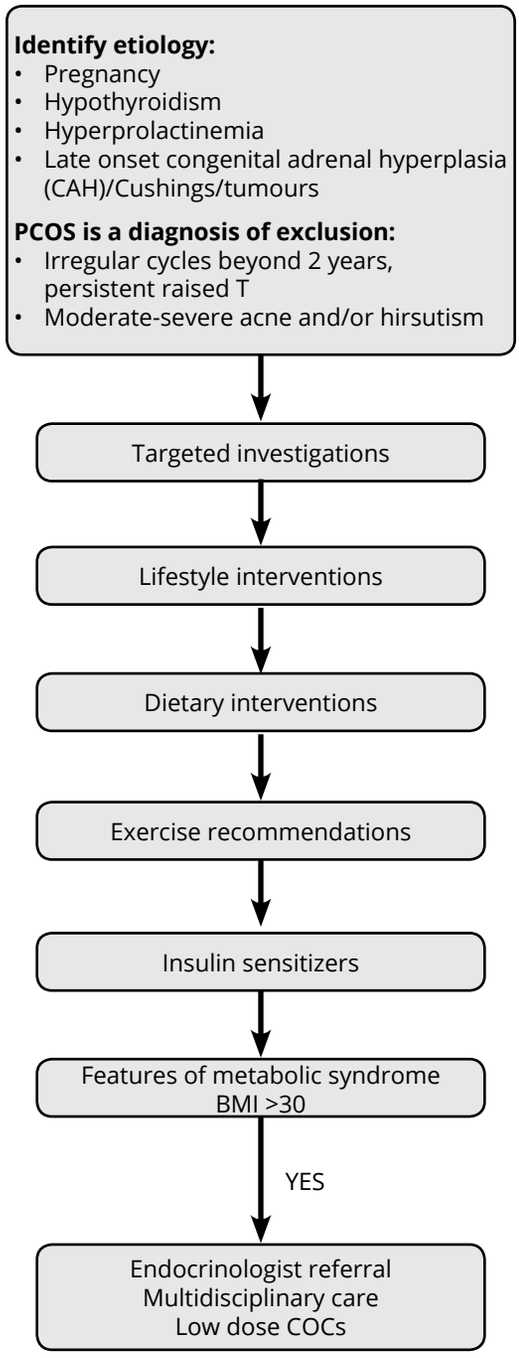
- Weight reduced
- Glucose tolerance improved, hyperinsulinemia ameliorated and there was some improvement in the lipid profile.
- After a year, normal ovulatory menstrual cycles without progesterone medication was reported.

# Irregular cycles, amenorrhoea, and ovulatory dysfunction in adolescents




COCs: combined oral contraceptives.

## Obesity in adolescents




COCs: combined oral contraceptives; BMI: body mass index.

## Irregular cycles and ovulatory dysfunction[1]

Irregular menstrual cycles are defined as:

- Normal in the first year post menarche as part of the pubertal transition
- > 1 to < 3 years post menarche: < 21 or > 45 days
- > 3 years post menarche to perimenopause: < 21 or > 35 days or < 8 cycles per year
- > 1 year post menarche > 90 days for any one cycle
- Primary amenorrhea by age 15 or > 3 years post thelarche (breast development)

When irregular menstrual cycles are present a diagnosis of PCOS should be considered and assessed according to the guidelines.

## Obesity and BMI in Asian Indians

| | Indian | Caucasian |
|---|---|---|
| Normal | 18–23 | 20–25 |
| Overweight | 23–24 | 25–29 |
| Obese | 25–30 | 30–35 |
| Morbidly obese | >30 | >35 |

For diagnosis of Adolescent PCOS, all three components hyperandrogenism, ovulatory dysfunction, and PCO morphology must be present as per Rotterdam criteria.[2, 3]

Accepted diagnostic factors and pathognomonic markers include:[4]

- Early acne or hirsutism; persistent hirsutism
- Persistent severe acne; frequent relapse in acne
- Acanthosis nigricans
- Alopecia
- Family history in sibling and mother
- Obesity and inadequate lifestyle
- Markers of lipid dysregulation

Targeted investigations should include:

| | |
|---|---|
| Urine pregnancy test | Pregnancy |
| FSH LH | Hypo- / hyper- gonadism |
| Prolactin assessment | Hyperprolactinemia |
| Thyroid function tests | Hypothyroidism |
| 17-OH-progesterone | Late onset CAH |
| Lipid profile | Early metabolic syndrome |
| CAH: congenital adrenal hyperplasia; FSH: follicle-stimulating hormone; LH: luteinizing hormone. | |

## Role of ultrasound[1]

- Ultrasound should not be used for the diagnosis of PCOS in those with a gynecological age of < 8 years (< 8 years after menarche), due to the high incidence of multi-follicular ovaries in this life stage.
- The transvaginal ultrasound approach is preferred in the diagnosis of PCOS, if sexually active and if acceptable to the individual being assessed.
- Using endovaginal ultrasound transducers with a frequency bandwidth that includes 8MHz, the threshold for PCOM should be on either ovary, a follicle number per ovary of > 20 and/or an ovarian volume ≥ 10ml, ensuring no corpora lutea, cysts or dominant follicles are present.

- In transabdominal ultrasound in adolescents, reporting is best focused on ovarian volume with a threshold of ≥ 12mL for both ovaries or a single ovary ≥ 15 mL, given the difficulty of reliably assessing follicle number with this approach.[5]

# Obesity management

## Lifestyle interventions[1]

- Lifestyle intervention (preferably multicomponent including diet, exercise and behavioural strategies) should be recommended in all those with PCOS and excess weight, for reductions in weight, central obesity and insulin resistance.
- Achievable goals such as 5% to 10% weight loss in those with excess weight yields significant clinical improvements and is considered successful weight reduction within six months. Ongoing assessment and monitoring is important during weight loss and maintenance in all women with PCOS.
- SMART (Specific Measurable, Achievable, Realistic and Timely), goal setting and self-monitoring can enable achievement of realistic lifestyle goals.

## Dietary intervention[1]

- To achieve weight loss in those with excess weight, an energy deficit of 30% or 500 - 750 kcal/day (1,200 to 1,500 kcal/day) could be prescribed for women, also considering individual energy requirements, body weight and physical activity levels.
- In women with PCOS, there is no or limited evidence that any specific energy equivalent diet type is better than another, or that there is any differential response to weight management intervention, compared to women without PCOS.

## Exercise recommendations[1]

### For weight maintenance

- At least 60 minutes of moderate to vigorous intensity physical activity/day, including those that strengthen muscle and bone at least 3 times weekly.
- Activity should be performed in at least 10-minute bouts or around 1000 steps, aiming to achieve at least 30 minutes daily on most days.

### For weight loss

- Adolescents should aim for a minimum of 250 min/week of moderate intensity activities or 150 min/week of vigorous intensity or an equivalent combination of both, and muscle strengthening activities involving major muscle groups on two non-consecutive days/ week.

### In general

- Daily, 10000 steps is ideal, including activities of daily living and 30 minutes of structured physical activity or around 3000 steps.

- Realistic physical activity SMART (Specific, Measureable, Achievable, Relevant, Time limited) goals could include 10 minute bouts, progressively increasing physical activity 5% weekly, up to and above recommendations.

## Insulin sensitizers[1]

- Insulin sensitizers in additional to lifestyle, could be considered in adolescents with a clear diagnosis of PCOS or with symptoms of PCOS before the diagnosis is made.

Where metformin is prescribed the following need to be considered:

- Adverse effects, including gastrointestinal side-effects that are generally dose dependent and self-limiting, need to be the subject of individualized discussion
- Starting at a low dose, with 500 mg increments 1–2 weekly and extended release preparations may minimize side effects
- Metformin use appears safe long-term, based on use in other populations, however ongoing requirement needs to be considered and use may be associated with low vitamin B12 levels
- Health professionals need to inform women and discuss the evidence, possible concerns and side effects.

## Inositols

The new generation of insulin sensitizers myo- and d-chiro-inositols (MI + DCI ) show significant promise in the correction of hormonal and metabolic abnormalities associated with PCOS. Recent studies have demonstrated that combined supplement containing both MI + DCI in their physiological plasma ratio 40:1 is able to improve the endocrine profile, ovarian function, and the insulin resistance in PCOS patients.[6]

Potential benefits of supplementation of MI/DCI in ratio 40:1[6]

- There is better reduction of insulin resistance, androgens levels, and cardiovascular risk.
- There is better restoration of spontaneous ovulation and menstrual cycle.
- Improvement with combination is more quicker compared to MI alone.
- Better results in terms of weight reduction, resumption of spontaneous ovulation, and spontaneous pregnancy compared with metformin.

A meta-analysis published in 2017 including 9 RCTs with nearly 500 patients showed significant decrease in fasting insulin and testosterone level with increase in SHBG.[7] These results highlight the beneficial effect of MI as regards metabolic profile and hyperandrogenism and hence these molecules can be considered for non-hormonal treatment of adolescent PCOS.

MI and DCI may be considered as alternatives in patients who are unable to tolerate metformin and experience side effects with the traditional drug. More robust data, especially in the Indian population is as yet awaited.

## Bariatric surgery

- Bariatric surgery should be considered an experimental therapy in adult women with PCOS, for the purpose of having a healthy baby, with risk to benefit ratios currently too uncertain to advocate this as fertility therapy.[1]
- It is not recommended in the adolescent age group.
- Rather, multidisciplinary care with an endocrinologist referral and low dose combined hormonal oral contraceptive pills should be considered in obese adolescents with a BMI >30 who are refractory to lifestyle interventions including dietary modifications and exercise.

# CASE 2

## CASE PRESENTATION

*A 16-year-old presented to the clinic with excessive hair growth on the face and body (hirsutism), alopecia, acne, skin problems, and irregular or absent periods. The patient reported to not having menstruated in past 1 year. She craved carbohydrates "all the time," even after eating dinner, and complained that her weight had been increasing over the past year.*

*She had seen a dermatologist for acne on her chin after never having had an acne problem before. She also had visited her primary care physician for dizziness, feeling shaky, and irregular menses. She was already on a birth control pill to regulate her periods. All of these symptoms negatively affected the emotional health of the patient and was damaging her self-image.*

## Examination and investigations

### Family history

- The patient was overweight; and had high BMI

### Laboratory tests

- High serum testosterone and luteinizing hormone levels
- Elevated fasting blood glucose with an abnormal increase during an oral glucose tolerance test (OGTT)
- High TSH
- Abnormal lipid profile; elevated TG, LDL, TC, and Low HDL

### Radiographic evaluation

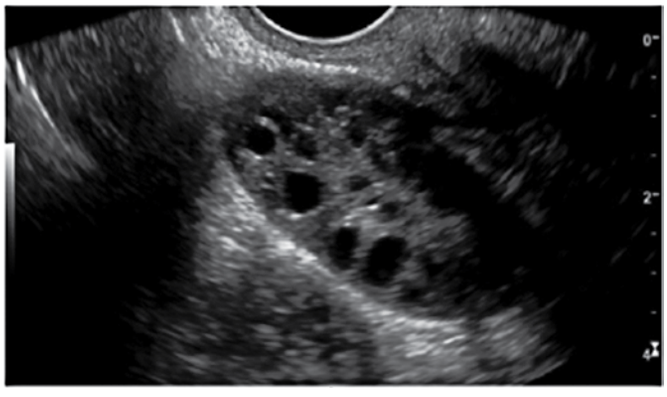


**Figure 1: Transverse ultrasound image of the right ovary demonstrating the classic "string of pearls" appearance of a polycystic ovary.**

## Diagnosis

**PCOS was diagnosed based on menstrual irregularity for over six months, hyperandrogenism; and ultrasonographic appearance of the polycystic ovary.**

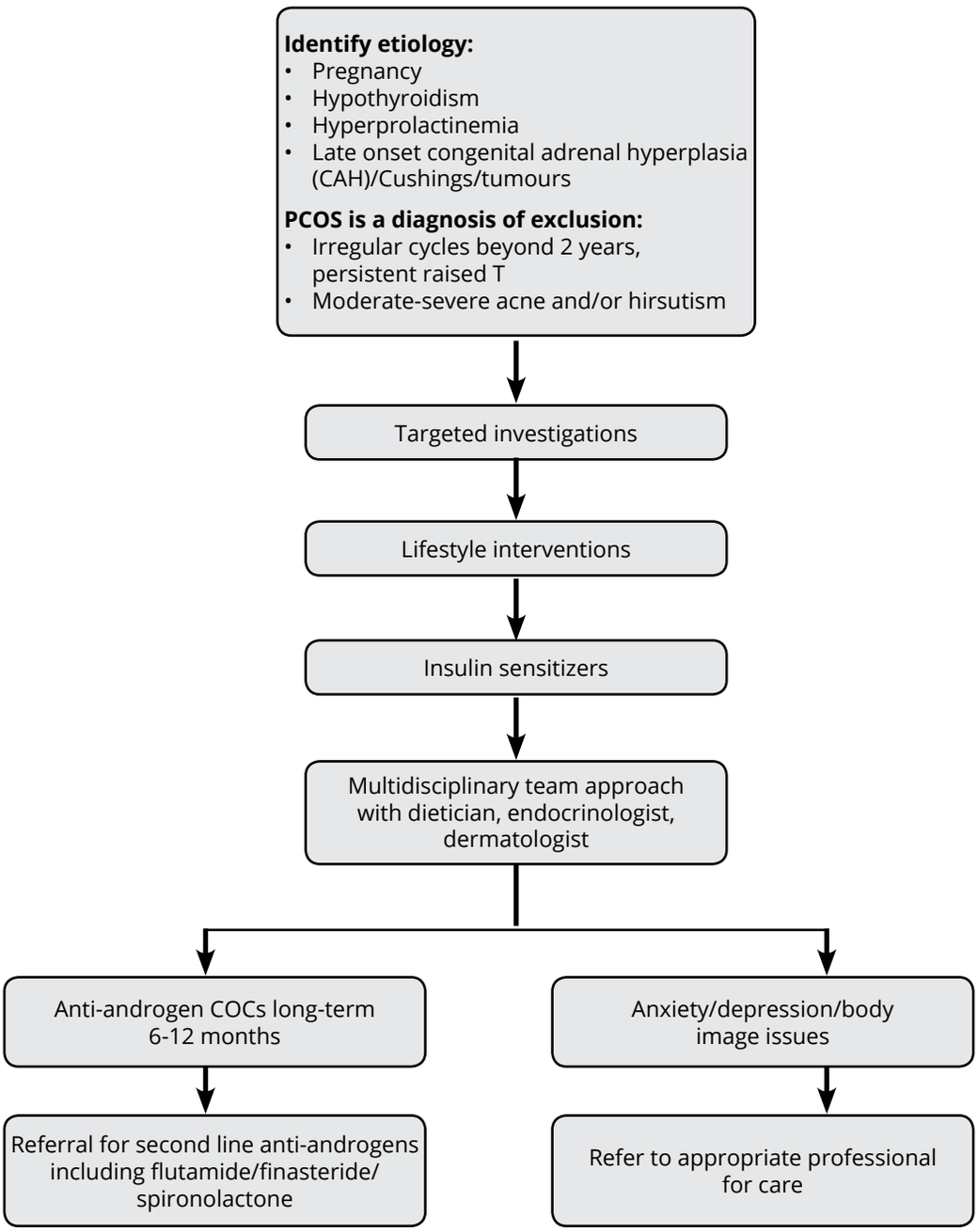
### Intervention

- Exercise, low carbs diet, physical activity
- Contraceptive pills were suggested to be continued
- D-chiro-Inositol 27.6 mg +Folic acid 100 mcg + Myo-inositol 1100 mg was prescribed
- Thyroxine was prescribed to manage hypothyroidism

### Follow-up after 6 months

- Improved glucose tolerance and normalized menstrual cycles after 6 months of treatment.

## Hirsutism and mental health issues in adolescents




## Biochemical hyperandrogenism[1]

- Calculated free testosterone, free androgen index or calculated bioavailable testosterone should be used to assess biochemical hyperandrogenism in the diagnosis of PCOS.
- High quality assays such as liquid chromatography–mass spectrometry (LCMS)/mass spectrometry and extraction/chromatography immunoassays, should be used for the most accurate assessment of total or free testosterone in PCOS.
- Androstenedione and dehydroepiandrosterone sulfate (DHEAS) could be considered if total or free testosterone are not elevated; however, these provide limited additional information in the diagnosis of PCOS.
- Direct free testosterone assays, such as radiometric or enzyme-linked assays, preferably should not be used in assessment of biochemical hyperandrogenism in PCOS, as they demonstrate poor sensitivity, accuracy, and precision.

### Antimullerian hormone (AMH)[1]

- Serum AMH levels should not yet be used as an alternative for the detection of PCOM or as a single test for the diagnosis of PCOS.

## Clinical hyperandrogenism[1]

- A comprehensive history and physical examination should be completed for symptoms and signs of clinical hyperandrogenism, including acne, alopecia and hirsutism and, in adolescents, severe acne and hirsutism.
- Standardized visual scales are preferred when assessing hirsutism, such as the modified Ferriman Gallwey score (mFG) with a level ≥ 4– 6 indicating hirsutism, depending on ethnicity, acknowledging that self-treatment is common and can limit clinical assessment.
- The Ludwig visual score is preferred for assessing the degree and distribution of alopecia.

### Combined oral contraceptives[1]

- The COCP should be considered in adolescents with a clear diagnosis of PCOS for management of clinical hyperandrogenism and/or irregular menstrual cycles.
- The COCP could be considered in adolescents who are deemed "at risk" but not yet diagnosed with PCOS, for management of clinical hyperandrogenism and irregular menstrual cycles.
- In an Indian population, cyproterone acetate is more beneficial in the treatment of acne when compared to drospirenone and desogestrel.[4]

## Anxiety and depression[1]

- Anxiety and depressive symptoms should be routinely screened in all adolescents and women with PCOS at diagnosis.
- If the screen for these symptoms and/or other aspects of emotional wellbeing is positive, further assessment and/or referral for assessment and treatment should be completed by suitably qualified health professionals.
- Assessment of anxiety and or depressive symptoms involves assessment of risk factors, symptoms and severity. Symptoms can be screened using the following stepped approach:

**Step 1: Initial questions could include:**

- Over the last 2 weeks, how often have you been bothered by the following problems?
- Feeling down, depressed, or hopeless?
- Little interest or pleasure in doing things?
- Feeling nervous, anxious or on edge?
- Not being able to stop or control worrying?

**Step 2: If any of the responses are positive, further screening should involve:**

- Assessment of risk factors and symptoms and/or refer to an appropriate professional for further assessment.

## Negative body image[1]

Negative body image, can be screened according to regional guidelines or by using the following stepped approach:

### Step 1: Initial questions could include:

- Do you worry a lot about the way you look and wish you could think about it less?
- On a typical day, do you spend more than 1 hour per day worrying about your appearance? (More than 1 hour a day is considered excessive)
- What specific concerns do you have about your appearance?
- What effect does it have on your life?
- Does it make it hard to do your work or be with your friends and family?

### Step 2: If an issue is identified, health professionals could further assess by:

- Identifying any focus of concern of the patient and respond appropriately
- Assessing the level of depression and/or anxiety
- Identifying distortion of body image or disordered eating

## Eating disorders[1]

Eating disorders and disordered eating can be screened using the following stepped approach:

### Step 1: The SCOFF (Sick, Control, One stone, Fat, Food) screening tool can be used or initial screening questions can include:

- Does your weight affect the way you feel about yourself?
- Are you satisfied with your eating patterns?

### Step 2: If the SCOFF tool or any of these questions are positive, further screening should involve:

- Assessment of risk factors and symptoms
- Referral to an appropriate health professional for further mental health assessment and diagnostic interview

## Behavioural strategies[1]

- Lifestyle interventions could include behavioural strategies such as goal-setting, self-monitoring, stimulus control, problem solving, assertiveness training, slower eating, reinforcing changes and relapse prevention, to optimize weight management, healthy lifestyle and emotional wellbeing in women with PCOS.
- Comprehensive health behavioural or cognitive behavioural interventions could be considered to increase support, engagement, retention, adherence, and maintenance of healthy lifestyle and improve health outcomes in women with PCOS.

## References

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# HORMONAL THERAPY IN MENSTRUAL IRREGULARITIES

**FOGSI President** : **Dr. Nandita Palshetkar**

**Moderators** : **Dr. Rishma Dhillon Pai**

**Dr. Sujata Dalvi**

**Panelists** : **Dr. Ritu Hinduja**

**Dr. Rutvij Dalal**

**Dr. Guruprasad Pednekar**


**From left to right:** Dr. Rutvij Dalal, Dr. Sujata Dalvi, Dr. Rishma Pai, Dr. Ritu Hinduja

# CASE 1

## CASE PRESENTATION

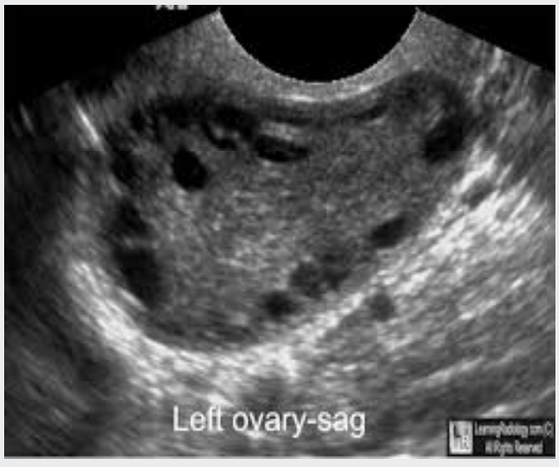
- *27-years-old presented with metabolic syndrome for last 2 years with history of irregular periods*
- *Currently employed at job which involves lot of travelling*
- *Periods at an interval of 30 – 45 – 60 days, spontaneous, with flow lasting for 4 days, heavy on first 2 days with moderate pain*
- *Using barrier methods for contraception since 6 months*
- *No history of acne/extra hair growth*
- *No significant medical/surgical history*
- *Strong family history of diabetes mellitus*
- *Desired to regularize her periods*
- *Was on combined hormonal pills for 1 year which she stopped 6 months ago*

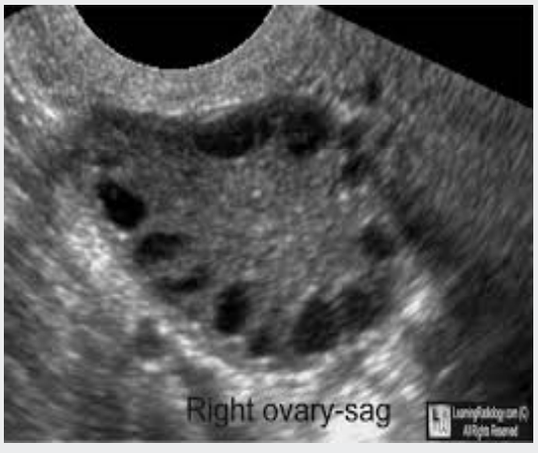
## Past history

### Investigations

- BMI: 27
- Blood profiles were normal except fasting serum insulin which was higher than normal
- Pelvic ultrasound – Both ovaries PCO pattern with ovarian volume 12/14 cc

### Ultrasound of pelvis - ovaries (1 year ago)




- While on combined hormonal pill (EE + cyproterone 2 mg) she complained of weight gain of 5 kgs and depression
- Also put on metformin 500 mg 1 tab daily after breakfast

**Diagnosed as PCOD with menstrual irregularity**

## Present complaints

### Vitals

- BMI - 29
- Vital are normal
- No acne / no hirsuitism/ no acanthosis

### Investigations

- Complete blood count: 9.5 gm/dl
- Anti-Müllerian hormone (AMH) : 6 ng/ml
- Lipid profile
  - » Total cholesterol: 200mg/dl
  - » LDL: 110mg/dl
  - » HDL: 50 mg/dl
  - » Triglycerides: 170 mg/dl
- Fasting insulin: 18 mIU/L
- Fasting blood sugar (FBS): 100 mg/dl
- Postprandial blood sugar: 136 mg/dl
- Glycated hemoglobin ($HbA_{1C}$): 5.9
- Thyroid-stimulating Hormone (TSH): 1.5 mIU
- Prolactin (PRL): 23 ng/ml
- Repeat sonography: Uterus normal, ovaries bulky, ovarian volume of 14 and 16 cc, peripherally arranged multiple follicle > 18 per ovary

## Diagnosis: Polycystic ovarian disease with irregular menstrual cycles

### Intervention

- Life style modification
  - » Diet: Low carbohydrate/high fibre/carbohydrate with low glycemic index/lots of fruits and vegetables
  - » Increase in physical activities
  - » Leisure time physical activities such as walking or cycling, occupational work, household chores, games, sports or planned exercise, in context of daily, family and community activities with 10,000 steps per day being ideal
  - » Activity must be performed in at least 10 minutes bouts or around 1000 steps, aiming to achieve at least 30 minutes daily on most days
- Oral iron therapy (sodium feredetate)
- Continue metformin - started at 500 mg per day gradually increased to three times daily
- Inositol (in any form) should currently be considered an experimental therapy in women with PCOS
- However many studies suggest benefit of Inositols for improving symptoms of PCOS
- Dydrogesterone 10 mg BD starting from 15$^{th}$ day of her periods for 10 days to be continued for 6 months

## Discussion

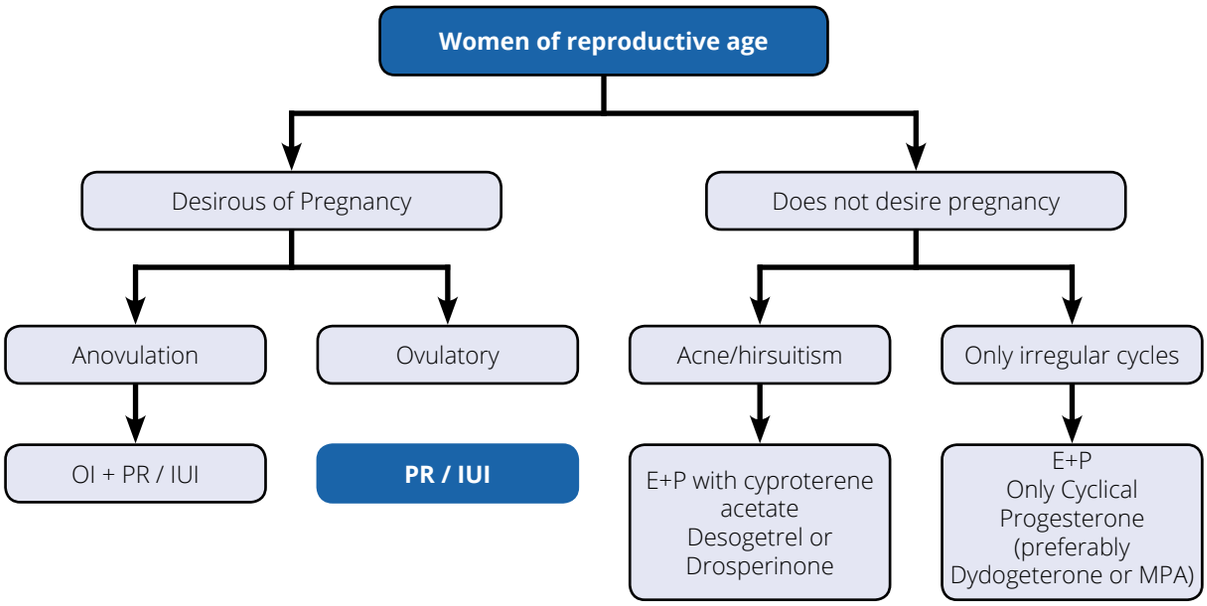
- Serum anti-Müllerian hormone (AMH) levels NOT to yet to be used as an alternative for detection PCOS or as single test for diagnosis of PCOS
- With improved standardization of assays - it may become useful test in future
- Using ultrasound transducers with a frequency > 8MHz, threshold for PCOS should be follicle number per ovary of ≥ 18 and/or an ovarian volume > 10 ml, ensuring no corpora lutea, cysts or dominant follicles are present in one or both ovaries
- In patients with irregular menstrual cycles and hyperandrogenism, an ovarian ultrasound is not necessary for PCOS diagnosis; however ultrasound will identify complete PCOS phenotype

## Treatment options

### The European Society of Human Reproduction and Embryology (ESHRE) Guidelines

- 35 μg ethinyl estradiol and cyproterone acetate preparations should not be considered first-line in adults and adolescents with PCOS as per general population guidelines
- Other combined COCs using EE with drospirenone or desogestrel have similar anti-androgenic effects, regulation of periods and relief of PCOS symptoms, however, the risk of thrombosis and alteration of lipid profile should be taken into consideration.
- Lower dose estrogen preparations and natural estrogen preparations (such as 20–30 mcg of ethinyl estradiol or equivalent) should be considered balancing efficacy, metabolic risk profile and side effects
- In combination with combined hormonal pills, metformin should be considered in women with PCOS for management of metabolic features or if BMI >25
- Metformin use appears safe long-term and its use maybe associated with low vitamin B12 levels
- Use of dydrogesterone cyclically for 10-12 days every month in patients with no obvious signs of PCOS except for irregular periods, will help regularize menstrual cycles
- Side-effects of weight gain, bloating and depression which are often faced by patients on combined O C pills will not be encountered
- Use of dydrogesterone - diminished risk of thromboembolism
- As this patient is using only barrier method of contraception, in case of accidental pregnancy, dydrogesterone will be safe

## PCOD




DRAFT International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome 2018

OI: ovulation induction; IUI: intrauterine insemination; PR: pregnancy rate; MPA: medroxyprogesterone acetate; E: estrogen; P: progestogen

# CASE 2

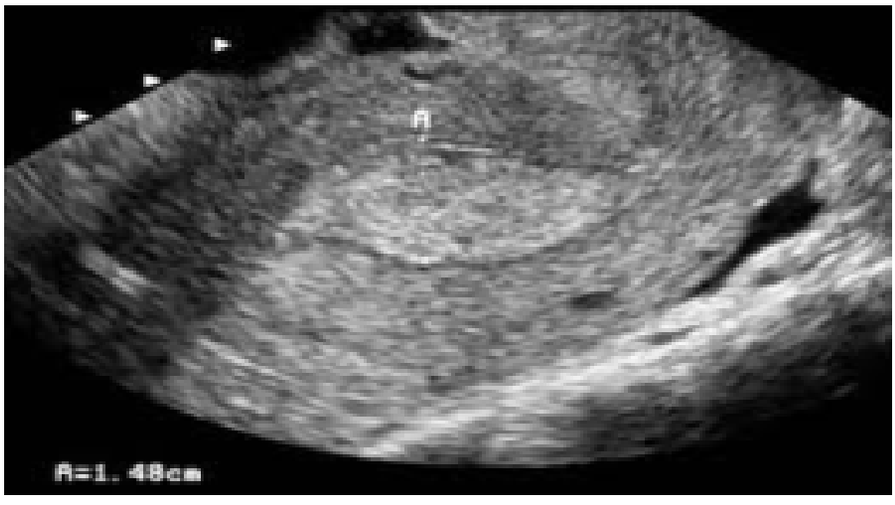
## CASE PRESENTATION

- *A 45-year-old woman, married since last 20 years*
- *Complaints of heavy menstrual flow with history of passing blood clots on first 3 days of periods with lower abdominal pain and low backache since last 6 months*
- *Cycles are irregular at an interval of 20–45 days*
- *Has 2 FTND – conceived with treatment*
- *Tubal ligation done*
- *Family hitory of diabetes*
- *Known hypertensive – On treatment since last 1 year*

## Examination

| Investigations | Investigations |
|---|---|
| • BMI: 30<br>• BP – 130/90 mmHg<br>• Mild pallor<br>• Clinically bulky uterus with clear fornices | • Hemoglobin: 9 gm%, platelets adequate<br>• Fasting blood sugar/Postprandial blood sugar – Normal<br>• Thyroid-stimulating hormone (TSH)/Prolactin (PRL): Normal<br>• Coagulation profile - Normal<br>• Respiratory function tests (RFTs)/Liver function tests (LFTs)/lipid profile: Normal<br>• Transvaginal sonography (mid cycle ): Bulky uterus with ET of 15 mm<br>• Both ovaries - Normal |

**Transvaginal sonography (TVS) – thickened endometrium**




**Pap smear and mammography normal**

**Diagnosed as abnormal uterine bleeding (AUB - O), ovulatory dysfunction**

## Classificaton of menorrhagia

| Underlying cause | Characteristics | Treatment |
|---|---|---|
| Ovulatory | | • Nonsteroidal anti-inflammatory drugs<br>• Anti-fibrinolytics<br>• COCPs<br>• Endometrial ablation<br>• Hysterectomy |
| Anovulatory | • Irregular bleeding, often heavy<br>• More common in adolescents and perimenopausal women<br>• Higher-risk of endometrial hyperplasia | • COCPs<br>• LNG-IUS<br>• Cyclic progestins<br>• Androgens<br>• Gonadotropin-releasing hormone agonists<br>• Endometrial ablation<br>• Hysterectomy |
| Anatomic | • Caused by fibroids, polyps, or adenomyosis<br>• Often heavy bleeding, pain<br>• Uterus might be enlarged | • COCPs<br>• Anti-fibrinolytics<br>• LNG-IUS<br>• Androgens<br>• Gonadotropin-releasing hormone agonists<br>• Uterine fibroid embolization<br>• Myomectomy<br>• Hysterectomy |

COCPs Combined oral contraceptive pills, LNG-IUS: levonorgestrel intra-uterine system

## Management

- Lifestyle modification for weight loss
- Iron supplementation
- Diagnostic hysteroscopy with endometrial sampling - HP report 'simple endometrial hyperplasia'
- Hormonal therapy
- Associated therapy: Tranexamic acid

### Treatment options

- Levonorgestrel-releasing intrauterine system (LNG-IUS) for a period of 5 years is recommended
- However, this patient has had bad experience with Copper-T and despite counsellig, did not want any intra-uterine device

- Cyclic progesterone therapy for 10-12 days every month to be continued for a period of 6-9 months
- Medroxyprogesterone acetete (MPA) 10 mg daily or Norethisterone 10 mg daily or Dydrogesterone 10-20 mg bid - any can be recommended

## Discussion

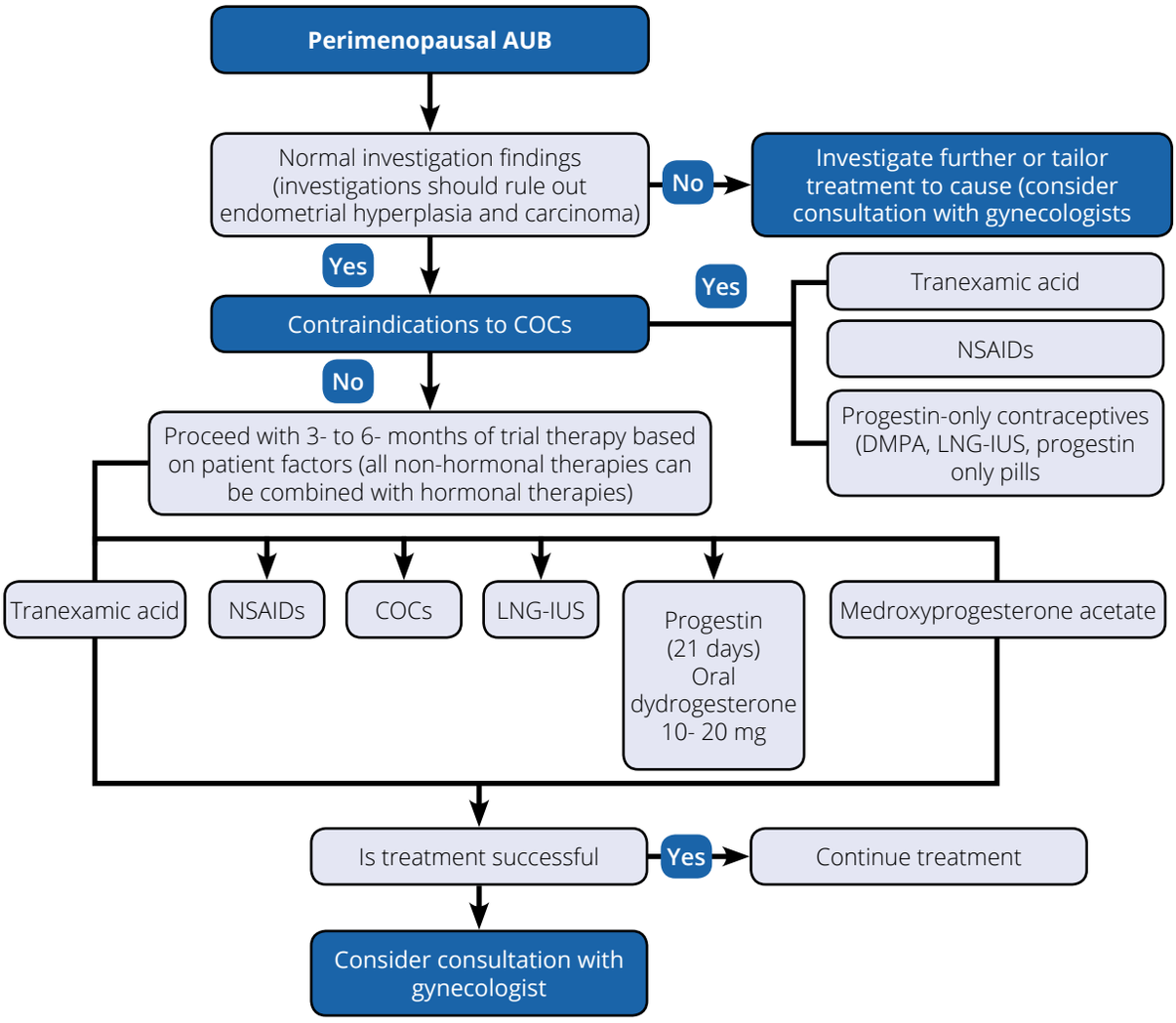
### NICE Guidelines 2018

- Consider an LNG-IUS as first treatment for heavy menstrual bleeding in women with no identified pathology or fibroids less than 3 cm in diameter, which are not causing distortion of uterine cavity or suspected or diagnosed adenomyosis
- If woman with heavy menstrual bleeding declines an LNG-IUS or it is not suitable, consider following pharmacological treatments
  - » Non-hormonal
    - — Tranexamic acid
    - — NSAIDs (non-steroidal anti-inflammatory drugs)
  - » Hormonal
    - — Combined hormonal contraception
    - — Cyclical oral progestogens
- This patient, combined contraceptive pills might not be recommended due to her age, hypertension history and presence of endometrial hyperplasia
- Many different oral progesterone agents can be effectively used in patients with peri-menopausal menstrual irregularities
- Dydrogesterone regularizes and improves duration of menstrual cycle, reduces amount of bleeding, relieves menstrual pain and prevents relapse of irregular cycles at six months after discontinuation of treatment
- Medroxyprogesterone acetate is beneficial, however, previous history of breast cancer, thrombosis and impaired liver function is contraindication
- Norethisterone, in dose of 5 mg tid, from cycle day 5–26 of menstrual cycle can be used for treatment of perimenopausal menstrual irregularity. However, it can worsen fluid retention and hence cause problems in patients with hypertension, migraine, epilepsy. Contraindications for its use are thromboembolism, liver disease, and breast cancer
- In non-complaint patients, usage of injectable depomedroxyprogesterone acetate (DMPA) 150 mg once every 3 months can be considered

- Endometrial ablation will give relief from menorrhagia, however, will not take care of hyperplasia which will still need to be monitored
- To monitor patients with endometrial hyperplasia, apart from TVS, endometrial (pipelle) biopsy should be considered
- Lastly, hysterectomy would be last resort

| Medication | Action |
|---|---|
| **NSAIDs**<br>• Mefenamic acid 250 mg<br>• Naproxen 250–275 mg<br>• Ibuprofen 200–400 mg<br>• Dose: 1–2 tablets before or at beginning of menses, then 1 tablet ever 6–8 hrs as required | • Inhibit prostaglandin synthesis, might also alleviate menstrual pain<br>• No evidence of difference in clinical efficacy of individual NSAIDs |
| **Antifibrinolytics**<br>• Tranexaic acid (500 mg-1000 mg every 6–8 h as required | • Counteract increased fibronolytic activity, significantly reduce mean blood loss compared with placebo, NSAIDs (mefenamic acid), and oral luteal phase progestins (level 1 evidence) |
| **Combined oral contraceptives** | • Useful for anovulatory bleeding, might have benefit for ovulatory bleeding (although lack of good-quality data) |
| **Progestins**<br>• Levonorgestrel intrauterine system<br>**Oral progestins**<br>• Medroxyprogesterone acetate (5–10 mg/d for 10–14 days initially and repeated for 10 days) | • Stabilizes endometrium<br>• T-shaped intrauterine device releases a steady amount of levonorgestrel (20 mcg/24 h), low level of circulating hormone minimizes systemic side effects, training in insertion is advised |
| • Oral dydrogesterone 10–20 mg | • Induce regular menstrution with symptomatic relief, reduces blood loss and reduce days of bleeding<br>• Represses reactive oxygen species formulation, exerts modulating effects on nitric oxide synthesis and on the expression of endothelial nitric oxide synthase<br>• Reduces severity of menstruation-related symptom (lower abdominal pain, low back pain, headache, nausea/vomiting) |

IM: intramuscularly, NSAIDs: nonsteroidal anti-inflammatory drugs, SC: subcutaneously

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# LUTEAL PHASE SUPPORT

**FOGSI President** : Dr. Nandita Palshetkar

**Moderators** : Dr. Nandita Palshetkar

Dr. Hrishikesh Pai

**Panelists** : Dr. Kundan Ingale

Dr. Nilan Rodrigo

Dr. Milind Colvalkar

Dr. Rohan Palshetkar

Dr. Manisha Kundnani

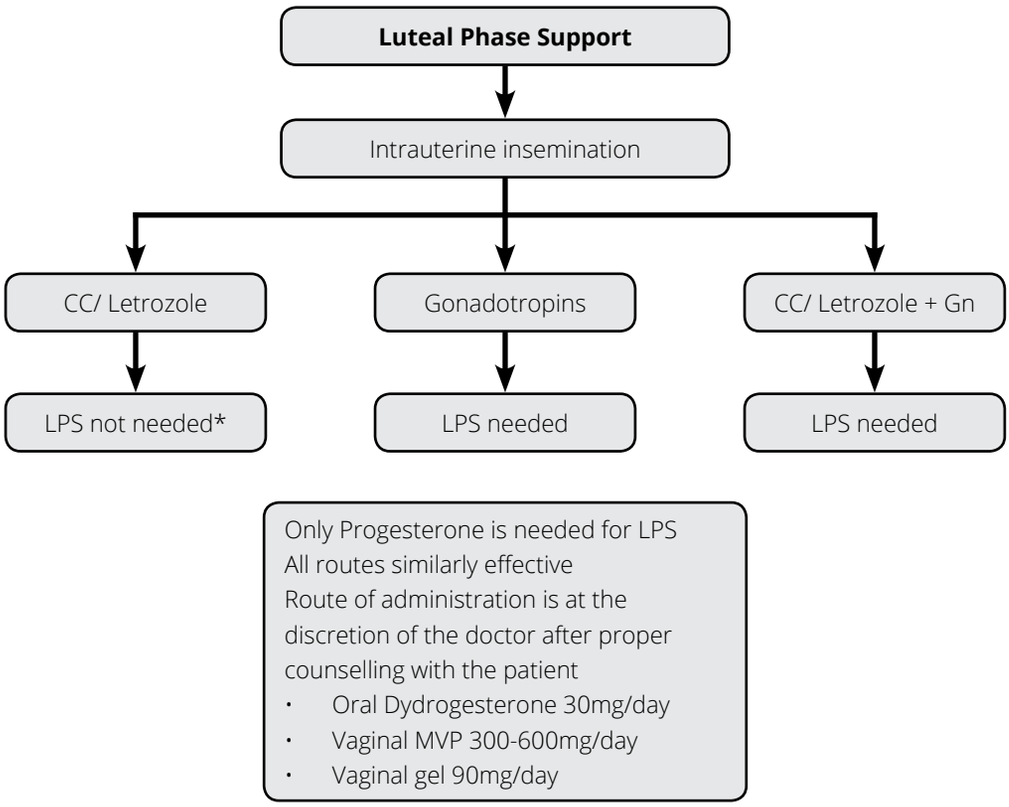
Dr. Padam Raj Pant


**From left to right:** Dr. Padam Raj Pant, Dr. Milind Kolwalkar, Dr. Manisha Kundnani, Dr. Hrishikesh Pai, Dr. Nandita Palshetkar, Dr. Nilan Rodrigo, Dr. Kundan Ingale, Dr. Rohan Palshetkar

# CASE 1

## CASE PRESENTATION

- *A 30-year-old female married since 3 years with regular menstruation. Endocrine profile normal, HSG shows b/l patent tubes. HSA is normal. BMI is 26. Past history of 5-6 cycles of OI+PR without any resultant pregnancy.*
- *She underwent OI with CC+HMG, hCG trigger was given when two leading follicles were more than 17 mm. IUI was done 36 hours later. Dydrogesterone 10 mg TID was started on the day of IUI. It was continued for 14 days. β-hCG was positive after 14 days. Luteal Support was continued until 12 weeks gestation. USG at 6 weeks showed single live intrauterine gestation.*




*In LPD/PCOS cases, LPS is needed even if CC/Letrozole is alone

CC: clomiphene citrate; LPS: luteal phase support; Gn: gonadotropins; MPV: micronized vaginal progesterone

# CASE 2

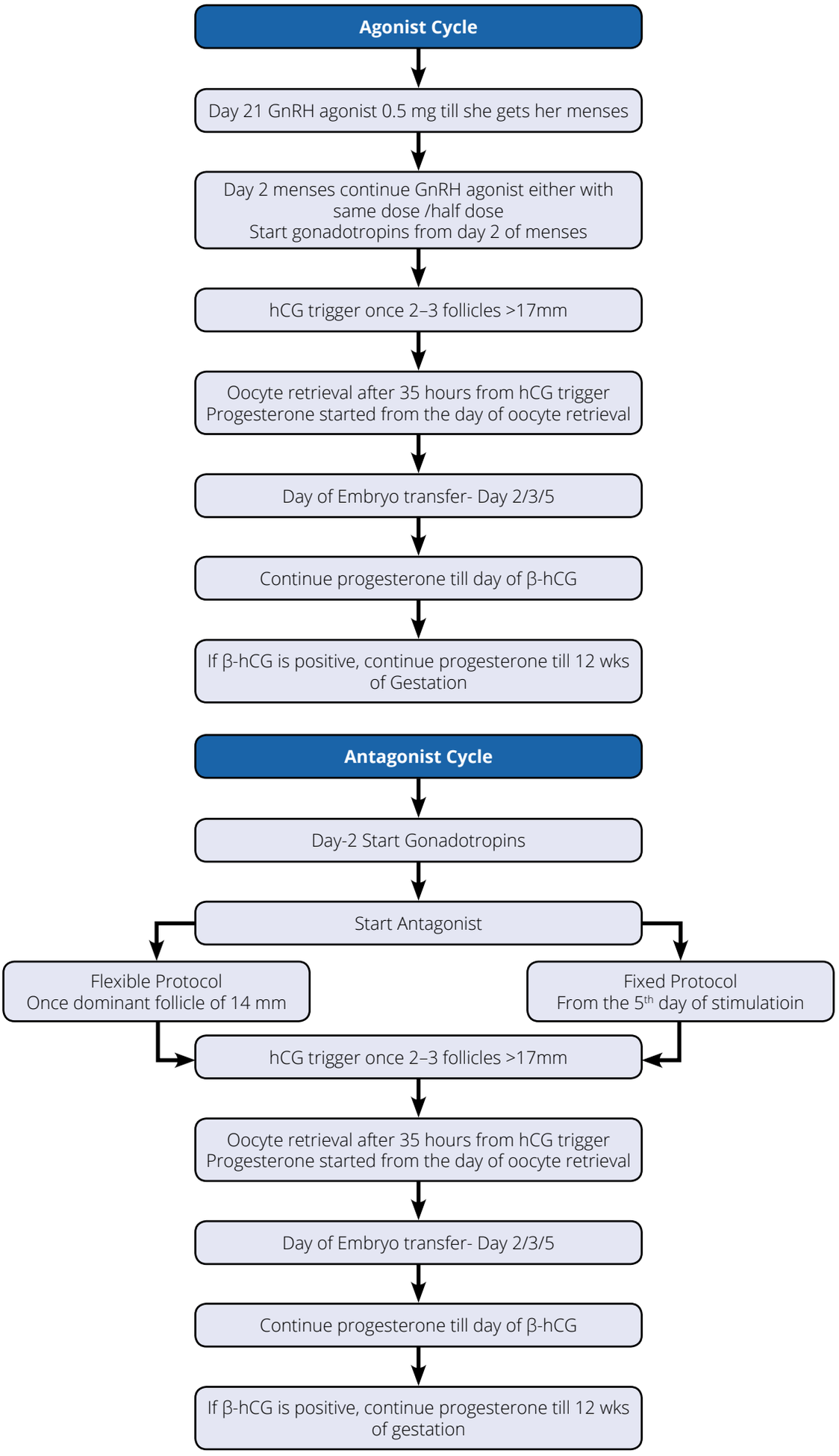
## CASE PRESENTATION

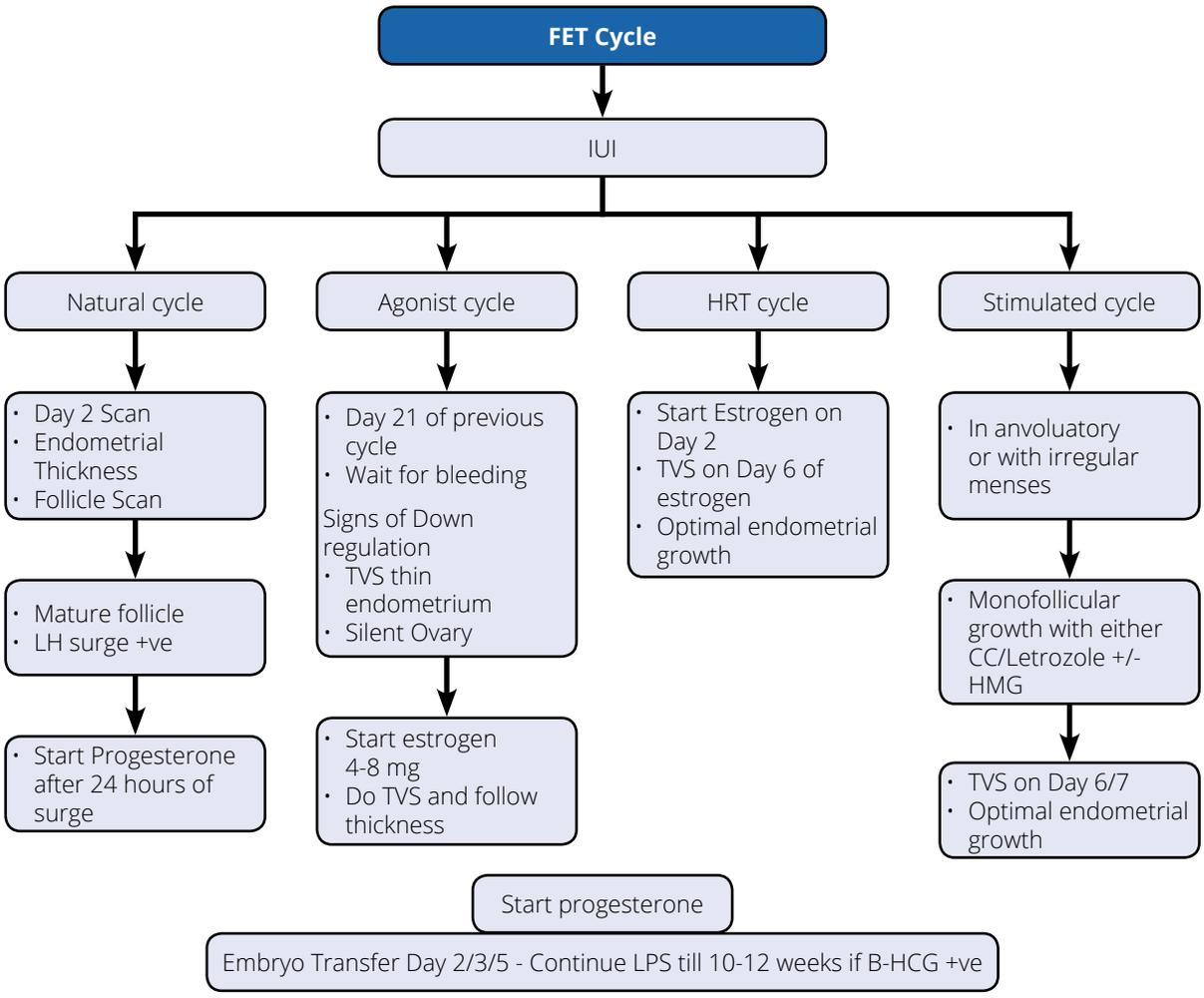
- *A 35-year-old married since 6 years with regular menstruation with husband semen analysis of 2 million with 10% motility. Endocrine profile is normal. USG shows no significant pelvic pathology.*
- *AMH: 2.65 ng/ml. AFC 8-10 in each side.*

## Discussion

The patient was recommended to undergo In vitro fertilisation (IVF)-Intracytoplasmic sperm injection (ICSI) cycle as it was a case of severe male factor infertility. Patient was subjected to antagonist protocol. Due to mild hyperstimulation, agonist trigger was given.

- Antagonist protocol was used.
- Patient went into mild ovarian hyperstimulation syndrome (OHSS) due to which agonist trigger was used.
- Oocyte pick-up (OPU) was done after 36 hours.
- ICSI was performed and all embryos were frozen and patient was started on cabergolin.
- Subsequent cycle frozen-thawed embryo transfer (FET) was planned after endometrial preparation by hormone replacement therapy (17-β estradiol, estradiol valerate 2 mg TID).
- Once optimal endometrial thickness was attained, dydrogesterone 10 mg TID was started.
- Embryo transfer was done after 5 days.
- Estrogen and progesterone support was continued.
- Beta-human chorionic gonadotropin (β-hCG) was positive after 2 weeks.
- Luteal phase support continued till 12 weeks.


Agonist Cycle
Day 21 GnRH agonist 0.5 mg till she gets her menses
Day 2 menses continue GnRH agonist either with same dose /half dose
Start gonadotropins from day 2 of menses
hCG trigger once 2–3 follicles >17mm
Oocyte retrieval after 35 hours from hCG trigger
Progesterone started from the day of oocyte retrieval
Day of Embryo transfer- Day 2/3/5
Continue progesterone till day of β-hCG
If β-hCG is positive, continue progesterone till 12 wks of Gestation
Antagonist Cycle
Day-2 Start Gonadotropins
Start Antagonist
Flexible Protocol
Once dominant follicle of 14 mm
Fixed Protocol
From the 5th day of stimulatioin
hCG trigger once 2–3 follicles >17mm
Oocyte retrieval after 35 hours from hCG trigger
Progesterone started from the day of oocyte retrieval
Day of Embryo transfer- Day 2/3/5
Continue progesterone till day of β-hCG
If β-hCG is positive, continue progesterone till 12 wks of gestation




B-HCG: beta-human chorionic gonadotropin; CC: Clomiphine citrate; FET: frozen-thawed embryo transfer; HMG: human menopausal gonadotropin; HRT: hormone replacement therapy; LPS: luteal phase support; TVS: transvaginal sonography.

## Management

| Drugs | Dose | Benefits |
|---|---|---|
| **1. Oral**<br>Dydrogesterone | 30 mg/day | • Better bioavailaiblity<br>• No estrogenic, androgenic, corticoid activity<br>• Better pre-gestational and immunomodulatory activity |
| **2. Vaginal Progesterone**<br>a. Micronized progesterone capsule | 300–600 mg/day | • Bypass 1st pass metabolism<br>• Higher concentration in uterine circulation |
| b. Micronized Progesterone gel | 90 mg/day | • Same as above |
| **3. Injectable**<br>a. Micronized Progesterone (oil based) IM | 50–100 mg/day | • High plasma concentration |
| b. Micronized Progesterone (oil based) SC/IM | 25–50 mg/day | • High plasma concentration<br>• Pain at injection site |

| Drugs | Dose | Benefits |
|---|---|---|
| **1. Oral** | | |
| a. Estradiol Hemihydrate | Starting Dose - 4–8 mg/day<br>Maximum Dose - 12 mg/day | • Better compliance<br>• Minimum liver load |
| b. Estradiol Valerate (2 mg) | Starting Dose - 4–8 mg/day<br>Maximum Dose - 12 mg/day | • Better compliance |
| **2. Transdermal**<br>a. 17-β Estradiol | Starting Dose - 4–8 mg/day<br>Maximum Dose - 12 mg/day | • Decreases the chance of deep vein thrombosis and venous thromboembolism in post menopausal and older women |

## Conclusion

- LPS has been proven to be necessary in ART.
- The modalities may be adding progesterone, GnRH agonists, and estrogen.
- Progesterone can be supplemented administerd orally, vaginally, intramuscular or subcutaneous, oral route is preffered.
- Dydrogesterone is recommended for LPS as it has minimal side-effects, better bio-availability, and comparable outcomes.
- We recommend that LPS should be continued until 12 weeks.

# BLEEDING IN FIRST-TRIMESTER

**FOGSI President** : Dr. Pratap Kumar
**Moderators** : Dr. Ameya Purandare
**Panelists** : Dr. Geeta Gurung
Dr. Rajendra Nagarkatti
Dr. Dilip Walke
Dr. Selvapriya Saravanan
Dr. Parita Dalvi


**From left to right:** Dr. Dilip Walke, Dr. Rajendra Nagarkatti, Dr. Pratap Kumar, Dr. Ameya Purandare, Dr. Geeta Gurung (Nepal), Dr. Parita Dalvi, Dr. Selvapriya Saravanan

# CASE 1

## CASE PRESENTATION

- *29-year-old Primi*
- *10 weeks pregnancy*
- *Vaginal bleeding*
- *Mild abdominal pain*
- *No other medical/surgical illness*
- *Receiving prenatal care from her obstetrician*

- Bleeding is common complication in 1st trimester (1 in 3)
- Ominous threat to both fetus and mother

## Examination and investigations

| **General condition/vital signs** | **Investigations** |
|---|---|
| • Pulse<br>• BP<br>• Pallor<br>• PA | • USG Pelvis- TA or TVS (preferable)<br>• CBC<br>• Blood group and Rh<br>• B-hCG<br>• PT INR (selected cases such as in cases of missed abortion and patients on anticoagulants) |
| **USG Pelvis**<br>• SLIUG of 10 weeks<br>• Following are seen<br>» Gestational sac<br>» Yolk sac<br>» Trophoblastic rim<br>» Embryo with fetal cardiac activity<br>» Small sub chorionic bleed (3 x 0.5 cm) noted | **Diagnosis: Threatened abortion** |

BP: blood pressure; CBC: complete blood count; hCG: human chorionic gonadotropin; SLIUG: single live intrauterine gestation; PT: prothrombin time; TA: transabdominal; TVS: transvaginal; USG: ultrasonography.

# Management

## Progesterone[1]

- Treatment of miscarriage with progestogens (dydrogesterone) compared to placebo or no treatment probably reduces the risk of miscarriage; (RR 0.64, 95% CI: 0.47 to 0.87; 7 trials; 696 women; moderate-quality evidence).
- Progestogens are probably effective in the treatment of threatened miscarriage but may have little or no effect in the rate of preterm birth.
- Progesterone use not associated with significant risk of congenital anomalies.

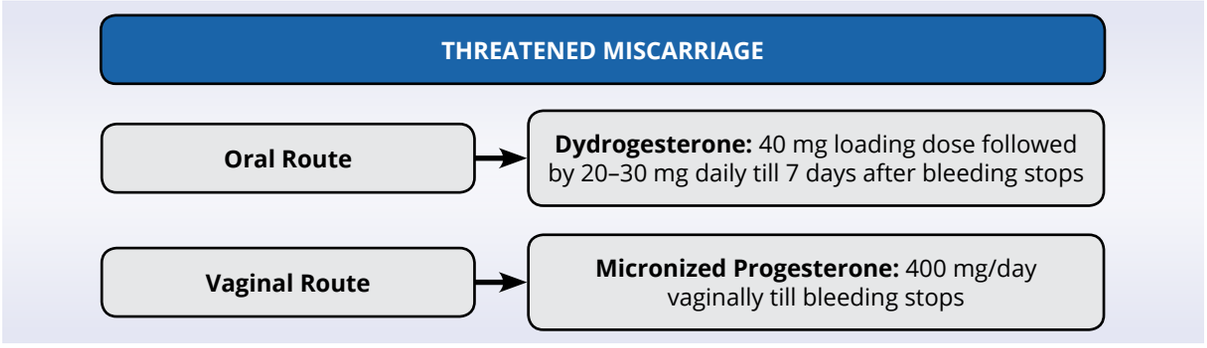
## Threatened miscarriage – Progesterone studies, meta-analyses, and guidelines

| Studies | Length of dydrogesterone treatment | Miscarriage rate | | p value |
|---|---|---|---|---|
| Omar[2] | Until bleeding stopped | 4.1% | 13.8% | p=0.037 |
| El-Zibdeh[3] | 1 week after bleeding stopped | 17.5% | 25.0% | p≤0.05 |
| Pandian[4] | Until week 16 | 12.5% | 28.4% | p<0.05 |

| Meta-analysis | Studies included | Results | |
|---|---|---|---|
| Wahabi 2011[1] | 2 vaginal progesterone (n=84)<br>2 dydrogesterone (n=337) | Significant reduction of miscarriage by progestogens vs. placebo or no treatment | 0.53 (CI = 0.35–0.79) |
| Carp 2012[5] | 5 dydrogesterone (n=660) | Significant reduction with dydrogesterone for miscarriage compared to standard care | 0.47 (CI = 0.31–0.7) |
| Lee HJ et al[6] | Randomized trials (n=9)<br>Vaginal progesterone vs. placebo<br>Oral dydrogesterone vs. placebo | Incidence of miscarriage was significantly lower with oral dydrogesterone | 11.7% vs 22.6%; odds ratio, 0.43; 95% CI, 0.26 to 0.71; p=0.001; $I^2$, 0%) |
| Wang XX et al[7] | Randomized controlled trials (n=8)<br>Dydrogesterone vs natural progesterone and vaginal progesterone | Dydrogesterone reduced the risk of miscarriages than natural progesterone compared to vaginal administration | RR = 0.55, 95% CI 0.38-0.79<br>RR = 0.58, 95% CI 0.28-1.21 |

| Guidelines | Recommendation |
|---|---|
| 2013 Australian and New Zealand Guidelines[8] | For women presenting with a clinical diagnosis of threatened miscarriage, there is now preliminary evidence of a reduction in the rate of spontaneous miscarriage with the use of progestins |
| 2015 European Progestin Club Guidelines for the Treatment of Threatened Miscarriage[9] | For women presenting with a clinical diagnosis of threatened miscarriage, there is a reduction in the rate of spontaneous miscarriage with the use of dydrogesterone |

## Progesterone: FOGSI position statement 2015[10]




A number of small clinical trials have shown that progesterone therapy improves pregnancy outcomes in women with bleeding in early pregnancy. The PRISM Current Controlled Trials supported by National Institute for Health Research Health Technology Assessment program, a multicenter, randomized, double-blind, placebo-controlled trial evaluated progesterone vs with placebo in women with vaginal bleeding in early pregnancy. The study included 4,153 women who were assigned to receive progesterone (2,079 women) or placebo (2,074 women). The incidence of live births after at least 34 weeks of gestation was 75% in the progesterone group as compared to 72% in the placebo group. The study reported that for women with bleeding in early pregnancy, progesterone therapy administered during the first trimester did not result in a significantly higher incidence of live births as compared to placebo.[11]

However, as mentioned earlier, the meta-analysis and Cochrane review have reported that dydrogesterone is known to be effective to reduce miscarriage rate.[1,5-7]

## Follow-up

The patient was adviced for:

- Follow-up after 2 weeks, if no further bleeding/SOS
- Repeat ultrasound after 2 weeks/SOS
- Progesterone to be continued
    - » Till 12 weeks or till vaginal bleeding ceases, whichever is later
    - » To be continued in the presence of sub-chorionic bleed
- Strict bed rest not mandatory
- Coitus and strenuous activity to be avoided
- Continue folic acid

# CASE 2

## CASE PRESENTATION

- *39-year-old, primigravida with Rh-negative*
- *6 weeks pregnancy*
- *In vitro fertilization (IVF) conception on tablet aspirin and Injection low-molecular-weight heparin (LMWH)*
- *Post coital spotting PV that lasted for 1 day*
- *No passage of tissue or clot like material*
- *Mild abdominal pain*

## Examination

| Vitals | Lab tests |
|---|---|
| **Gentle per speculum exam**<br>• Bleeding from OS present, polyp ruled out<br>**Per vaginal examination**<br>• Uterine size approximately 6 weeks, cervical os closed, cervix long<br>• Ultrasound showing<br>• Single IU gestational sac less than 6 weeks [Mean sac diameter (MSD): 18 mm]<br>• Foetal pole not visualized at present. | • Complete blood count: Normal<br>• Quantitative beta-human chorionic gonadotropin (B-hCG) levels were 2400 IU/L and repeat values done after 48 hours were 3100 IU/L<br>• Husbands blood grouping and Rh typing was done |
| **Diagnosis: A case of threatened abortion in the first-trimester** | |
| **Intervention**<br>• Withhold aspirin and LMWH<br>• Tablet dydrogesterone 40 mg stat followed by 10 mg three times a day till 12 weeks of pregnancy<br>• Strict bed rest is not mandatory<br>• Restricted activity and avoid coitus<br>• Injection Anti-D 100–300 microgram intramuscular | **Follow up**<br>HCG and ultrasound as per algorithm |

# CASE 3

## CASE PRESENTATION

- *28-year-old, G3A2*
- *2 months pregnancy*
- *History of first trimester abortions*
- *Complaint of single episode of spotting PV the previous day*

## Examination

| Vitals | Lab tests |
|---|---|
| • Normal<br>• Per speculum: No bleeding at present<br>• Per vaginum: Uterine size approximately 6 weeks, cervical os closed<br>• Ultrasound: Single intrauterine gestation showing CRL 7 mm with cardiac pulsations, Subchorionic haematoma (3cm x 0.5cm) | • Complete blood count with blood grouping and Rh typing<br>• Serum HCG levels |

**Diagnosis: A case of threatened abortion**

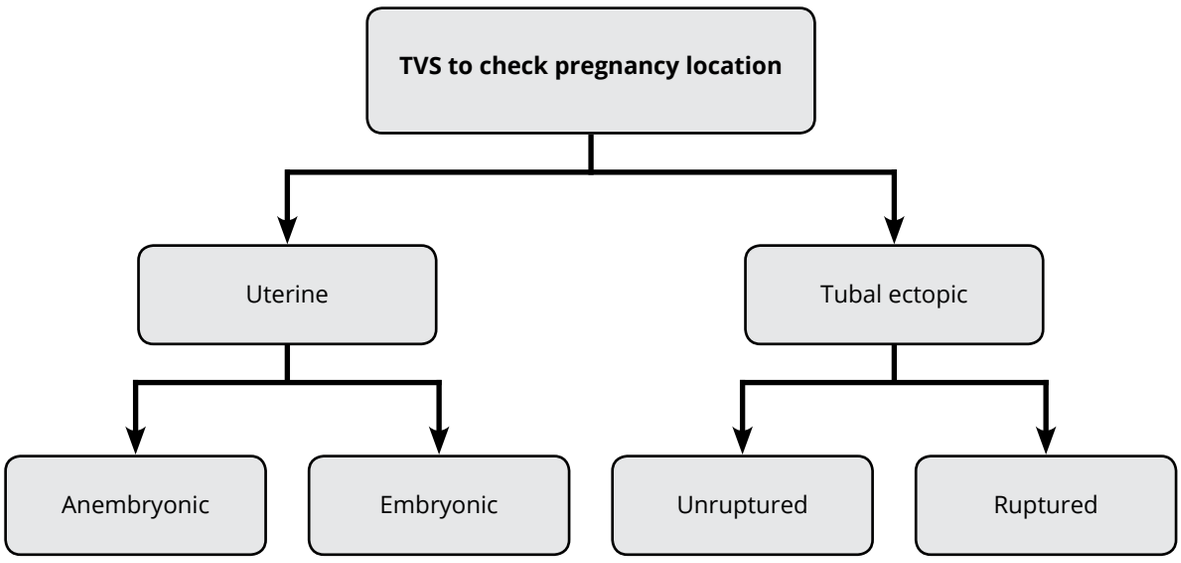
**Intervention**

- Tablet dydrogesterone 40 mg stat followed by 10 mg three times a day till 12 weeks of pregnancy
- Strict bed rest is not mandatory
- Restricted activity and avoid coitus
- Follow up ultrasound for resolution of hematoma
- Further evaluation and appropriate management for recurrent pregnancy loss

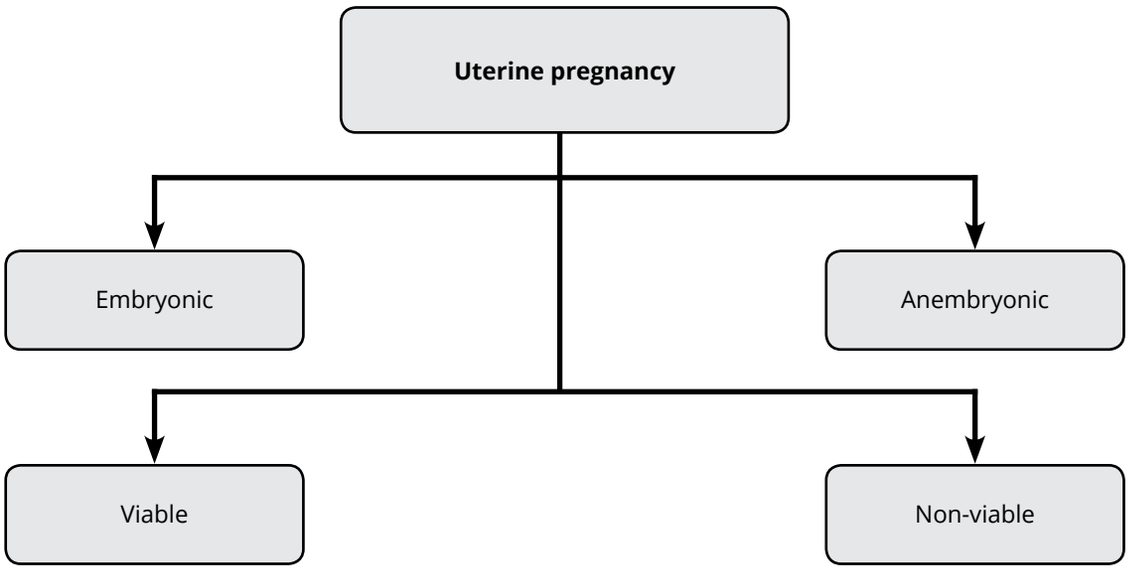
## Routes for progesterone

- Can be administered orally, vaginally or intramuscularly.
- Oral administration ensures optimal compliance. Dydrogesterone is similar to the natural progesterone but with higher bioavailability, fewer side-effects and high specificity for progesterone receptor.[9]
- The vaginal route results in higher concentrations in the uterus but does not reach high and constant blood levels.[10] In the presence of vaginal bleeding, its use is often difficult or it may even be washed out with severe vaginal bleeding. Dosage of vaginal micronized progesterone: 400–800 mg/day
- Intramuscular injections may cause pain and non-septic abscesses, although it results in optimal blood levels. Intramuscular progesterone can be given as 50–100mg/day.
- The current evidence does not support the routine use of hCG in the treatment of threatened miscarriage.[11]
- Anti fibrinolytic agents such as tranexamic acid can be used in certain cases with bleeding.
- Hospitalization should be considered after appropriate patient counseling.
- Patient and relatives should be counselled regarding the prognosis and about the outcome of pregnancy in at-risk patients

## Transvaginal scan (TVS) to check pregnancy location



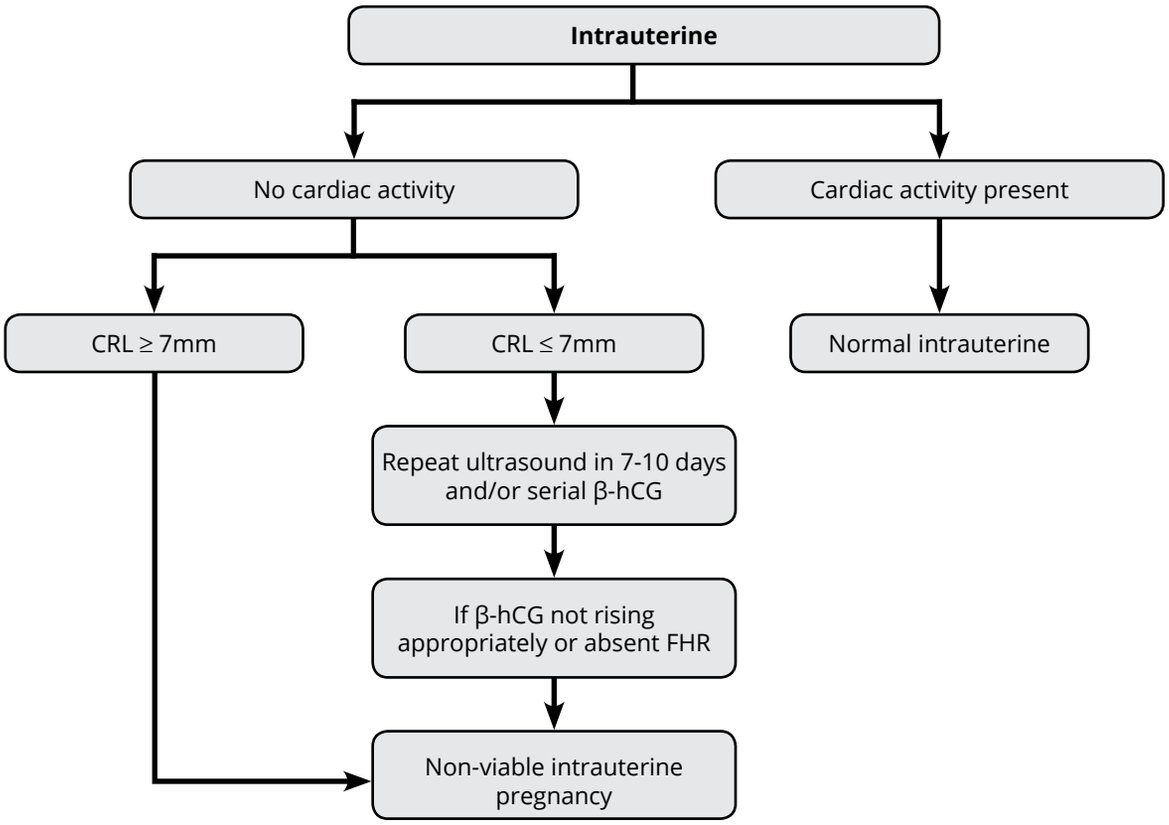
## Uterine pregnancy



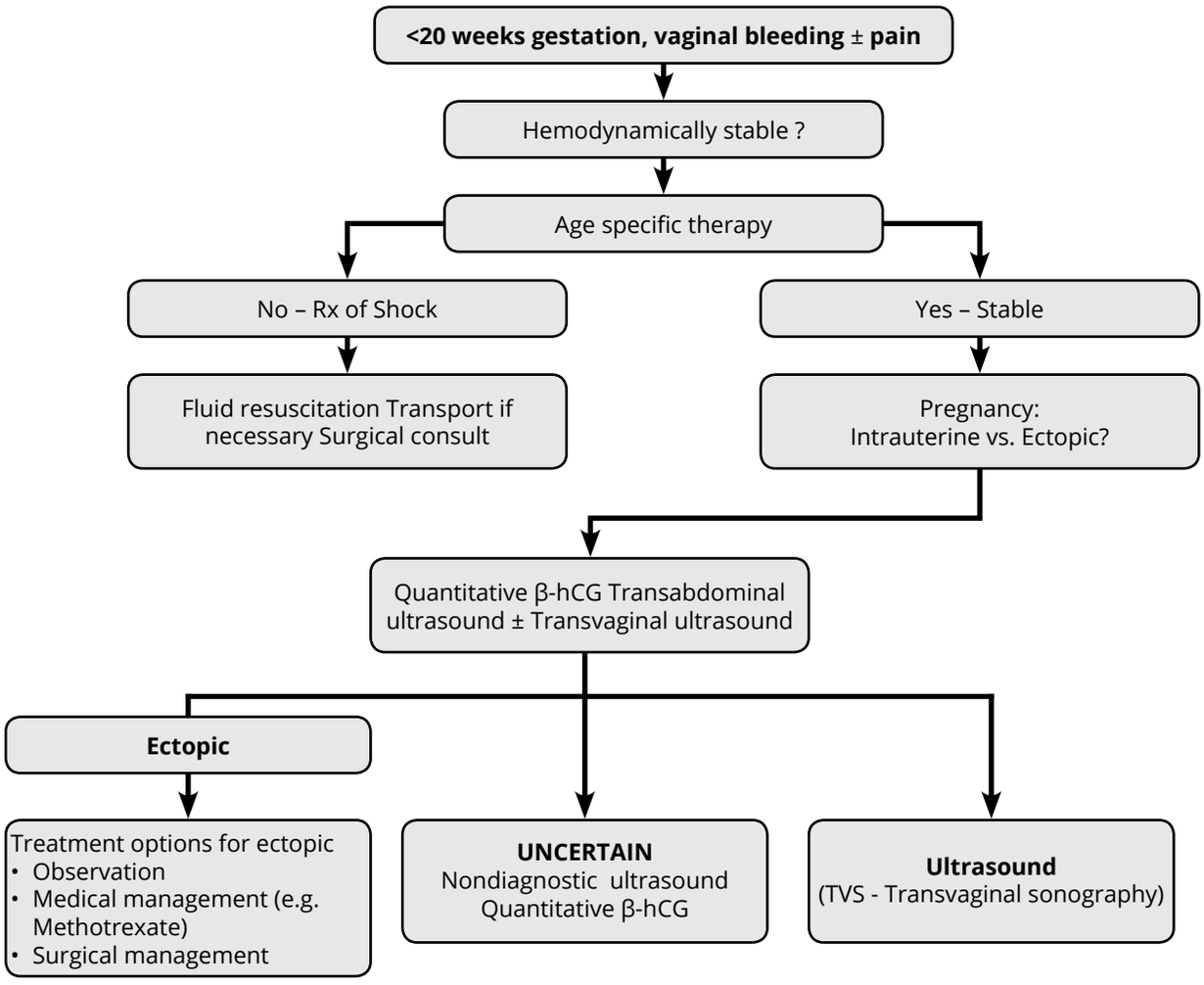

### Society of Radiologists in Ultrasound guidelines for transvaginal ultrasonographic diagnosis of early pregnancy loss (ACOG 2015)[12]

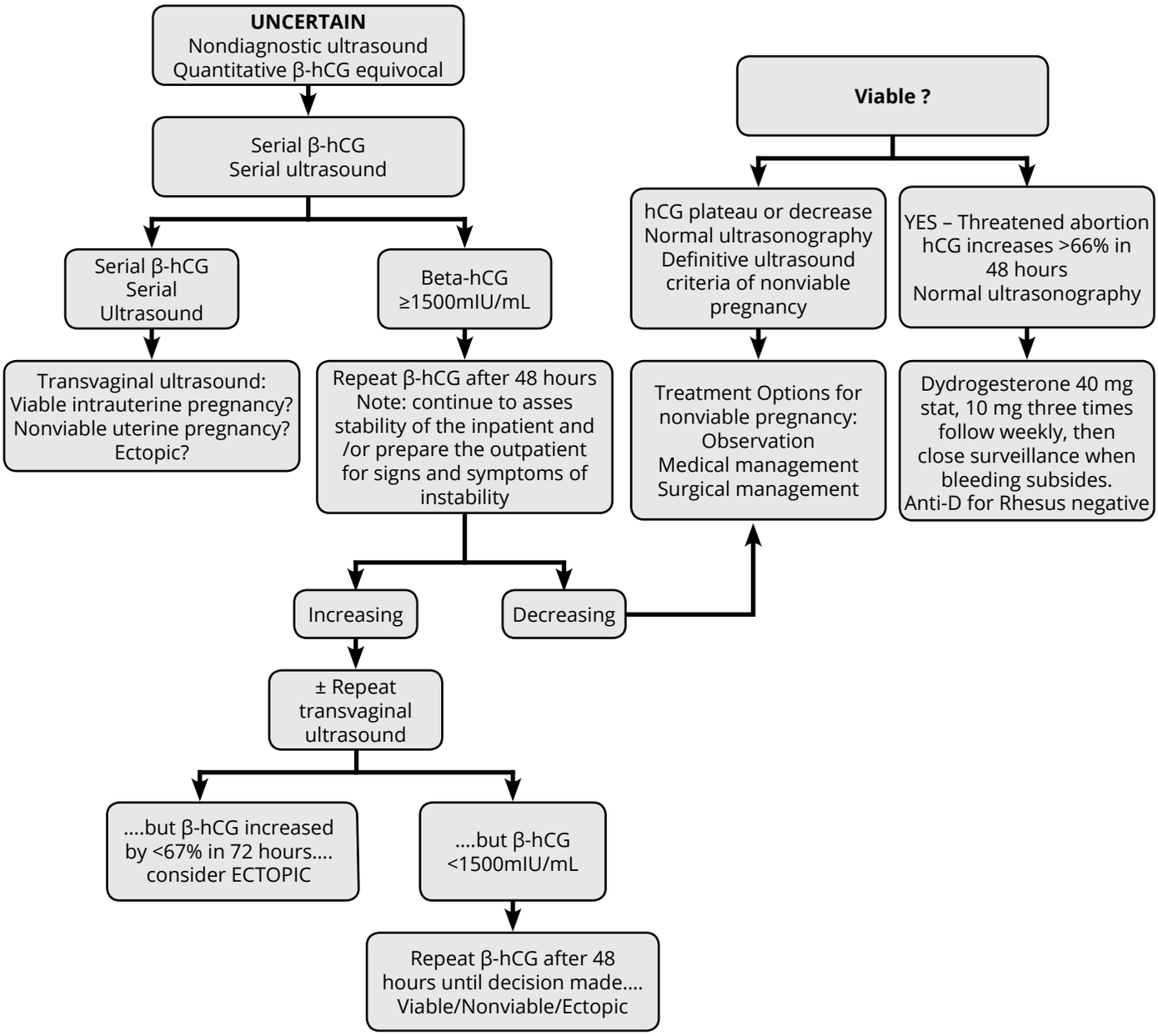
| Findings diagnostic of early pregnancy loss | Findings diagnostic of early pregnancy loss |
|---|---|
| • Crown–rump length of 7 mm or greater and no heartbeat<br>• Mean sac diameter of 25 mm or greater and no embryo<br>• Absence of embryo with heartbeat 2 weeks or more after a scan that showed a gestational sac without a yolk sac<br>• Absence of embryo with heartbeat 11 days or more after a scan that showed a gestational sac with a yolk sac | • Crown–rump length of less than 7 mm and no heartbeat<br>• Mean sac diameter of 16–24 mm and no embryo<br>• Absence of embryo with heartbeat 7–13 days after an ultrasound scan that showed a gestational sac without a yolk sac<br>• Absence of embryo with heartbeat 7–10 days after an ultrasound scan that showed a gestational sac with a yolk sac<br>• Absence of embryo for 6 weeks or longer after last menstrual period<br>• Empty amnion (amnion seen adjacent to yolk sac, with no visible embryo)<br>• Enlarged yolk sac (greater than 7 mm)<br>• Small gestational sac in relation to the size of the embryo (less than 5 mm difference between mean sac diameter and crown–rump length) |

## Frist trimester intrauterine pregnancy

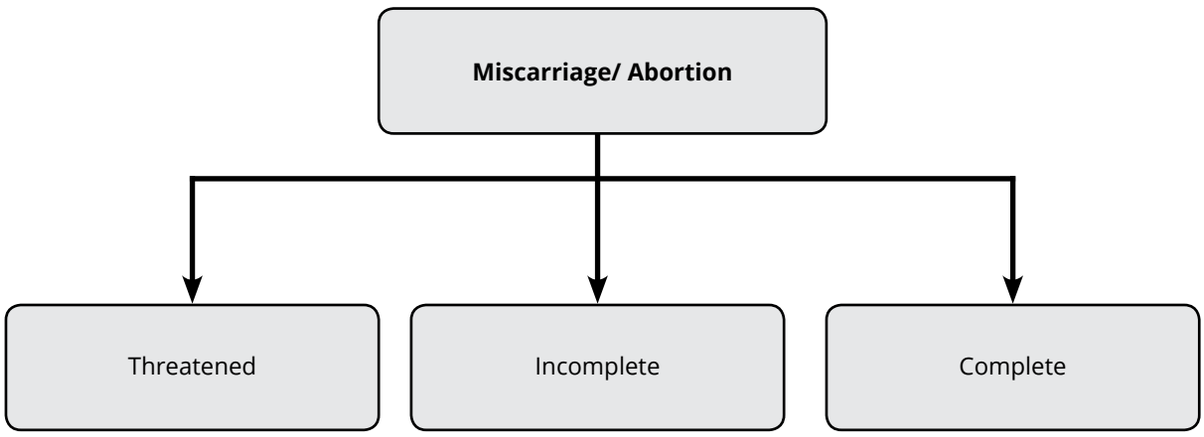



## Frist trimester vaginal bleeding






## Frist trimester uterine bleeding



## Other causes

Molar pregnancy

- B-hCG +++++
- USG: snowstorm appearance

Local causes: Cervical and vaginal

- Polyps
- Erosions
- Trauma
- Infection

## Conclusions

- Bleeding in first trimester is common complication.
- Ominous for maternal and fetal outcome – appropriate evaluation and management essential for optimal pregnancy outcome.
- Serial evaluations with ultrasound and β-hCG mainstay of diagnosis.
- Use of progesterone in threatened miscarriage is beneficial (Evidence and experience based).
- Tubal pregnancy: Early diagnosis and conservative management (medical and laparoscopic) is paradigm of change.
- Dydrogesterone may effectively reduce the miscarriage rate in women with threatened miscarriage. It has a good oral availability along with a good safety and tolerability profile.

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# HYPERGLYCEMIA IN PREGNANCY

**FOGSI President** : Dr. Nandita Palshetkar

**Moderators** : Dr. Ashis Kumar Mukhopadhyay
Dr. Partik Tambe

**Panelists** : Dr. Vanita Raut
Dr. Mandakini Megh
Dr. Rukshan Cleophas
Dr. Amol Tilve
Dr. Mansi Medekar


**From left to right:** Dr. Ashis Mukhopadhyay, Dr. Vanita Raut, Dr. Mansi Medekar, Dr. Rukshan Cleophas (Sri Lanka), Dr. Mandakini Megh, Dr. Pratik Tambe, Dr. Amol Tilve

# CASE 1

## CASE PRESENTATION

- *A 28-year-old women, married since 3 years*
- *Using barrier contraception.*
- *Planning pregnancy since 4 months with missed period*
- *LMP 6 weeks back*
- *Visits you with routine ANC profile*

## Examinations

### Investigations

- Random blood sugar: 150 mg/dl
- HbA1c: 8%
- Rest investigations were normal

### Counselling

- Risks involved and expected turn of events
- No abortion needed as early pregnancy – organogenesis started
- Strict sugar control – diabetologist, nutritionist
- Timely routine nuchal translucency scan (NT scan) and anomaly scan to evaluated anomalie

**Diagnosed as hyperglycemia in pregnancy**

# CASE 2

## CASE PRESENTATION

- *A 26-year-old lady 6 months post marriage*
- *Irregular menses since 3-4 months*
- *History of weight gain*
- *Family history of diabetes*
- *Weight 62 kg height 145 cm BMI 29*
- *USG s/o Bilateral PCOS*
- *Basic investigation including TSH, Sugars normal*

## Counselling

**Preconceptional counselling**

- Weight loss
- Lifestyle modification
- Contraception till optimal BMI and her desire of pregnancy
- Counselling about risks in pregnancy
- Universal pre-conceptional screening
- She comes after 6 months with a missed period
- UPT positive
- Weight 56 Kg
- ANC profile normal

## Screening and diagnosis: Universal screening

### DIPSI criteria

| | | |
|---|---|---|
| 75 gm<br>2 hr venous plasma glucose<br>irrespective of time of meal | < 120 mg/dL | Normal |
| | 120-140 mg/dL | Gestational glucose intolerance (GGI) |
| | 140 mg/dL | Gestational diabetes mellitus (GDM) |
| **Frequency of DIPSI:** At first visit, at 24-28 weeks, 32-34 weeks | | |

> 200 mg% postprandial plasma glucose or random plasma glucose with symptoms of diabetes is referred as overt diabetes/diabetes in pregnancy

## Management

| | |
|---|---|
| **Diet** | • Carbohydrate 40%, protein 20 %, fat 40 %<br>• Eat locally available food<br>• Complex carbohydrates<br>• Low glycemic index food<br>• Health education leaflet |
| **Exercise** | • 30 min walk per day OR<br>• 15 min after each meal |
| **Self monitoring of sugars** | • Capillary blood glucose – targets – set at lower levels<br>• Advise pregnant women with any form of diabetes to maintain their capillary plasma glucose below the following target levels, if these are achievable without causing problematic hypoglycemia:<br>» Fasting: 95 mg/dl<br>» 1 hour after meals: 140 mg/dL<br>» 2 hours after meals: 120mg/dL |
| **Pharmacological treatment** | • Target levels not maintained after 2 weeks of medical nutritional therapy (MNT) and exercise<br>• Multidisciplinary care<br>• Endocrinologist/Diabetologist involvement<br>• Physician and nutritionist<br>• Insulin: Drug of choice<br>• Metformin: Resource settings, lack of storage facilities, poor patient compliance and/or refusal of insulin<br>• Documentation of options given and choice made<br>• Dose of insulin and OHD individualized |
| **PCOS and metformin** | • Metformin if started earlier in a woman with PCOS can be continued during pregnancy, although not evidence based.<br>• No teratogenicity reported with metformin, has to be given after taking informed consent.<br>• No opinion regarding up to which POG |
| **Inositol** | • Antenatal supplementation with inositol during pregnancy shows a potential benefit for reducing the incidence of gestational diabetes<br>• Reduces the level of insulin resistance in pregnancy<br>• During pregnancy shows a potential benefit for reducing the incidence of gestational diabetes. |
| **ANC visit** | • Up to 32 weeks - 4 weekly<br>• 32 – 36 weeks - 2 weekly<br>• Post 36 weeks - weekly |
| OHD: oral hypoglycemic drugs; PCOS; polycystic ovarian syndrome. | |

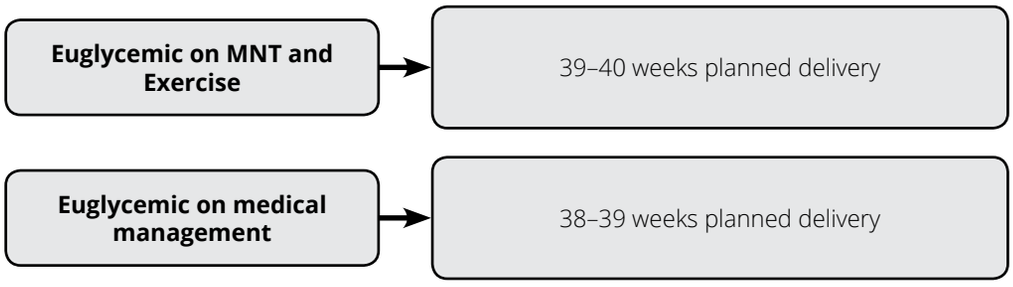
## Antepartum surveillience

| | |
|---|---|
| **28 weeks** | • Offer ultrasound monitoring of fetal growth and amniotic fluid volume.<br>• Educate women regarding Daily Fetal Movement Count (DFMC) |
| **32 weeks** | • Offer ultrasound monitoring of fetal growth and amniotic fluid volume.<br>• AC on USG > 75th percentile suggestive of macrosomia<br>• Offer all routine investigations normally scheduled for 32 weeks in routine antenatal care. |
| **34 weeks** | • Non Stress Test and Ultrasound monitoring<br>• Frequency of these tests should be individualized depending on glycemic control and other obstetric and medical complications<br>• Educate regarding risks<br>• BP monitoring |
| **36 weeks** | • Offer ultrasound monitoring of fetal growth and amniotic fluid volume.<br>• Provide information and advice about:<br>» Aiming, mode and management of birth<br>» Analgesia and anesthesia<br>» Changes to blood glucose-lowering therapy during and after birth<br>» Care of the baby after birth<br>» Initiation of breastfeeding and the effect of breastfeeding on blood<br>» Glucose control<br>» Contraception and follow-up |
| **37 – 38 weeks** | • Offer induction of labor, or cesarean section if indicated |
| **39 weeks** | • Offer tests of fetal wellbeing.<br>• Advise women with uncomplicated gestational diabetes to give birth no later than 40 weeks. |

## Mode and timing of delivery

Mode of delivery depends on:

- Bishops score
- Estimated baby weight
- Associated medical and obstetric indication




* If delivery plan less than 38 weeks Prophylactic steroids for fetal lung maturity indicated with proper monitoring of sugar and tight glycemic control

MNT: medical nutrition therapy.

## Intrapartum monitoring

- 2 hourly capillary blood sugar monitoring
- Blood sugar to be maintained between 70–100 mg/dL
- Avoid maternal hyperglycemia
- Intravenous fluids: Normal saline/Dextrose normal saline with neutralizing dose of insulin
- In case of lower segment Cesarian section (LSCS) omit morning dose of insulin and oral hypoglycemic drugs

## Postpartum care

- 6 weeks post-partum screening – Fasting blood sugar, post lunch blood sugar
- To continue advice and exercise
- Explain increased risk of gestational diabetes mellitus, type 2 diabetes, and cardiovascular risk
- Contraceptive advice: Oral contraceptive pills not contraindicated, postpartum Intrauterine contraceptive device [long-acting reversible contraception (LARC)]

# CHOLESTASIS IN PREGNANCY

**FOGSI President** : Dr. Nandita Palshetkar

**Moderators** : Dr. Girija Wagh

Dr. Krishna Kumari M

**Panelists** : Dr. Sejal Ajmera

Dr. Shailesh Kamath

Dr. Ajit Mopkar

Dr. Madhuri Mehendhale

Dr. Mohit Saraogi


**From left to right:** Dr. Sejal Ajmera, Dr. Madhuri Mehendhale, Dr. Girija Wagh, Dr. Krishna Kumari M, Dr. Mohit Saraogi, Dr. Ajit Mopkar, Dr. Shailesh Kamat

# CASE 1

## CASE PRESENTATION

- *A 24-year-old primigravida pregnant women presented with the chief complaints of severe pruritus and jaundice in the 30th week of pregnancy.*
- *No complaints of nausea, vomiting, headache, fever or fatigue.*

## Examination

| | |
|---|---|
| **Family history**<br>• The patient's mother had a history of third-trimester pruritus with milder symptoms and no history of fetal death or preterm delivery in her previous pregnancies. | **Physical examination**<br>• Physical examination revealed scleral icterus<br>• Blood pressure and other general examination findings were normal<br>• There were excoriation marks seen on palms and abdomen |
| **Laboratory examinations**<br>• Increased levels of direct bilirubin (D-Bil), aspartate transaminase (AST), alanine aminotransferase (ALT), total bile acid, were found<br>• Viral markers tests (hepatitis A, B, and C) were negative<br>• Urine test: No proteinuria or ketonuria were noted | **USG findings**<br>• Liver, gall bladder, and spleen normal |
| **Final diagnosis: Intrahepatic cholestasis of pregnancy with severe symptoms** | |
| **Intervention**<br>The patient was treated with 300 mg of ursodeoxycholic acid (UDCA) twice daily from the day of diagnosis.<br>• After administration of UDCA, the patient's pruritus slowly improved and D-Bil, AST, ALT, and bile acid levels slowly returned to the normal levels<br>• Electively induced at 37 weeks of pregnancy and delivered a healthy baby | |
| **Follow-up**<br>• Immediately after delivery, UDCA was discontinued and no symptom recurrence or increase in the level of hepatobiliary enzymes was observed.<br>• Biochemical markers were repeated after 10 days.<br>• There was a decrease in the level observed. | |

## Discussion

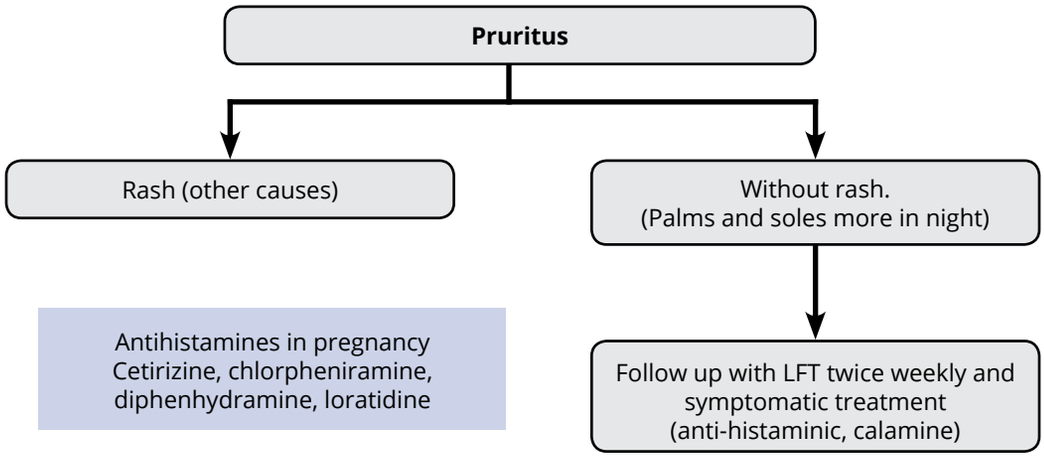
- Intrahepatic cholestasis of pregnancy is a diagnosis of exclusion more commonly presenting in the 2nd half of pregnancy with primary complaints of pruritus without rash usually starting over the palms and soles especially at night.
- Bile acid levels with values more than 40 micro IU/L is associated with a poor fetal outcome.
- Common differentials for the condition are:
  - » Infective hepatitis
  - » Severe preeclampsia/HELLP
  - » AFLP (acute fatty liver of pregnancy)
  - » Acute obstruction secondary to gall stones
  - » Drug induced (methyldopa)
  - » Auto immune

## Ursodeoxycholic acid (UDCA)

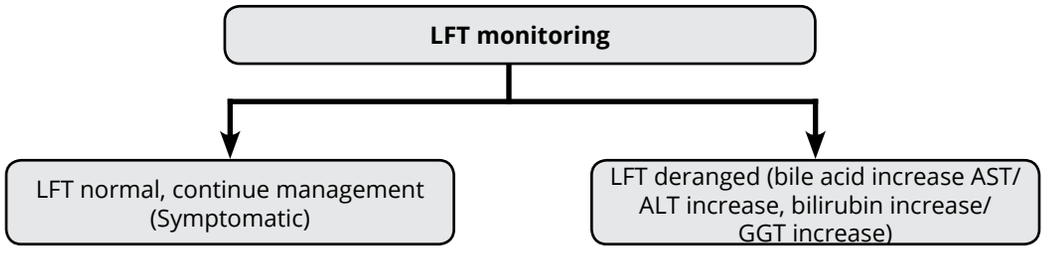
- Increases hepatobiliary excretion of bile acids.
- Direct protective action on hepatocytes and cholangiocytes from bile acids.
- Reduces cholesterol absorption in the intestine and in turn reduces bile acid production.
- Doses – 15 mg/kg day in divided doses till maximum of 2 g per day.
- Recent clinical trials suggested the satisfactory efficacy of UDCA in treating ICP with less adverse reactions.
- In cases of patients with prolonged prothombin time, administration of vitamin K may help. It can be administered orally (as a water soluble salt).
- According to recent guidelines dexamethasone has no benefit in the treatment of this condition.
- In case of no response or inadequate response to UDCA supplement the treatment with SAM (S-adenosine methionine)/rifampin.

# Management

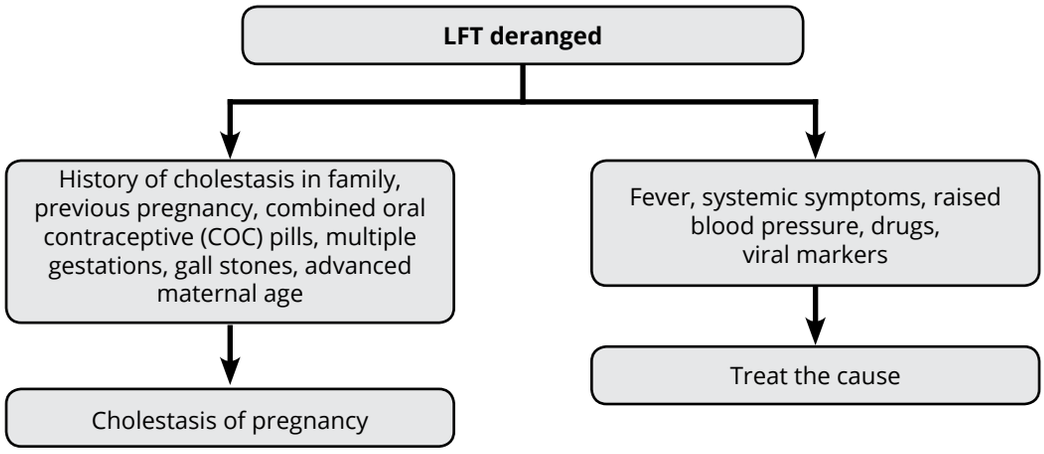
## Pruritus




## Liver function tests (LFT) monitoring




## LFT deranged

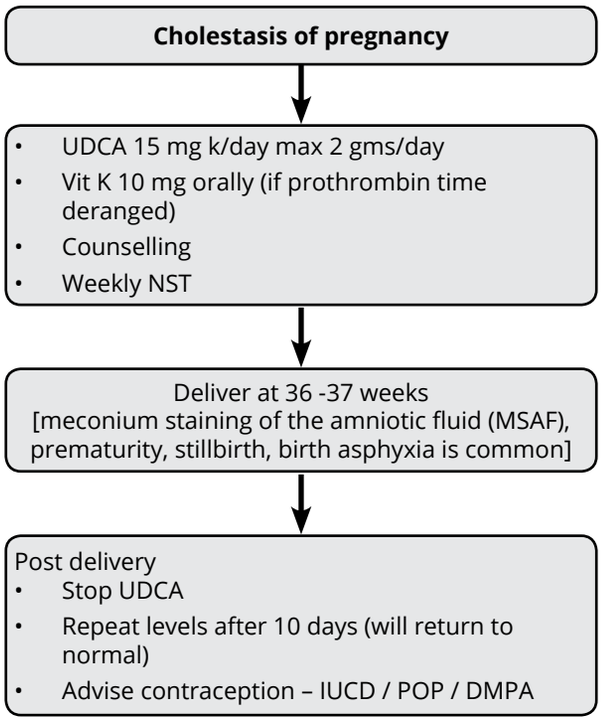


## LFT interpretation

| Disease | AST/ALT IU/l | Total bilirubin mg/dl |
|---|---|---|
| HELLP | <500 | <2 indirect |
| AFLP | <1000 | 2-10 ( direct ) |
| IHCP | <500 | < 5 direct, bile acids + |
| Viral hepatitis | 500 – 3000 | 5 -10 direct and indirect |

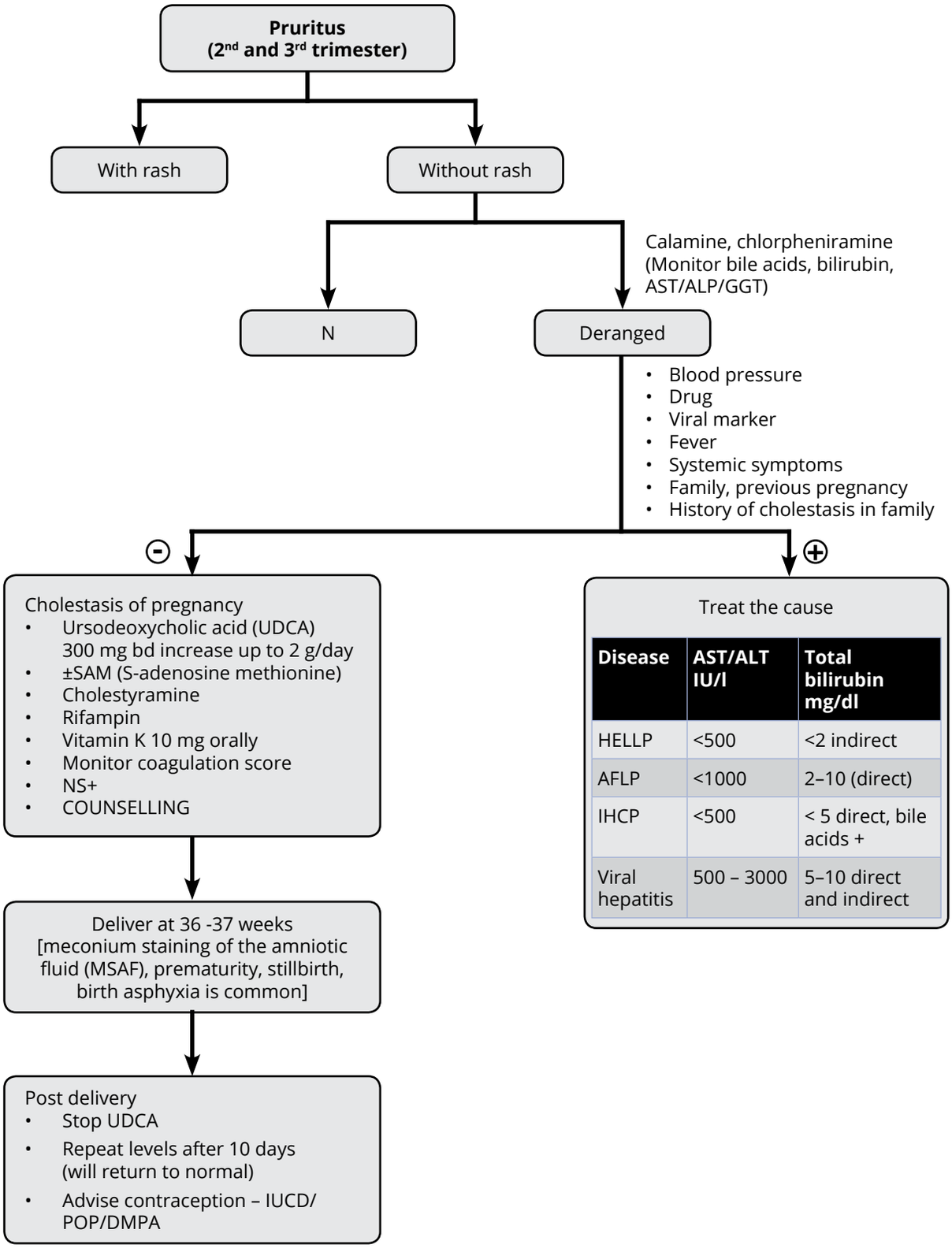
HELLP: Haemolysis, elevated liver enzymes, low platelet count; AFLP: acute fatty liver of pregnancy; IHCP: Intrahepatic cholestasis of pregnancy; AST: Aspartate transaminase; ALT: Alanine aminotransferase

# Management of cholestasis of pregnancy




DMPA: Medroxyprogesterone acetate; IUD: Intrauterine device; POP: Progestogen-only pill

# Management of pruritus in 2nd and 3rd trimester




| Disease | AST/ALT IU/l | Total bilirubin mg/dl |
|---|---|---|
| HELLP | <500 | <2 indirect |
| AFLP | <1000 | 2–10 (direct) |
| IHCP | <500 | < 5 direct, bile acids + |
| Viral hepatitis | 500 – 3000 | 5–10 direct and indirect |

AFLP: acute fatty liver of pregnancy; ALT: Alanine aminotransferase; AST: Aspartate transaminase; DMPA: Medroxyprogesterone acetate; HELLP: Haemolysis,elevated liver enzymes, low platelet count; IHCP: Intrahepatic cholestasis of pregnancy; IUD: Intrauterine device; POP: Progestogen-only pill.

Abbott

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# Strengthens its presence in Women's Health

## Novelon®

Desogestrel & Ethinylestradiol Tablets USP

Each uncoated tablet contains: Desogestrel BP: 0.15mg, Ethinylestradiol IP: 0.03mg

The pill with excellent cycle control[1]

Novelon® is indicated for contraception

## Femilon®

Desogestrel & Ethinylestradiol Tablets USP

Each uncoated tablet contains: Desogestrel BP: 0.15mg, Ethinylestradiol IP: 0.02mg

*The light* pill for starters*[1]

Femilon® is indicated for Contraception.

**Select Safety Information**

Well tolerated, with most commonly reported side effects (i.e., nausea, headache, nervousness and breast tenderness).

**Reference**

**1. Comparato, et al**: Contraceptive efficacy and acceptability of a monophasic oral contraceptive containing 30 mcg ethinylestradiol and 150 mcg desogestrel in Latin-American women. Advances in Contraception 1998:14:15-26.

**Study Design**

**Comparato, et al:** In this study contraceptive efficacy, subject acceptability (cycle control, side-effects, acne score and weight gain) and blood pressure of a monophasic oral contraceptive containing 30 micrograms ethinylestradiol (Marvelon®) were assessed in an open-label, 6-cycle multicenter study in Argentina (7 centers) and Venezuela (5 centers). Of the participating women, 389 (95.6%) completed six cycles of treatment, providing data for a total of 2383 cycles. Marvelon® is available as Novelon® in India

ABRIDGED PRESCRIBING INFOMRATION

Tablet containing 0.150 mg desogestrel and 0.030 mg ethinylestradiol

**INDICATIONS:** Contraception. **DOSE, METHOD OF ADMINISTRATION AND USAGE:** Tablets must be taken in the order directed on the package every day at about the same time with some liquid as needed. One tablet is to be taken daily for 21 consecutive days. Each subsequent pack is started after a 7-day tablet-free interval, during which time a withdrawal bleed usually occurs. This usually starts on day 2-3 after the last tablet and may not have finished before the next pack is started. No preceding hormonal contraceptive use tablet-taking has to start on day 1 of the woman's natural cycle. Changing from a combined hormonal contraceptive (combined oral contraceptive (COC), vaginal ring, or transdermal patch); The woman should start with COC containing 0.150 mg desogestrel and 0.030 mg ethinylestradiol preferably on the day after the last active tablet of her previous COC. In case a vaginal ring or transdermal patch has been used, the woman should start using COC containing 0.150 mg desogestrel and 0.030 mg ethinylestradiol preferably on the day of removal. If the woman has been using her previous method consistently and correctly and if it is reasonably certain that she is not pregnant she may also switch from her previous combined hormonal contraceptive on any day of the cycle. Changing from a progestogen-only-method (minipill, injection, implant) or from a progestogen-releasing intrauterine system (IUS)The woman may switch any day from the minipill (from an implant or the IUS on the day of its removal, from an injectable when the next injection would be due), but should in all of these cases be advised to additionally use a barrier method for the first 7 days of tablet-taking. Following delivery or second-trimester abortion Women should be advised to start at day 21 to 28 after delivery or second-trimester abortion. **USE IN SPECIAL POPULATION:** Pregnancy and lactation: COC containing 0.150 mg desogestrel and 0.030 mg ethinylestradiol is not indicated during pregnancy. The use of COCs should generally not be recommended until the nursing mother has completely weaned her child. **CONTRA-INDICATIONS:** Combined oral contraceptives (COCs) should not be used in the presence of any of the conditions listed below. Should any of the conditions appear for the first time during COC use, the product should be stopped immediately. Presence or a history of venous or arterial thrombotic/thromboembolic events (e.g., deep venous thrombosis, pulmonary embolism, myocardial infarction) or of a cerebrovascular accident. Presence or history of prodromi of a thrombosis (e.g. transient ischaemic attack, angina pectoris). History of migraine with focal neurological symptoms. Diabetes mellitus with vascular involvement. The presence of a severe or multiple risk factor(s) for venous or arterial thrombosis may also constitute a contraindication. Pancreatitis or a history thereof if associated with severe hypertriglyceridaemia. Presence or history of severe hepatic disease as long as liver function values have not returned to normal. Presence or history of liver tumors (benign or malignant). Known or suspected sex steroid-influenced malignancies (e.g., of the genital organs or the breasts). Undiagnosed vaginal bleeding. Known or suspected pregnancy. Hypersensitivity to the active substances or to any of the excipients. COC containing 0.150 mg desogestrel and 0.030 mg ethinylestradiol is contraindicated for use with the Hepatitis C virus combination drug regimen ombitasvir/ paritaprevir/ritonavir with or without dasabuvir **WARNINGS AND PRECAUTIONS:** Circulatory Disorders Epidemiological studies have shown an association between the use of CHCs and an increased risk of arterial and venous thrombotic and thromboembolic diseases such as myocardial infarction, stroke, deep venous thrombosis, and pulmonary embolism. The use of CHCs is associated with an increased risk of venous thromboembolism (VTE) manifesting as deep venous thrombosis and/or pulmonary embolism. The risk is highest during the first year a woman ever uses a CHC. The risk of venous thromboembolism increases with: increasing age; a positive family history (i.e. venous thromboembolism ever in a sibling or parent at a relatively early age); obesity (body mass index over 30 kg/m2); prolonged immobilisation, major surgery, any surgery to the legs, or major trauma. In these situations, it is advisable to discontinue COC use (in the case of elective surgery at least four weeks in advance) and not to resume until two weeks after complete remobilisation. and possibly also with superficial thrombophlebitis and varicose veins. There is no consensus about the possible role of these conditions in the etiology of venous thromboembolism. The risk of arterial thromboembolic complications increases with: increasing age; smoking dyslipoproteinaemia; obesity (body mass index over 30 kg/m2); hypertension; migraine; valvular heart disease; atrial fibrillation; a positive family history (i.e. arterial thrombosis ever in a sibling or parent at a relatively early age). If a hereditary predisposition is suspected, the woman should be referred to a specialist for advice before deciding about any hormonal contraceptive use. 2. Tumours: The most important risk factor for cervical cancer is persistent human papilloma virus (HPV) infection. Epidemiological studies have indicated that long-term use of COCs contributes to this increased risk, but there continues to be uncertainty about the extent to which this finding is attributable to confounding effects, like increased cervical screening and difference in sexual behavior including use of barrier contraceptives, or a causal association. Hepatitis C During clinical trials with the HCV combination drug regimen ombitasvir /paritaprevir/ritonavir with and without dasabuvir, ALT elevations greater than 5 times the upper limit of normal (ULN) were significantly more frequent in women using ethinylestradiol-containing medications such as CHCs. COC containing 0.150 mg desogestrel and 0.030 mg ethinylestradiol must be discontinued prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir **UNDESIRABLE EFFECTS:** Common/Uncommon: Weight increased, fluid retention, headache, migraine, libido decreased, depressed mood, mood altered, nausea, vomiting, abdominal pain, diarrhea, rash, urticaria, breast pain, breast tenderness, breast hypertrophy. Rare: hypersensitivity, weight decreased, libido increased, contact lens intolerance, erythema nodosum, erythema multiforme, vaginal discharge, breast discharge. **PRESENTATION:** Blister pack of 21 tablets. **STORAGE CONDITIONS:** Do not store above 30°C. Do not freeze. Store in the original package, in order to protect from light and moisture. Before prescribing COC containing 0.150 mg desogestrel and 0.030 mg ethinylestradiol, please refer to the full prescribing information.

**Select Safety Information**

Most frequently reported adverse events (AEs) were headache, bleeding irregularity, back pain, vaginitis, sinusitis and upper respiratory tract infection. Majority of AEs were considered to be mild to moderate in intensity.

**Reference**

1. Egarter, et al: Low Dose Oral Contraceptives and Quality of Life. Contraception 1999; 59:287-291.

**Study Design**

**Egarter, et al**This study investigated the effects of a low dose oral contraceptive (OC) (Mercilon) on women's satisfaction and quality of life based on a detailed questionnaire. A total of 614 first-time users of oral contraceptives were enrolled by 102 gynecologists for a treatment period of 4 months. Mercilon® is available as Femilon in India.

ABRIDGED PRESCRIBING INFORMATION

FEMILON®

Tablet containing 0.150 mg desogestrel and 0.020 mg ethinylestradiol

**INDICATIONS:** Contraception. **DOSE, METHOD OF ADMINISTRATION AND USAGE:** Tablets must be taken in the order directed on the package every day at about the same time with some liquid as needed. One tablet is to be taken daily for 21 consecutive days. Each subsequent pack is started after a 7-day tablet-free interval, during which time a withdrawal bleed usually occurs. This usually starts on day 2-3 after the last tablet and may not have finished before the next pack is started. No preceding hormonal contraceptive use tablet-taking has to start on day 1 of the woman's natural cycle. Changing from a combined hormonal contraceptive (combined oral contraceptive (COC), vaginal ring, or transdermal patch); The woman should start with Femilon® preferably on the day after the last active tablet of her previous COC. In case a vaginal ring or transdermal patch has been used, the woman should start using Femilon® preferably on the day of removal. If the woman has been using her previous method consistently and correctly and if it is reasonably certain that she is not pregnant she may also switch from her previous combined hormonal contraceptive on any day of the cycle. Changing from a progestogen-only-method (minipill, injection, implant) or from a progestogen-releasing intrauterine system (IUS); The woman may switch any day from the minipill (from an implant or the IUS on the day of its removal, from an injectable when the next injection would be due), but should in all of these cases be advised to additionally use a barrier method for the first 7 days of tablet-taking. Following delivery or second-trimester abortion; Women should be advised to start at day 21 to 28 after delivery or second-trimester abortion. **USE IN SPECIAL POPULATION:** Pregnancy and lactation: Femilon is not indicated during pregnancy. The use of COCs should generally not be recommended until the nursing mother has completely weaned her child. **CONTRA-INDICATIONS:** Combined oral contraceptives (COCs) should not be used in the presence of any of the conditions listed below. Should any of the conditions appear for the first time during COC use, the product should be stopped immediately. Presence or a history of venous or arterial thrombotic/thromboembolic events (e.g., deep venous thrombosis, pulmonary embolism, myocardial infarction) or of a cerebrovascular accident. Presence or history of prodromi of a thrombosis (e.g. transient ischaemic attack, angina pectoris). History of migraine with focal neurological symptoms. Diabetes mellitus with vascular involvement. The presence of a severe or multiple risk factor(s) for venous or arterial thrombosis may also constitute a contraindication. Pancreatitis or a history thereof if associated with severe hypertriglyceridaemia. Presence or history of severe hepatic disease as long as liver function values have not returned to normal. Presence or history of liver tumors (benign or malignant). Known or suspected sex steroid-influenced malignancies (e.g., of the genital organs or the breasts). Undiagnosed vaginal bleeding. Known or suspected pregnancy. Hypersensitivity to the active substances or to any of the excipients. Femilon® is contraindicated for use with the Hepatitis C virus combination drug regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir. **WARNINGS AND PRECAUTIONS:** Circulatory Disorders; Epidemiological studies have shown an association between the use of combined hormonal contraceptives (CHCs) and an increased risk of arterial and venous thrombotic and thromboembolic diseases such as myocardial infarction, stroke, deep venous thrombosis, and pulmonary embolism. The use of CHCs is associated with an increased risk of venous thromboembolism (VTE) manifesting as deep venous thrombosis and/or pulmonary embolism. The risk is highest during the first year a woman ever uses a CHC. The risk of venous thromboembolism increases with: increasing age; a positive family history (i.e. venous thromboembolism ever in a sibling or parent at a relatively early age); obesity (body mass index over 30 kg/m2); prolonged immobilisation, major surgery, any surgery to the legs, or major trauma. In these situations it is advisable to discontinue COC use (in the case of elective surgery at least four weeks in advance) and not to resume until two weeks after complete remobilization; and possibly also with superficial thrombophlebitis and varicose veins. There is no consensus about the possible role of these conditions in the etiology of venous thromboembolism. The risk of arterial thromboembolic complications increases with: increasing age; smoking; dyslipoproteinaemia; obesity (body mass index over 30 kg/m2); hypertension; migraine; valvular heart disease; atrial fibrillation; a positive family history (i.e. arterial thrombosis ever in a sibling or parent at a relatively early age). If a hereditary predisposition is suspected, the woman should be referred to a specialist for advice before deciding about any hormonal contraceptive use. Tumours: The most important risk factor for cervical cancer is persistent human papilloma virus (HPV) infection. Epidemiological studies have indicated that long-term use of COCs contributes to this increased risk, but there continues to be uncertainty about the extent to which this finding is attributable to confounding effects, like increased cervical screening and difference in sexual behavior including use of barrier contraceptives, or a causal association. Hepatitis C virus (HCV): During clinical trials with HCV combination drug regimen ombitasvir /paritaprevir/ritonavir with and without dasabuvir, ALT elevations greater than 5 times the upper limit of normal (ULN) were significantly more frequent in women using ethinylestradiol-containing medications such as CHCs. Femilon® must be discontinued prior to starting therapy with the combination drug regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir. **UNDESIRABLE EFFECTS:** Common/Uncommon (more than 1/1000): Increased weight, fluid retention, headache, migraine, decreased libido, depressed mood, altered mood, nausea, vomiting, abdominal pain, diarrhea, rash, urticaria, breast pain, breast tenderness, breast hypertrophy. **Rare:** Hypersensitivity, decreased weight, increased libido, contact lens intolerance, erythema nodosum, erythema multiforme, vaginal discharge, breast discharge. **PRESENTATION:** Blister pack of 21 tablets. **STORAGE CONDITIONS:** Do not store above 30°C. Do not freeze. Store in the original package, in order to protect from light and moisture.

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MSD INVENTING FOR LIFE



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Abbott

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