

# Clinical Gynecology for Family medicine

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### **LEARNING OBJECTIVES:**

- 1. Understand causes and treatment of amenorrhoea
- 2. Understand endocrinology of menstrual disorders
- 3. Management of abnormal uterine bleeding
- 4. Causes of infective vaginal discharge and treatment



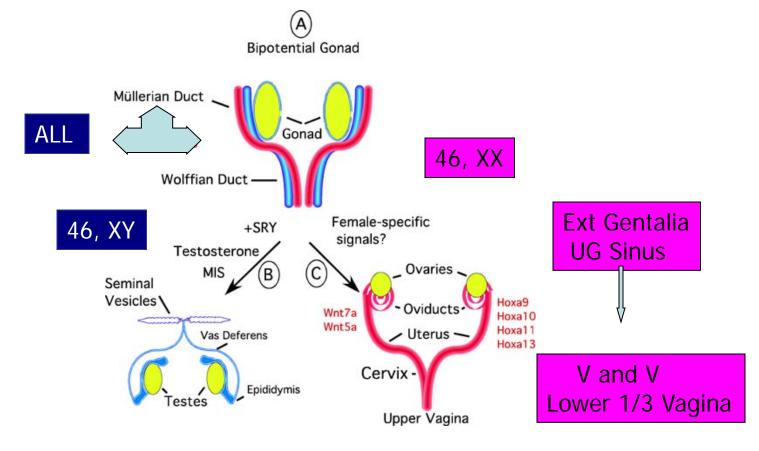
# PRIMARY AMENORRHOEA

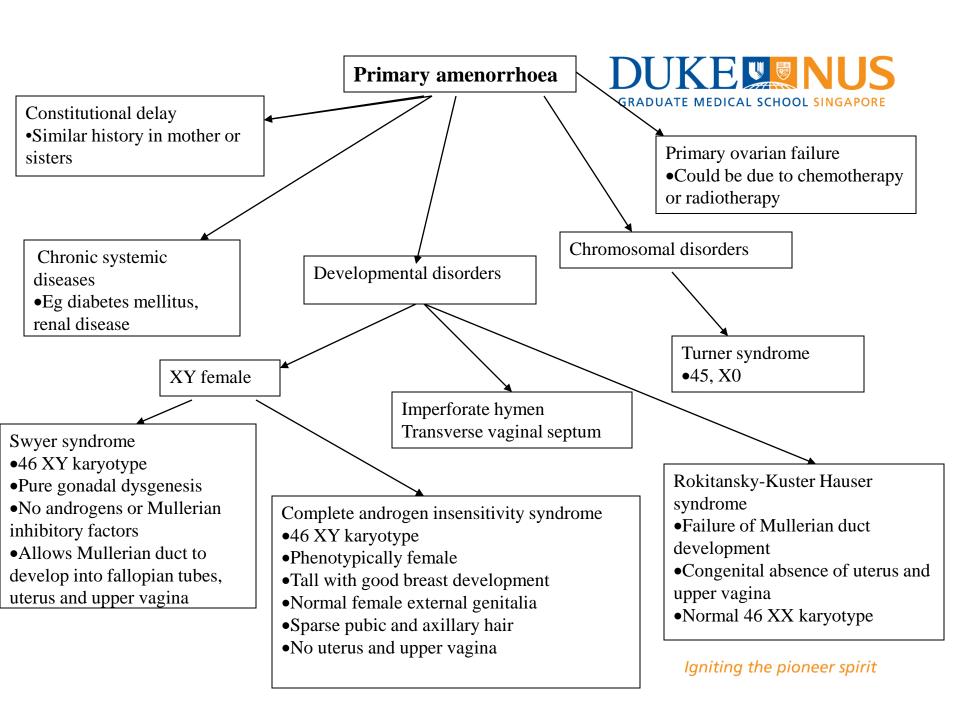
# **Definition**

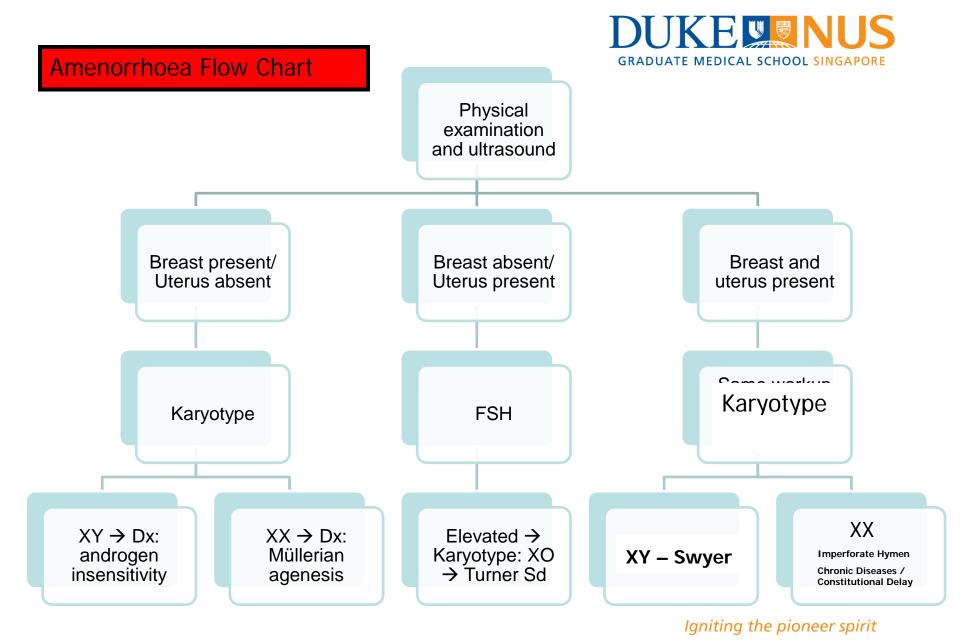
Never experienced menstrual period by 16 yo



# **Embryology of reproductive organs**







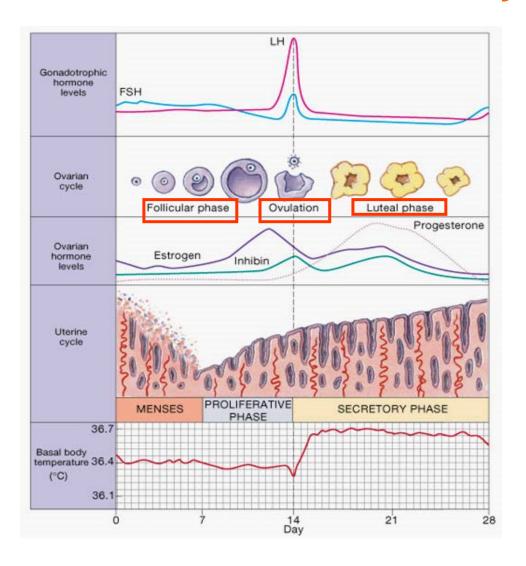




- •Refer OBGYN for investigations and management of primary amenorrhoea
- •For constitutional delay, no treatment is needed except reassurance
- •For chromosomal disorders and primary ovarian failure, small dose of ethinyl oestradiol 1µg daily can be started for 6 months, increasing to 2, 5, 10 and eventually 20 µg with increments at six monthly intervals. This is then followed by combined oral contraceptive pills.
- •For vaginal and mullerian agenesis, vaginal reconstruction is necessary. This could be achieved by vaginal dilators or surgical procedures like William's vulvo-vaginoplasty, McIndoe's procedure or skin graft.
- •For XY female, counseling with the parents is important to discuss on psychological issues of gender of rearing and gender identity. Management includes gonadectomy as the dysgenetic testes have a high lifetime risk of malignancy (30%).



# **Endocrine Control of Menstrual Cycle**





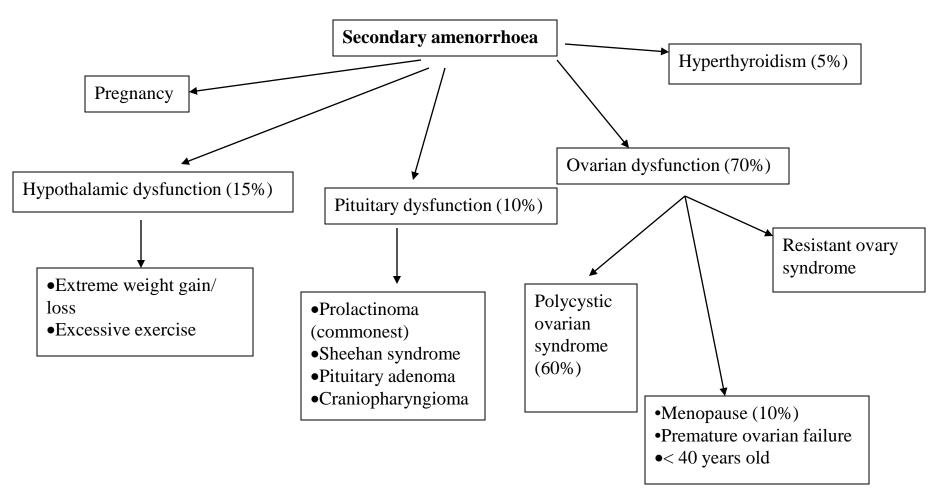
# **SECONDARY AMENORRHOEA**

### **DEFINITION**

Cessation of menses for 6 months

Hypothalamus	Diagnosis Hypogonadotrophic hypogonadism Weight loss, anorexia, Exercise Kallmann's syndrome Tumours (craniopharyngioma)	Features Low or normal gonadotrophins Negative withdrawal bleed
Ant	Hyperprolactinaemia Prolactinoma Drugs Sheehan's syndrome	Raised prolactin Negative withdrawal bleed
FSH LH Ovary	Chromosomal Gonadal agenesis Resistant ovary syndrome Premature ovarian failure latrogenic	Raised gonadotrophins Negative withdrawal bleed
	Polycystic ovarian syndrome	Raised LH:FSH Pos withdrawal bleed
Oestrogen Progesterone Uterus  Menses	Cryptomenorrhoea Hypoplasia or absence of vagina Testicular feminization Asherman's syndrome Infection	Normal hormone profile  Negative oestrogen and progesterone withdrawal bleed  Abnormal scan or examination









# **PCOS - Diagnosis**

- Oligo- and/or anovulation
  - Fewer than 8 menstrual cycles / year
- Hyperandrogenism
  - Clinical: Ferriman Gallwey score
  - Biochemical : Total Testosterone
- Polycystic ovaries (PCO)
  - presence of > 12 follicles (2-9 mm) in, or
  - increased ovarian volume (>10 ml)
     Only one ovary fitting this definition sufficient

2/3 of these criteria and exclusion of other etiologies (CAH, androgen-secreting tumours, Cushing's syndrome)

ESHRE/ASRM 2003

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# **Investigations:**



### Urine pregnancy test to exclude pregnancy

### 2. Follicular stimulating hormone (FSH)

- Suggests ovarian failure if > 30 IU/L
- Low level suggests hypothalamic/ pituitary dysfunction
- Reversal of LH/FSH ratio > 3:1 suggests PCOS

### 3. Serum prolactin level

Hyperprolactinaemia could cause secondary amenorrhoea

### 4. Thyroid function test

Hyperthyroidism could cause secondary amenorrhoea

### 5. Progestogen challenge test

- Give 5mg oral norethisterone bd for 5 days
- If there is withdrawal bleeding, there is presence of oestrogen and would mean that the patient would need cyclical progestogen for withdrawal bleeding to protect the endometrium from endometrial hyperplasia and carcinoma
- If there is no withdrawal bleeding, then combined oral contraceptive pill would be needed



# AUB and women's health

➤ Women with AUB less likely to rate their health as excellent or good

- ➤ Women with AUB work an average of 3.6 weeks (24 days) less per year
  - Work loss is estimated to be USD\$1700 per woman
- ➤ Estimated total direct cost USD\$37billion annually



### ABNORMAL UTERINE BLEEDING (AUB)

### **Definition**

The normal menstrual cycle lasts between **24 and 38 days** with menstrual flow lasting **2-8 days**.

Any disturbance in the menstrual cycle or flow pattern is termed as abnormal uterine bleeding (AUB). (FIGO 2012)

### **Steps in workup of AUB**

- (1) Look for pallor. If pale, check HB.
- (2) Ensure haemodynamical stability. Quantify severity of bleeding eg. number of pads used / day and presence of blood clots or episodes of flooding
- (3) Clinical examination to exclude cervical lesion and do a PAP smear if last PAP smear >1 year ago

# " Volume" revisited

- ➤ Traditionally in research, bleeding measured by volume of menstrual blood lost (>80 ml)
  - Actual women of MBL/ cycle <u>is not</u> the main reason women seek care for heavy menstrual bleeding

Heavy menstrual bleeding (HMB) is defined as excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life. It can occur alone or in combination with other symptoms.

**UK-NICE 2007** 

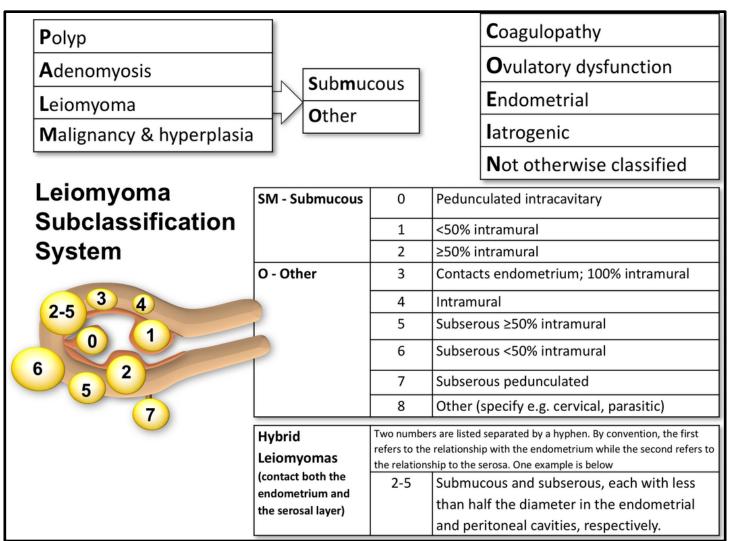
### Menstrual Diary Recording



Category	Days (past 6 months)	Normal or Abnormal	$\square$
		Absent (no periods or bleeding) = amenorrhea	
Frequency	every □□□days	Frequent (<24 days)	
rrequency		Normal (24 to 38 days)	
		Infrequent (>38 days)	
Duration	shortest:□□ days	Prolonged (>8 days)	
Duration	longest:□□ days	Normal (up to 8 days)	
Do avido vite.	shortest: □□□ days	Regular variation (shortest to longest ≤ 9 days)	
Regularity	longest: □□□ days	Irregular ( shortest to longest 10+ days)	
Flow volume	As determined by the	Heavy	
	patient - based on her assessment of the impact	Normal	П
	on her quality of life	Light	
•			
	None		
Intermenstrual Bleeding	Random		П
(IMB) Bleeding between cyclically		Early Cycle	Ш
regular onset of menses	Cyclic (Predictable)	Mid Cycle	
		Late Cycle	
Unscheduled Bleeding on	Not Applicable (not on hormone medication)		₽
Hormone Medication (eg Birth			╁┼┦
Control Pills, Rings or Patches)	Present		

## FIGO PALM- COEIN (2011)





Eg AVM, endometritis

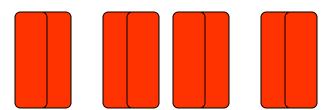
# AUB - O

DUKE SUR NUS
GRADUATE MEDICAL SCHOOL SINGAPORE

Infrequent menses

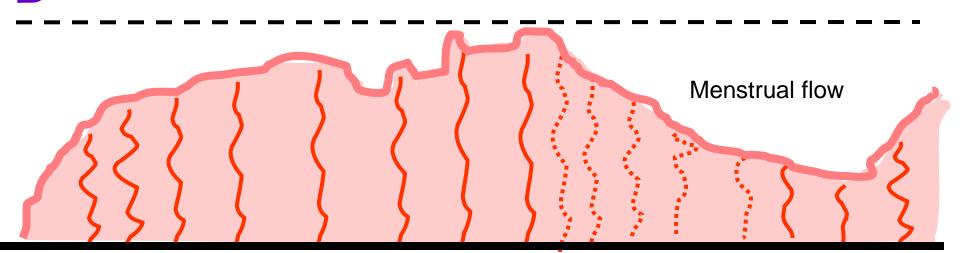
**HMB** 

Anovulation with P4 deficiency



Absence of Progesterone

Estrogen



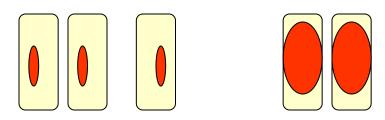
# AUB - E



#### **HEAVY AND REGULAR**

Caused by local disturbances in endometrial function/deficiencies or

excesses of fibriolytic activity that have an impact on coagulation



Estrogen

Progesterone

D1 D14



# **P**olyp

**A**denomyosis

Leiomyoma

Malignancy & Hyperplasia

BIOG An International Journal of Obstetrics and Gynaecology

# Coagulopathy

**O**vulatory Dysfunction

**E**ndometrial

Latrogenic

Not Otherwise Classified

# von Willebrand disease in women with menorrhagia: a systematic review

Meena Shankar, Christine A. Lee, Caroline A. Sabin, Demetrios L. Economides, Rezan A. Kadir

**Results** Prevalence was 13% (95% CI 11–15.6%). In the European studies—18% (95% CI 15–23%) compared with that in North American studies—10% (95% CI 7.5–13%).

This difference (P= 0.007) is likely to be the result of differences in method of recruitment of study population, method of assessing MBL, ethnic composition of study population,

criteria for diagnosis and values for von Willebrand factor.

# **INVESTIGATIONS**



- Perform UPT to exclude pregnancy related problems (threatened miscarriage, inevitable miscarriage or ectopic pregnancy)
- If there are bleeding tendencies, exclude blood dyscrasias for adolescents (13-18 years old)
- If there are symptoms of thyroid disorder or galactorrhoea, check thyroid function test or prolactin level
- Perform pelvic ultrasound scan to exclude pelvic pathology (fibroids/ adenomyosis)

### Endometrial biopsy (Sampling or D and C) recommended

- First line in all women over age 45 years
- ➤ Patients younger than 45 years with history of unopposed E2 (obesity, PCOS), failed medical management or persistent AUB

# Case study

45 y.o. non pregnant woman with 5 years of heavy and regular menstrual bleeding. She experiences severe cramping and passes blood clots. Coagulopathy screen negative. On exam – her uterus enlarged (16 week size) and small trickle of blood seen from the cervival os.

What etiologies are in your differential diagnosis?

	Y	N
Р	X	
A	X	
L	X	
M	X	

	Y	N
С		X
0		X
Е	X	
I		X
N		X

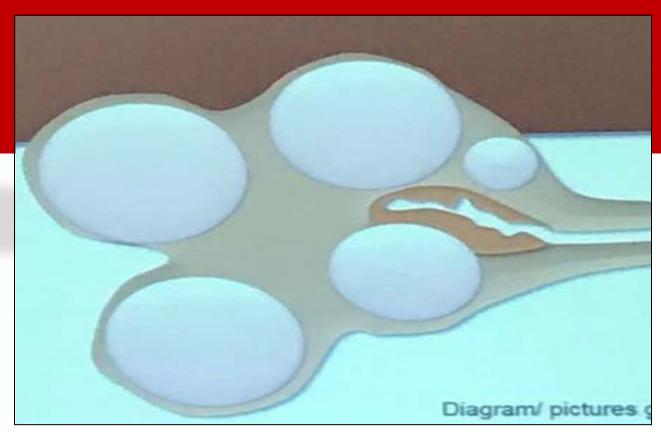
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45 y.o. non pregnant woman with 5 years of heavy and regular menstrual bleeding.

Ultrasound images represented below and endometrial biopsy with disordered proliferative endometrium. What is your differential diagnosis now?

	Y	N
P		X
Α		X
L	X	
M		X

	Y	N
C		X
0		X
E		X
I		X
N		X



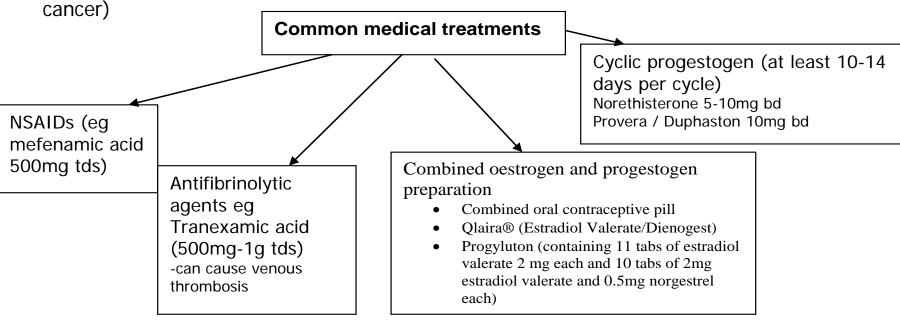
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### Goals of Rx



- Alleviate acute bleeding. Give IM progesterone 100 mg stat
- Prevent future episodes of noncyclic bleeding aim to give a bleed which is predictable in timing and amount

• Decrease risk of long term complications (eg development of endometrial



**Refer OBGYN** for endometrial assessment and further treatment if failed conventional initial treatment or age 45and above

### **PROGYLUTON**



- Cyclical sequential combined HRT (2mg estradiol valerate for first 11 days and 2mg E2V with 0.5mg norgestrel for next 10 days)
- Regulates menstrual cycle and does not affect endogenous hormone production
- Does not interfere with ovulation
- Can be used by pre- and peri- menopausal patients



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- First oral therapy approved for heavy menstrual bleeding (HMB) with contraceptive effect (E2V and Dienogest)
- Novel dosing regimen of 26 + 2 (ie 26 days "active" pills and 2 days of "placebo" pills, which provides good cycle control
- Reduces menstrual blood loss by 88% after 6 cycles of treatment
- Rapid and significant reduction of menstrual blood loss by 70 % after two cycles
- Low discontinuation rate of 3% with favourable safety profile



# **Qlaira**

Table 1 Contents and order of pills contained in each wallet of Qlaira

Number of pills	Colour	Estradiol Valerate (mg)	Dienogest (mg)
2	Dark yellow	3	0
5	Medium red	2	2
17	Light yellow	2	3
2	Dark red	1	0
2	White	0	0

# Mirena IUS



- Releases 20ug of LNG daily which affects endometrium locally
- Lasts 5 years
- Low local hormonal effect in endometrium which provides shorter and lighter menses and reduces dysmenorrhea
- 20% amenorrhoea after 1 year
- 20% intermittent per-vaginal spotting in 1st 6 months
- Lower risks of pelvic inflammatory disease and ectopic pregnancy compared with copper-IUCD



# **Depot Provera**

- Intramuscular Depot Provera 150mg every 3 monthly
- · Induce endometrial atrophy and amenorrhoea
- · Irregular bleeding in first 3 months
- · Side-effects: abdominal bloating, breast tenderness, weight gain, depression, water retention



### Gonadotrophin Releasing Hormone analogue (GnRHa)

- Continuous treatment with GnRHa causes down-regulation of pituitary gland and subsequent decrease in gonadotrophins and ovarian steroids
- · Causes amenorrhoea (90%)
- Side-effects are related to hypo-oestrogenism and post-menopausal in type (hot flushes, insomnia, mood swings)
- Not recommended for more than 6 months of continuous usage due to the risk of osteoporosis unless with hormonal add-back therapy
- Subcutaneous injection Zoladex (Goserelin) 3.6mg monthly, subcutaneous injection Lucrin (Leuprorelin) 3.75mg monthly / 11.25mg every 3-monthly, intra-muscular injection Decapetyl (Triptorelin) 3.75mg monthly

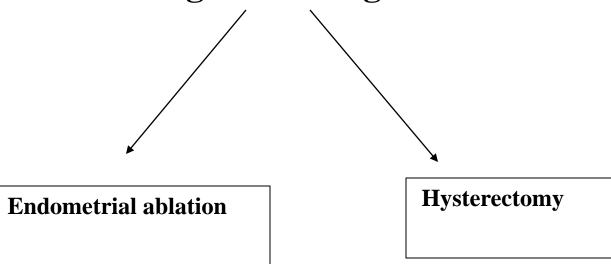


## **Danazol**

- Induce amenorrhoea in majority if taken in moderate/ high dose (> 400 mg daily)
- If taken at low dose (200 400 mg daily) it will induce amenorrhoea in some while others may experience light but often unpredictable bleed
- Masculinising side-effects such as hirsutism, acne, voice change (irreversible)



# **Surgical Management**





### THE HEALTHY VAGINA

- The vagina serves as a passageway between external environment and reproductive organs
- pH balance of vagina is acidic (pH 3.8-4.4) prevents infections
- Acidic environment is created by normally-occurring bacteria (lactobacilli)
- Vaginal secretions can be physiological
- Vaginal discharge is poorly indicative of STI



### **Pathological Causes**



Non-Infective

Infective

**CANDIDIASIS** 

TRICHOMONAS VAGINALIS

BACTERIAL VAGINOSIS



Retained tampon or condom

Chemical irritation

Allergic responses

Ectropion

Endocervical polyp

Fistula / Neoplasia



# Should a patient with vaginal discharge be investigated?

- High risk of STI
- Symptoms suggestive of upper genital tract infection (e.g. abdominal pain, dyspareunia or fever)
- Failed previous treatment
- Postnatal, post-miscarriage, or postabortion
- Within 3 weeks of insertion of IUCD
- Requested by patient



- Overgrowth of anaerobes (Gardnerella vaginalis, Mycoplasma hominis and Mobiluncus species)
- Replacement of lactobacilli and an increase in pH (from < 4.5 to 7.0)</li>
- Spontaneous onset and remission of BV.
- Not considered a STI but occurs more commonly amongst sexually active women.

## Treatment of BV



### **General Measures**

Avoid vaginal douching or use of antiseptic agents
 Grade C, Level 3

### **Indications**

1) All symptomatic women, pregnant or non pregnant.

Grade A, Level 1+

2) Asymptomatic women before surgical procedures.

**Grade A, Level 1+** 



# Recommended regimens DUKE NUS



	Regimes	Grade and Level of evidence
1	Clindamycin cream 2% (5 g) intravaginally daily x 3 days or Clindamycin site-released (SR) cream 2% (5 g) intravaginally x single application	Grade A, Level 1+
	OR	
2	Clindamycin 300 mg orally bid x 7 days	Grade A, Level 1+
	OR	
3	Metronidazole gel 0.75% (5 g) intravaginally daily x 5 days	Grade A, Level 1+
	OR	
4	Metronidazole pessary (500 mg) intravaginally bid x 7 days or daily x 14 days	Grade A, Level 1+
	OR	
5	Metronidazole 400 mg orally bid x 7 days	Grade A, Level 1+
	OR	
6	Tinidazole 2 g orally single dose	Grade A, Level 1+

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### Recurrent BV

- Occurs within 3/12 Rx (15-30%).
- Few published studies evaluating the optimal approach to frequent BV recurrences.
- Consider suppressive regimes but evidence to support their effectiveness is limited.



### Recurrent BV

#### Suggested suppressive therapy:

	REGIME	Grade and Level of evidence
1	Metronidazole gel 0.75% (5 g) twice weekly for 4 - 6 months	Grade A, Level 1+
	OR	
2	Metronidazole 400 mg orally bid for 3 days at the start and end of menstruation	Grade C, Level 3

#### Suggested maintenance regime:

• Acetic acid vaginal gel use at time of menstruation and following unprotected sexual intercourse to maintain acidic vaginal pH.

Grade B, Level 2+



#### Recurrent BV

#### Follow up

- Follow-up not necessary if symptoms resolve.
- Test of cure not required.

#### **Management of sex partners**

- No clinical counterpart is recognised in males and screening and treatment has not shown to be beneficial for the patient or the male partner.
- Some studies reported a high incidence of BV in female partners of lesbian women with BV, but no study looks into treatment of partners of lesbian women simultaneously.



# Vulvovaginal candidiasis (VVC)

- Candida albicans (80-90%).
- Non-albicans species include C. glabrata, C. tropicalis, C. krusei, C.parapsilosis, and Saccharomyces cerevisiae.



# Vulvovaginal candidiasis (VVC)

- Risk factors: Pregnancy, DM, prolonged steroid therapy, antibiotics treatment, and immunosuppression.
- Lab tests include Gram-stain or wet mount (saline or 10% KOH) of swabs from vulva / vaginal wall which reveal budding yeast cells and pseudohyphae (sensitivity 60%), vaginal pH 4 - 4.5 and culture on Sabouraud medium.



# **Vulvovaginal candidiasis (VVC)**

#### Note:

- Isolation of Candida species in absence of symptoms and signs does not suggest infection and is not an indication for treatment as 10-20% of women during reproductive years may be colonized with Candida species.
- None of the symptoms or signs pathognomonic.
- Symptoms and signs no guide to underlying causative species.

# Treatment of Candidiasis **DUKE DUKE DUKE**



	REGIME	Grade and Level of evidence
1	Butoconazole1-sustained released (SR) cream site 2% (5 g) intravaginally x single application	Grade A, Level 1+
	OR	
2	Clotrimazole pessary 200 mg intravaginally daily x 3 days or 100 mg or 1% cream (5 g) intravaginally daily x 7 days or 500 mg x single application	Grade A, Level 1+
	OR	
3	Fluconazole 150 mg orally single dose	Grade A, Level 1+
	OR	
4	Isoconazole pessary 600 mg intravaginally x single application	Grade A, Level 1+
	OR	
6	Itraconazole 200 mg orally bid x 1 day	Grade A, Level 1+
	OR	
7	Miconazole pessary 200 mg intravaginally daily x 3 days or 100 mg or 2% cream (5 g) intravaginally daily x 7 days	Grade A, Level 1+
	OR	
8	Nystatin pessary 100,000 U daily x 14 days	Grade A, Level 1+

## **Treatment of Candidiasis**



#### Note:

- All topical and oral azole therapies give a clinical and mycological cure rate of 80-90% in uncomplicated VVC.
   Nystatin preparations give 70-90% cure rate.
- Treatment choice personal preference, availability and affordability as well as familiarity of the clinician.
- Topical azole treatment may damage latex condoms and diaphragms. Barrier methods not recommended as contraception during treatment.
- Topical azole treatment may cause vulvo-vaginal irritation and this should be considered if symptoms worsen.

## Treatment of Candidiasis DU



## Follow up

- Follow-up not necessary if symptoms resolve.
- Test of cure is not required.

## Management of sex partners

 No evidence to support treatment of asymptomatic male sexual partners in acute or recurrent VVC.



# Recurrent vulvovaginal candidiasis

- Defined as 4 or more episodes of symptomatic vulvovaginal candidiasis in a year.
- May have partial resolution of symptoms between episodes.
- Positive microscopy or moderate/heavy growth of Candida on at least two episodes.
- 5% acute VVC will develop recurrent VVC.
- Usu due to C albicans although C.glabrata and other nonalbicans species observed in 10-20% of recurrent VVC.
- Evaluate predisposing factors. These include uncontrolled DM, immunosuppression, high E2 state (e.g. use of OCP and HRT), disturbance of normal vagina flora (e.g. use of broad-spectrum antibiotics) and steroid use.



### **Treatment of Recurrent VVC**

 Clinicians should be aware of psychosexual problems and depression.

 Principle of therapy involves an induction regimen to ensure clinical remission, followed immediately by a maintenance regime.



## **Treatment of Recurrent VVC**

	Induction Regimens	Grade and Level of evidence
1	Fluconazole 150 mg orally every 72 hours x 3 doses	Grade A, Level 1+
	OR	
2	Topical imidazole therapy x 7-14 days according to symptomatic response	Grade C, Level 3
	Maintenance Regimens	
1	Clotrimazole pessary 500 mg intravaginally once a week or 200 mg intravaginally twice a week	Grade B, Level 2++
	OR	
2	Fluconazole 150 mg orally once a week	Grade B, Level 2++



### **Treatment of Recurrent VVC**

### Note:

 Maintenance therapy should last 6 months. 90% of women remain disease-free during treatment.

Grade B, Level 2++

 For women with relapses between doses, consider twice-weekly 150 mg fluconazole or 50 mg fluconazole daily.

Grade C, Level 2+

Monitor LFT when on regular oral azole Rx.

Grade D, Level 4

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### Alternative treatment for VVC

## **Probiotics/Lactobacillus**

 Insufficient evidence to support use of oral or vaginal LB to prevent VVC although there are anecdotal reports of benefit.

# **Special groups**



## Candidiasis in diabetes mellitus

- Optimise glycaemic control.
- Increased prevalence of non-albicans species, in particular C glabrata.
- For treatment of symptomatic women with C glabrata, boric acid 600 mg intravaginal suppository once a day for 14 days is as effective as a single dose of fluconazole 150 mg.

Grade A, Level 1+

# **Special groups**



## **Candidiasis in HIV infection**

 VVC occurs more frequently and with greater persistence in women with HIV infection. Treat with conventional methods.

## Non-albicans VVC

- Majority due to C. glabrata susceptible to available azoles. C. krusei is intrinsically resistant to fluconazole.
- Optimal Rx of non-albicans VVC unknown.
- Non-albicans VVC may require longer courses (7-14 days).

#### **Treatment**



 Nystatin pessaries or non-fluconazole azole drug (oral or topical) are first line treatment for non-albicans VVC.

Grade C, Level 2+

 Consider Amphotericin B vaginal suppositories 50 mg once a day for 14 days.

### **Trichomoniasis**



- Caused by Trichomonas vaginalis.
- STI.
- 10 50% asymptomatic.
- Predominant symptoms: yellow-green and offensive discharge, vulval itch or dysuria.
- Vulva erythema or excoriations
- Cervical haemorrhages and ulcers can give the classical appearance of the "strawberry cervix" (2%).

### **Trichomoniasis**



### Management of sex partners

- Sexual contacts in preceding 60 days should be traced, screened and treated on epidemiologic grounds. If the last sexual exposure was >60 days, the patient's most recent partner should be treated.
- Patients should be advised to avoid sexual intercourse (including oral sex) until they and their partner(s) have completed treatment and follow-up.
- Screening for coexisting sexually transmitted infections should be undertaken in both the patients and their partners.
- Women should be informed that TV is a STI and partner management and treatment is recommended for all partners in last 2 months.

Grade C, Level 2+



### Follow-up

 Follow-up unnecessary for asymptomatic patients. Patients with persistent symptoms should be retreated with metronidazole 400 mg orally bid for 7 days.

Grade A, Level 1+

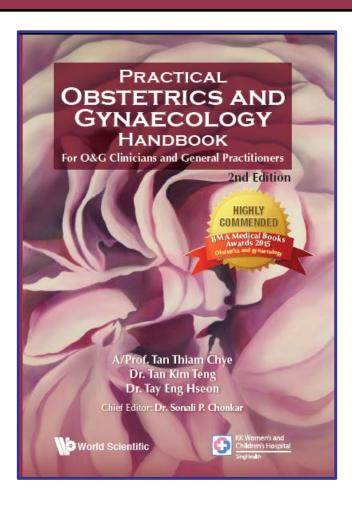
 If treatment failure occurs repeatedly, the patient can be treated with high dose oral metronidazole 2 g daily for 3 days.

Grade A, Level 1+

"This is a useful reference book and a fantastic educational resource. Multiple papers and NICE guidelines have been condensed and summarised into a readable format with beautiful illustrations, photos and diagrams. I will recommend this book to local GP trainees. Clear Photos. Useful diagrams and a good combination of medical and practical advice."

British Medical Association Book Awards 2015





## Thank you