GYNECOLOGY

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ANATOMY

A. EXTERNAL GENITALIA

❑ referred to collectively as the vulva

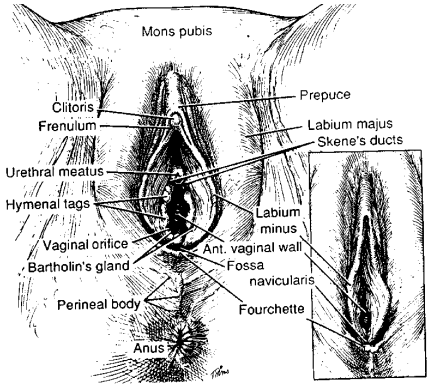

Figure 1. Vulva and Perineum

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B. VAGINA

C. UTERUS

❑ includes the cervix **(see Colour Atlas OB1)** and uterine corpus, joined by the isthmus

❑ 4 paired sets of ligaments:

- round ligaments: travel from anterior surface of uterus, through broad ligament, through inguinal canal, terminating in the labium majus; keep uterus anteverted
- uterosacral ligaments: arise from sacral fascia and insert into posterior inferior uterus; important mechanical support for uterus and contain autonomic nerve fibers
- cardinal ligaments: extend from lateral pelvic walls and insert into lateral cervix and vagina; important mechanical support, preventing prolapse
- broad ligaments: pass from lateral pelvic wall to sides of uterus; coursing through the broad ligament on each side is the fallopian tube, round ligament, ovarian ligament, nerves, vessels, and lymphatics

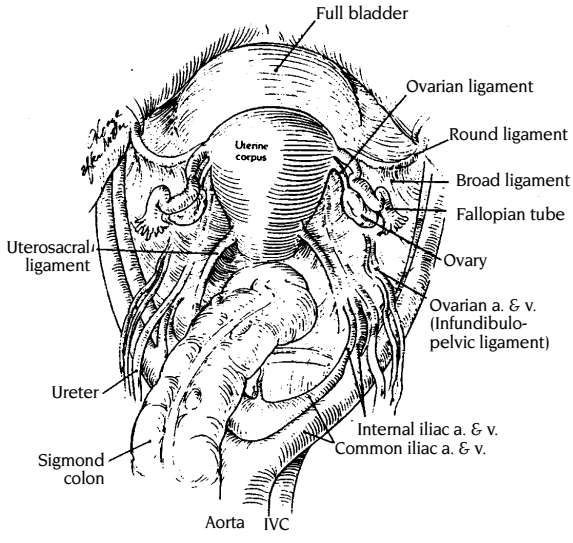

Figure 2. Posterior View of Internal Genital Organs

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D. FALLOPIAN TUBES

E. OVARIES

APPROACH TO THE PATIENT

HISTORY

❑ includes identifying history (IH), chief complaint (CC), history of present illness (HPI), past medical history (PMH), Meds, Allergies, etc.

Obstetrical History

❑ GTPAL (see Obstetrics Chapter)
❑ year, location, outcome, mode of delivery, duration of labour, sex, gestational age, weight, complications

Menstrual History

❑ LNMP, LMP (last menstrual period)
❑ age of menarche, menopause
❑ cycle length, duration, regularity
❑ flow
❑ associated symptoms: pain, PMS
❑ abnormal menstrual bleeding: intermenstrual, post-coital

Sexual History

❑ age when first sexually active
❑ number and sex of partners
❑ oral, anal, vaginal
❑ current relationship and partner's health
❑ dyspareunia or bleeding with intercourse
❑ satisfaction
❑ history of sexual assault or abuse

Contraceptive History

❑ present and past contraception modalities
❑ reasons for discontinuing
❑ compliance
❑ complications/failure/side-effects

Gynecological Infections

❑ sexually transmitted diseases (STDs), pelvic inflammatory disease (PID)
❑ vaginitis, vulvitis
❑ lesions
❑ include treatments, complications

Gynecological Procedures

❑ last Pap smear
    - history of abnormal Pap
    - follow-up and treatments
❑ gynecological or abdominal surgery
❑ previous ectopic pregnancies

PHYSICAL EXAMINATION

❑ height, weight, blood pressure (BP)
❑ breast exam
❑ abdominal exam
❑ pelvic exam including
    - inspection of external genitalia
    - speculum exam +/– smears and swabs
    - bimanual exam
        - cervix size, consistency, os, and tenderness
        - uterus size, consistency, contour, position, shape, mobility, and other masses
        - adnexal mass, tenderness
    - rectovaginal exam
    - rectal exam

INVESTIGATIONS

Bloodwork

❑ CBC
    - evaluation of abnormal uterine bleeding, preoperative investigation
❑ βhCG
    - investigation of possible pregnancy or ectopic pregnancy
    - work-up for gestational trophoblastic neoplasia (GTN)
    - monitored after the medical management of ectopic and in GTN to assess for cure and recurrences
❑ LH, FSH, TSH, PRL
    - amenorrhea, menstrual irregularities, menopause, infertility

Imaging

- ❑ ultrasound (U/S)
  - imaging modality of choice for pelvic structures
    - transvaginal U/S provides enhanced details of structures located near the apex of the vagina (i.e. intrauterine and adnexal structures)
  - may be used to
    - diagnose acute or chronic pelvic pain
    - rule in or out ectopic pregnancy, intrauterine pregnancy
    - assess uterine, adnexal, ovarian masses (i.e. solid or cystic)
    - determine uterine thickness
    - monitor follicles during assisted reproduction
- ❑ hysterosalpingography
  - x-ray after contrast is introduced through the cervix into the uterus
  - contrast flows through the tubes and into the peritoneal cavity if tubes are patent
  - used for evaluation of size, shape, configuration of uterus, tubal patency or obstruction
- ❑ sonohysterography
  - saline infusion into endometrial cavity under U/S visualization expands endometrium, allowing visualization of uterus and fallopian tubes
  - useful for investigation of abnormal uterine bleeding, uncertain endometrial findings on vaginal U/S, infertility, congenital/acquired uterine abnormalities (i.e. uterus didelphys, uni/bicornate, arcuate uterus)
  - easily done, minimal cost, extremely well-tolerated, sensitive and specific
  - frequently avoids need for hysteroscopy

Genital Tract Biopsy

- ❑ vulvar biopsy
  - under local anesthetic
  - Keye's biopsy or punch biopsy
  - hemostasis achieved with local pressure, Monsel solution or silver nitrate
- ❑ vaginal and cervical biopsy
  - punch biopsy or biopsy forceps
  - generally no anesthetic used
  - hemostasis with Monsel solution
- ❑ endometrial biopsy
  - in the office using an endometrial suction curette (Pipelle): hollow tube guided through the cervix used to aspirate fragments of endometrium (well-tolerated)
  - a more invasive procedure using cervical dilatation and curettage (D&C) may be done in the office or operating room (via hysteroscopy or during D&C)

Colposcopy

- ❑ diagnostic use
  - provides a magnified view of the surface structures of the vulva, vagina and cervix
  - special green filters allow better visualization of vessels
  - application of 1% acetic acid wash dehydrates cells and reveals white areas of increased nuclear density (abnormal) or areas with epithelial changes
  - biopsy of visible lesions or those revealed with the acetic acid wash allows early identification of dysplasia and neoplasia
- ❑ therapeutic use
  - cryotherapy
    - tissue destruction by freezing
    - for dysplastic changes, genital warts
  - laser
  - cervical conization
    - removes the cervical transformation zone and areas within the endocervical canal
    - methods include cold knife, laser excision, or electrocautery

DIFFERENTIAL DIAGNOSIS OF COMMON GYNECOLOGICAL COMPLAINTS

VAGINAL DISCHARGE

Physiological
❑ normal vaginal discharge (midcycle)
❑ increased estrogen states (e.g. pregnancy, oral contraceptive pill (OCP))

Infectious
❑ candida vulvovaginitis (*Candida albicans*)
❑ trichomonas vaginitis (*Trichomonas vaginalis*)
❑ bacterial vaginosis (*Gardnerella vaginalis*)
❑ *chlamydia*
❑ gonorrhea
❑ bartholinitis or Bartholin abscess
❑ PID

Neoplastic
❑ vaginal intraepithelial neoplasia (VAIN)
❑ vaginal squamous cell cancer
❑ invasive cervical cancer
❑ fallopian tube cancer

Other
❑ allergic/irritative vaginitis
❑ foreign body
❑ atrophic vaginitis
❑ enterovaginal fistulae

VAGINAL/VULVAR PRURITUS

Infectious
❑ candida vulvovaginitis
❑ trichomonas vaginitis
❑ herpes genitalis (herpes simplex virus (HSV))

Other
❑ postmenopausal vaginitis or atrophic vaginitis
❑ chemical vaginitis
❑ hyperplastic dystrophy
❑ lichen sclerosis
❑ vulvar cancer

GENITAL ULCERATION

Infectious
❑ painful
  - herpes genitalis (HSV)
  - chancroid (*Hemophilus ducreyi*)

❑ painless
  - syphilis (*Treponema pallidum*)
  - granuloma inguinale (*Calymmatobacterium granulomatis*)
  - lymphogranuloma venereum (C. *trachomatis* - serotypes L1-L3)

Malignant
❑ vulvar cancer

Other
❑ trauma
❑ foreign body
❑ Behçet's disease
(autoimmune disease resulting in oral and genital ulcerations with associated superficial ocular lesions)

INGUINAL LYMPHADENOPATHY

Infectious
❑ HSV
❑ syphilis
❑ chancroid
❑ granuloma inguinale (D. *granulomatis*)

Malignant
❑ vulvar cancer
❑ vaginal cancer
❑ anal cancer
❑ lymphoma

PELVIC MASS

Uterus, Asymmetrical
- ❑ leiomyomata
- ❑ leiomyosarcoma

Uterus, Symmetrical
- ❑ pregnancy
- ❑ adenomyosis
- ❑ endometrial cancer
- ❑ imperforate hymen
- ❑ hematometra/pyometra

Adnexal, Ovarian
- ❑ corpus luteum cyst
- ❑ follicular cyst
- ❑ theca lutein cyst
- ❑ endometrioma
- ❑ inflammatory cyst (tubo-ovarian abscess)
- ❑ luteoma of pregnancy
- ❑ polycystic ovary
- ❑ benign neoplasms
  - dermoid cyst (most common)
- ❑ malignant neoplasms
  - granulosa cell tumour (most common)
  - metastatic lesions (e.g. Krukenberg's tumour from stomach)

Adnexal, Non-ovarian
- ❑ gynecological
  - ectopic pregnancy
  - pelvic adhesions
  - paratubal cysts
  - pyosalpinx/hydrosalpinx
  - leiomyomata or fibroids
  - primary fallopian tube neoplasms
- ❑ gastrointestinal
  - appendiceal abscess
  - diverticular abscess
  - diverticulosis, diverticulitis
  - carcinoma of rectum/colon
- ❑ genitourinary
  - distended bladder
  - pelvic kidney
  - carcinoma of the bladder

DYSPAREUNIA
- ❑ atrophic vaginitis
- ❑ chemical vaginitis
- ❑ lichen sclerosis
- ❑ candida vulvovaginitis
- ❑ trichomonas vaginitis
- ❑ acute or chronic PID
- ❑ endometriosis
- ❑ fibroids
- ❑ adenomyosis
- ❑ congenital abnormalities of vagina (e.g. septate vagina)
- ❑ retroverted, retroflexed uterus
- ❑ ovarian cysts/tumours
- ❑ psychological trauma
- ❑ vaginismus
- ❑ vulvodynia

PELVIC PAIN

Acute Pelvic Pain
- ❑ gynecological causes
  - pregnancy-related
    - ectopic pregnancy
    - abortion (missed, septic, etc.)
  - ovarian
    - ruptured ovarian cyst
    - torsion of ovary or tube
    - mittelschmertz (ovulation pain as follicle ruptures into peritoneal space)
    - hemorrhage into ovarian cyst or neoplasm
  - uterine
    - degeneration of fibroid
    - torsion of pedunculated fibroid
  - infectious
    - acute PID

❑ non-gynecological causes
- urinary
  - urinary tract infection (UTI) (cystitis, pyelonephritis)
  - renal colic
- gastrointestinal
  - appendicitis
  - mesenteric adenitis
  - diverticulitis
  - inflammatory bowel disease (IBD)

Chronic Pelvic Pain (CPP)
❑ refers to pain of greater than 6 months duration
❑ gynecological causes of CPP
- chronic PID
- endometriosis
- adenomyosis
- invasive cervical cancer (late)
- leiomyomata
- uterine prolapse
- adhesions
- cyclic pelvic pain
  - primary dysmenorrhea
  - secondary dysmenorrhea
- ovarian remnant syndrome
- pelvic congestion syndrome
- ovarian cyst

❑ non-gynecological causes
- referred pain
- urinary retention
- urethral syndrome
- penetrating neoplasms of GI tract
- irritable bowel syndrome
- partial bowel obstruction
- inflammatory bowel disease (IBD)
- diverticulitis
- hernia formation
- nerve entrapment
- constipation
- psychological trauma
  - 20% of CPP patients have a history of previous sexual abuse/assault (remember to ask about it)

ABNORMAL UTERINE BLEEDING (see Figure 3)

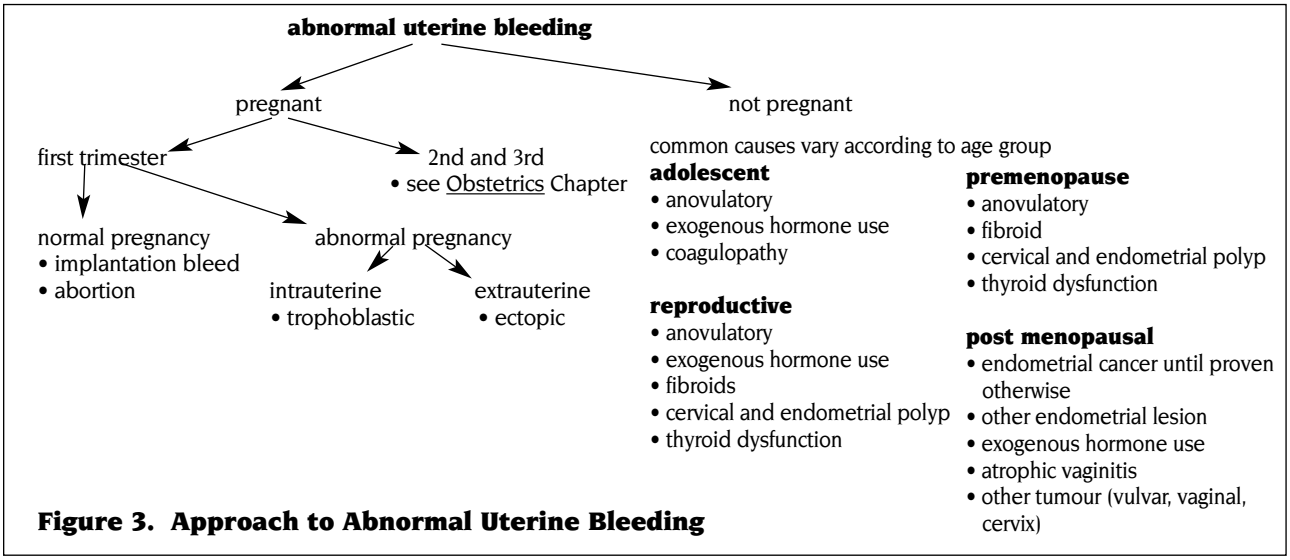

Figure 3. Approach to Abnormal Uterine Bleeding

Gynecological Causes
❑ increased bleeding with menses
- polyps
- adenomyosis
- leiomyomata
- endometriosis
- intrauterine device (IUD)

DIFFERENTIAL DIAGNOSIS OF COMMON GYNECOLOGICAL COMPLAINTS . . . CONT.

- ❑ bleeding following a missed period
  - ectopic pregnancy
  - abortion (missed, threatened, inevitable, incomplete, or complete)
  - implantation bleed
  - trophoblastic disease
  - placental polyp
- ❑ irregular bleeding
  - dysfunctional uterine bleeding
  - polycystic ovarian syndrome
  - vulvovaginitis
  - PID
  - benign or malignant tumours of vulva, vagina, cervix, or uterus
  - ovarian malignancy
  - anovulation (e.g. stress amenorrhea)
  - oral contraceptive use
  - polyps
- ❑ postmenopausal bleeding
  - endometrial cancer until proven otherwise
  - atrophic vaginitis (most common cause)
  - ovarian malignancy
  - benign or malignant tumours of vulva, vagina or cervix
  - withdrawal from exogenous estrogens
  - atrophic endometrium
  - endometrial/endocervical polyps
  - endometrial hyperplasia
  - trauma
  - polyps
  - lichen sclerosis

Non-Gynecological Causes

- ❑ thyroid disease (hyperthyroid/ hypothyroid)
- ❑ chronic liver disease
- ❑ von Willebrand's disease
- ❑ leukemia
- ❑ idiopathic thrombocytopenic purpura
- ❑ hypersplenism
- ❑ rectal or urethral bleeding
- ❑ renal failure
- ❑ adrenal insufficiency and excess
- ❑ drugs: spironolactone, danazol, psychotropic agents
- ❑ metastatic cancer

NORMAL MENSTRUATION AND MENOPAUSE

STAGES OF PUBERTY

- ❑ Tanner Staging (see Pediatrics Chapter)
  1. accelerated growth
  2. thelarche (breast budding)
  3. pubarche and adrenarche (growth of pubic and axillary hair)
  4. maximal growth (peak height velocity)
  5. menarche

MENSTRUAL CYCLE

Characteristics

- ❑ menarche at age 10-15 years (average age is decreasing)
- ❑ entire cycle 28 +/– 7 days, with bleeding for 1-6 days
- ❑ polymenorrhea if < 21 days
- ❑ oligomenorrhea if > 35 days
- ❑ 25-80 mL of blood loss per cycle

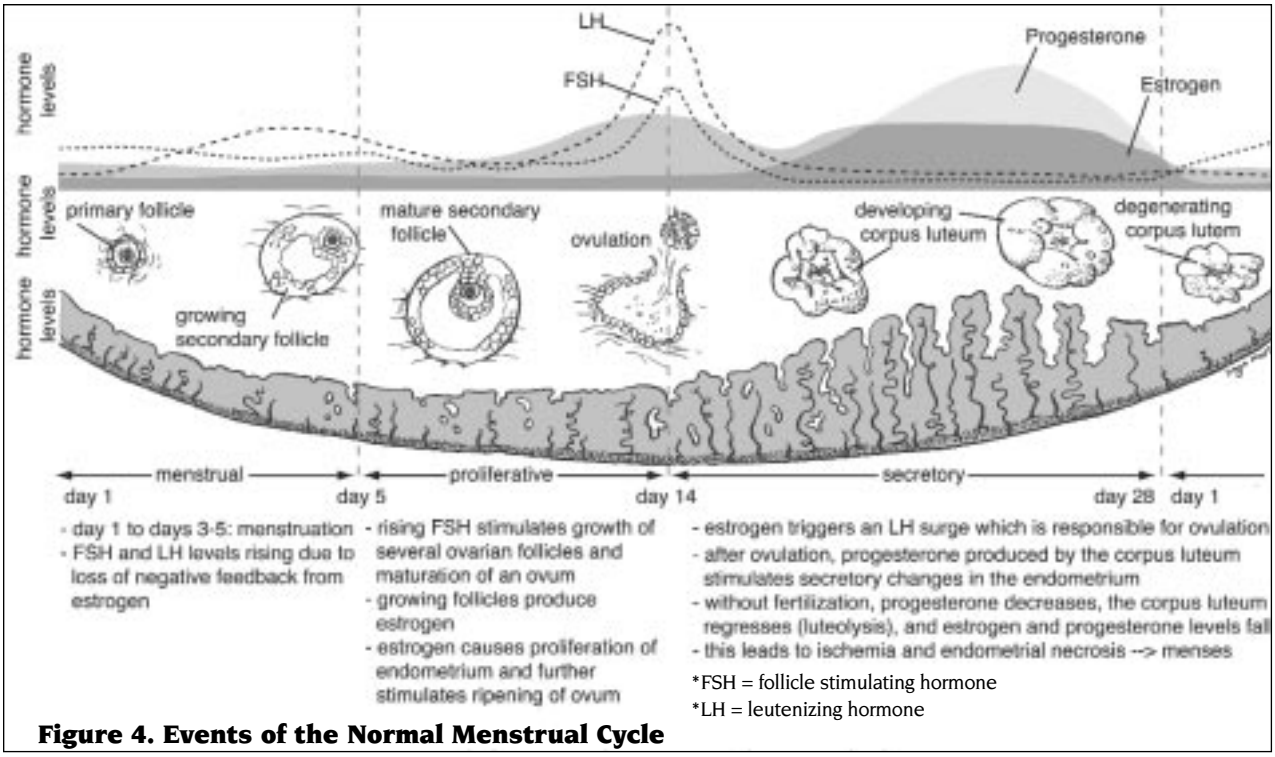

Figure 4. Events of the Normal Menstrual Cycle

Proliferative/Follicular Phase
- ❑ from first day of menses (day 1 of cycle) to preovulatory LH surge
- ❑ variable in length, estrogenic, low basal body temperature
- ❑ folliculogenesis and a rise in FSH levels begin during the last few days of the luteal phase of the previous cycle
- ❑ FSH secretion is affected by negative feedback from estrogen and progesterone; thus, initial FSH increase occurs due to regression of corpus luteum (in the preceding cycle), which causes a decrease in estrogen and progesterone, resulting in the escape of FSH secretion from negative feedback inhibition
- ❑ rising FSH leads to recruitment and growth of 3 ~ 30 follicles from which a single dominant follicle is chosen for ovulation; remainder of follicles become atretic
- ❑ LH begins to rise several days after rise in FSH, and continues to rise secondary to positive feedback from estrogen (produced by granulosa cells of the enlarging follicle)
- ❑ FSH alternatively decreases during the late follicular phase due to greater negative feedback from rising estrogen
- ❑ rising estrogen levels result in the proliferation of the endometrium and increased cervical vascularity/edema
- ❑ volume and elasticity of cervical mucus is also increased ('spinnbarkeit' = long stretchy threads)
- ❑ LH surge immediately precedes ovulation and marks the completion of the follicular phase

Ovulation
- ❑ 'ovulation' = release of ovum from the mature dominant follicle
- ❑ LH surge leads to ovulation (14 days before the onset of menses; 32 ~ 34 h after onset of LH surge)
- ❑ basal body temperature rise (0.5-1.0°C) due to the increase in progesterone level

Secretory/Luteal Phase
- ❑ from ovulation to the onset of menses
- ❑ fixed in length (14 days); corpus luteum (CL) formation
- ❑ characterized by suppression of both LH and FSH due to negative feedback from rising estrogen and progesterone
- ❑ CL develops from luteinized granulosa and thecal cells in ovary, and secretes progesterone and estrogen
- ❑ progesterone prepares endometrium for embryo implantation
- ❑ progesterone also causes endometrial glands to become coiled and secretory with increased vascularity
- ❑ without pregnancy —> decrease in progesterone —> regression of corpus luteum (luteolysis) —> withdrawal of estrogen and progesterone —> constriction of spiral arteries —> ischemia and endometrial necrosis —> menses
- ❑ additionally, the fall in estrogen and progesterone levels allows FSH to escape negative feedback; FSH begins to increase as a result, and this rise continues into follicular phase of next cycle

PREMENSTRUAL SYNDROME (PMS)

Definition
- ❑ variable cluster of symptoms that regularly occur prior to each menstrual episode
- ❑ more correctly called 'ovarian cycle syndrome' since symptoms depend on ovulation (see Table 4)
- ❑ also called 'menstrual molimina'
- ❑ etiology is unknown

Symptoms
- ❑ occur 7 -10 days before menses and relieved by onset of menses
- ❑ 7 day symptom-free interval must be present in first half of cycle
- ❑ physiologic and emotional symptoms
  - irritability
  - anxiety
  - depression
  - sleep disturbance
  - appetite change
  - libido change
  - fatigue
  - suicidal ideation
  - fluid retention
  - weight gain, bloating

Treatment
- ❑ no proven beneficial treatment, only suggested treatment
- ❑ psychological support
- ❑ diet
  - decreased sodium, fluids, carbohydrates
  - increased protein
  - avoidance of caffeine and alcohol
- ❑ medications
  - OCP
  - progesterone suppositories
  - diuretics for severe fluid retention
  - NSAIDs for discomfort, pain
  - danazol (an androgen that inhibits pituitary-ovarian axis)
  - over the counter (OTC): evening primrose oil (linoleic acid), vitamin B6
  - SSRI antidepressants in selected cases
  - regular exercise

MENOPAUSE

Definitions
- ❑ menopause
  - cessation of menses for > 6 months due to ovarian failure
- ❑ perimenopause
  - transitional period between ovulatory cycles and menopause
  - characterized by irregular menstrual cycles due to fluctuating ovarian function

Types of Menopause
- ❑ physiological (spontaneous menopause); average age = 51
- ❑ premature ovarian failure (< 40 y.o.)
- ❑ iatrogenic (surgical/radiation/chemotherapy)

Symptoms
- ❑ symptoms mainly associated with estrogen deficiency:
  - vasomotor (hot flushes/flashes, sleep disturbances, formication)
  - urogential (atrophic changes involving vagina, urethra, bladder)
    - dyspareunia, vaginal itching, bleeding
    - urinary frequency, urgency, incontinence
  - skeletal (osteoporosis, joint and muscle pain, backache)
  - skin and soft tissue (decreased breast size, skin thinning and loss of elasticity)
  - psychological (mood disturbances, irritability, fatigue, decreased libido, memory loss)

Diagnosis
- ❑ increased levels of FSH (> 40 IU/L)
- ❑ decreased levels of estradiol

Treatment
- ❑ hormone replacement therapy (HRT) (see Table 1)
- ❑ doses much lower than OCP
- ❑ estrogen (E)
  - oral or transdermal (e.g. patch, gel)
  - transdermal preferred for women with hypertriglyceridemia or impaired hepatic function
- ❑ progestin (P)
  - given in combination with E for women with an intact uterus (i.e. no hysterectomy) to prevent development of endometrial hyperplasia/cancer
- ❑ combination E + P patches and pills also available

- ❑ physical exercise, relaxation, yoga
- ❑ calcium + vitamin D supplement (to prevent bone loss)
- ❑ bisphosphonates if osteoporosis
- ❑ Selective Estrogen Receptor Modulators (SERMs: see below)
- ❑ phytoestrogen supplementation (e.g. products including soy and flaxseed); variable improvement in hot flushes and vaginal dryness
    - popular (but not evidence-based) OTC choices: Black cohosh(vasomotor symptoms), St. John's Wort (mood), Gingko biloba (memory), Valerian (sleep), evening primrose oil, Ginseng, Dong Quai

Table 1. Examples of HRT Regimens

HRT Regimen	Estrogen Dose	Progestin Dose	Notes
Unopposed Estrogen (if no uterus)	CEE 0.625 mg po od	N/A	
Standard-dose Continuous Combined	CEE 0.625 mg po od	MPA 2.5 mg po od	• withdrawal bleeding occurs in a spotty, unpredictable manner • usually abates after 6-8 months because of endometrial atrophy • once the patient has become amenorrheic on HRT, significant subsequent bleeding episodes require evaluation (endometrial biopsy)
Standard-dose Cyclic	CEE 0.625 mg po od	MPA 5 – 10 mg po on days 1 – 14 of menstrual cycle	• bleeding occurs monthly after day 14 of progestin and this can continue for years • PMS-like symptoms (breast tenderness, fluid retention, nausea, headache) more prominent with cyclical HRT
Pulsatile	CEE 0.625 mg po od	MPA low-dose	• 3 days on, 3 days off
Transdermal	Estradiol transdermal system (Estraderm) 0.05 - 0.1/24 h; Use 1 patch twice a week	MPA 2.5 mg po od	• use patch 3 weeks on, 1 week off • must use oral progestins • combined patches also available

CEE = conjugated equine estrogen (e.g. Premarin) HRT = hormone replacement therapy
MPA = medroxyprogesterone acetate (e.g. Provera)

Table 2. Benefits/Risks of Postmenopausal Hormone Replacement Therapy (HRT)

Variable	Effect	Benefit or Risk	Source of Data
Definite Benefits			
Symptoms of Menopause	Definite improvement	> 70-80% decrease	Observational studies and RCT
Osteoporosis	Definite increase in bone mineral density (BMD); probable decrease in risk of fractures	2-5% increase in BMD; 25-50% decrease in risk of fractures	Observational studies and limited data from RCT
Definite Risks			
Endometrial cancer	Definite increase in risk with use of unopposed E; no increase with use of combined E-P	Increase in risk by 8-10x with use of unopposed estrogen for >10 years; no excess risk with combined E-P	Observational studies and RCT
Venous Thromboembolism	Definite increase in risk	Increase in risk by 2.7x	Heart and Estrogen/Progestin Replacement Study (HERS) and Observational Studies
Probable Increase in Risk			
Breast Cancer	Probable increase in risk with long-term use (> 5 years)	Overall increase in risk by 1.35x with HRT use for > 5 years	Meta-analysis of 51 observational studies
Gallbladder Disease	Probable increase in risk	Increase in risk by 1.4x	HERS
Uncertain Benefits and Risks			
Cardiovascular Disease • Primary Prevention • Secondary Prevention	 Ranges from net benefit to net harm Probable early increase in risk	 Uncertain Uncertain	 Observational studies and RCT* Observational studies
Colorectal Cancer	Possible but unproven decrease in risk	20% decrease	Observational studies
Cognitive dysfunction	Unproven decrease in risk (inconsistent results)	Uncertain	Observational studies and RCT

* Observational data suggest a decrease in risk of 35-50%, whereas RCT data show no effect or a possible harmful effect during the first 1-2 years of use.

Modified from NEJM 2001 *July*; 345(1): 34-40.

Other Side Effects of HRT
- ❑ can be worse in progesterone phase of combined therapy
- ❑ abnormal uterine bleeding: requires endometrial biopsy if bleeding other than withdrawal bleeding with combined E/P therapy, or bleeding following prolonged amenorrhea
- ❑ mastodynia
- ❑ edema, bloating, heartburn, nausea
- ❑ mood changes (progesterone)

Contraindications of HRT
- ❑ absolute
  - undiagnosed vaginal bleeding
  - known or suspected uterine cancer
  - acute liver disease
  - acute vascular thrombosis or history of severe thrombophlebitis or thromboembolic disease
- ❑ relative
  - history of breast cancer
  - pre-existing uncontrolled hypertension
  - uterine fibroids and endometriosis
  - familial hyperlipidemias
  - migraine headaches
  - family history of estrogen-dependent cancer
  - chronic thrombophlebitis
  - diabetes mellitus
  - gallbladder disease
  - impaired liver function
  - fibrocystic disease of the breasts
  - obesity

Selective Estrogen Receptor Modulators (SERMs)
- ❑ e.g. Raloxifene (Evista)
- ❑ mimics estrogen effects on bone
- ❑ avoids estrogen-like action on breast and uterine tissue
- ❑ may be protective against breast cancer
- ❑ does not relieve hot flashes (may make them worse) or other menopausal symptoms
- ❑ is associated with decreased LDL and decreased HDL, although no proven reduction in adverse cardiovascular events

Table 3. Comparison of Treatment Modalities in Menopause

Condition	Estrogen Alone	Estrogen + Progestin	SERMs	Bisphosphonates
Hot flashes and urogenital symptoms	++	++	–	00
Mood, cognitive, libido changes	+	+	00	00
Osteoporosis	++	++	++	++
Coronary artery disease	+/-	+/-	0	00
Stroke	00	-	0	00
Breast cancer	-	-	++	00
Endometrial cancer	--	00	00	00
deep vein thrombus (DVT) or pulmonary embolus	--	--	--	00

++ proven benefit; + possible benefit; -- proven risk; – possible risk; 00 no effect; 0 no data.

Reference: *West J Med* 2001;175:32-34.

DISORDERS OF MENSTRUATION

AMENORRHEA

Definitions
❑ primary amenorrhea: absence of menses by age 15
❑ secondary amenorrhea: absence of menses for > 6 months after documented menarche, or > 3 consecutive cycles

Pathophysiology (3 main mechanisms) (see Table 4)
❑ failure of hypothalamic-pituitary-gonadal axis
❑ absence of end organs
❑ obstruction of outflow tract

Table 4. Causes of Primary and Secondary Amenorrhea

Anatomic	Ovarian Failure	Endocrine	Other

• pregnancy
• adhesion (intrauterine)
• gonadal dysgenesis
• imperforate hymen
• vaginal septum
• cervical stenosis
• gestational trophoblastic neoplasia
	• menopause
	• surgery, radiation, chemotherapy
	• chromosomal
	  • Turner Syndrome (XO)
	  • Androgen Insensitivity Syndrome (XY)
	• Resistant Ovary Syndrome
		• hypothalamic/pituitary tumours
		• hyperprolactinemia
		• isolated gonadotropin deficiency
		• hyperandrogenism
		  • PCOS
		  • ovarian/adrenal tumour
		  • testosterone injections
		• hypothyroidism
		• Cushing's Disease
			• stress
			• anorexia
			• post OCP
			• illness
			• exercise

History and Physical
❑ history
- menstrual history: age at menarche, LMP, previous menstrual pattern, diet, medications, stress
- galactorrhea, previous radiation therapy, chemotherapy, recent weight gain
- prolonged intense exercise, excessive dieting
- symptoms of estrogen deficiency (e.g. hot flushes, night sweats)
- sexual activity
- rule out pregnancy (most common cause of secondary amenorrhea)

❑ physical examination
- Tanner staging (breast development, pubic hair distribution)
- thyroid gland palpated for enlargement/nodules
- hair distribution (?androgen excess/insensitivity)
- external genitalia and vagina for atrophy from estrogen deficiency, or clitoromegaly from androgen excess; imperforate hymen, vaginal septum
- palpation of uterus/ovaries

Investigations (see Figure 5)
❑ progesterone challenge to assess estrogen status
- medroxyprogesterone acetate (Provera) 10 mg OD for 10 days
- any uterine bleed within 2 – 7 days after completion is considered to be a positive test/withdrawal bleed
- if withdrawal bleeding occurs —> adequate estrogen
- if no bleeding occurs —> hypoestrogenism

❑ karyotype if indicated
❑ U/S to rule out cyst, PCOS

Treatment
❑ hypothalamic dysfunction
- stop drugs, reduce stress, adequate nutrition, decrease excessive exercise
- clomiphene citrate (Clomid) if pregnancy desired
- otherwise OCP to induce menstruation

❑ hyperprolactinemia
- bromocriptine
- surgery for macroadenoma

❑ premature ovarian failure
- treat associated autoimmune disorders
- HRT to prevent osteoporosis and other manifestations of hypoestrogenic state

❑ hypoestrogenism
- karyotype
- removal of gonadal tissue if Y chromosome present

❑ polycystic ovarian syndrome
- see Polycystic Ovarian Syndrome section

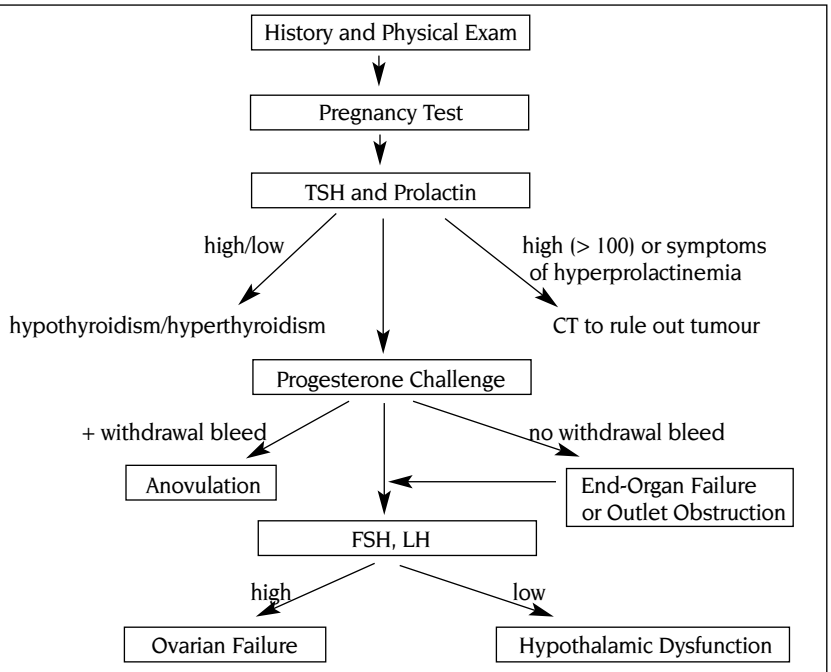

Figure 5. Diagnostic Approach to Amenorrhea

ABNORMAL UTERINE BLEEDING

❑ 90% anovulatory, 10% ovulatory

Hypermenorrhea/Menorrhagia

❑ cyclic menstrual bleeding occurring at regular intervals that is excessive in amount (> 80 mL) or duration (> 7 days)
- adenomyosis
- endometriosis
- leiomyomata
- endometrial hyperplasia or cancer
- hypothyroidism

Hypomenorrhea

❑ bleeding that occurs regularly but in small amounts (decreased menstrual flow or vaginal spotting)
- OCP

Oligomenorrhea

❑ episodic vaginal bleeding occurring at intervals > 35 days
- usually associated with anovulation

Polymenorrhea

❑ episodic vaginal bleeding occurring at intervals < 21 days
- usually associated with anovulation

Metrorrhagia

❑ uterine bleeding occurring at irregular intervals (i.e. between periods)
- organic pathology
- endometrial/cervical polyps or cancer
- anovulation
- estrogen withdrawal

Menometrorrhagia

❑ uterine bleeding irregular in frequency and excessive in amount
- organic pathology
- endocrine abnormality
- early pregnancy

Postmenopausal Bleeding

❑ any bleeding > 1 year after menopause
❑ investigations
- endometrial sampling - biopsy or D&C
- sonohysterogram for endometrial thickness and polyps
- hysteroscopy

DYSFUNCTIONAL UTERINE BLEEDING (DUB)

- ❑ abnormal bleeding with not attributable to organic (anatomic/systemic) disease
- ❑ a diagnosis of exclusion
- ❑ rule out anatomic lesions and systemic disease
  - blood dyscrasias, thyroid dysfunction, malignancy, PCOS, endometriosis, PID, fibroids, unopposed estrogen, polyps, or pregnancy
- ❑ > 90% of DUB is due to anovulation; thus "anovulatory bleed" is often used synonomously with DUB
  - during anovulatory cycles, failure of ovulation results in lack of progesterone, thus endometrium is exposed to prolonged unopposed estrogen stimulation
  - this results in overgrowth of endometrium that breaks down and bleeds (irregular estrogen-dependent breakthrough bleeding), unaccompanied by normal premenstrual molimina (premenstrual mood change, bloating, breast tenderness, dysmenorrhea)
- ❑ remaining 10% of DUB is due to dysfunction of corpus luteum such as inadequate progesterone production

Adolescent Age Group

- ❑ DUB due to immature hypothalamus with irregular LH, FSH, estrogen and progesterone pattern

Reproductive Age Group

- ❑ DUB due to an increase or decrease in progesterone level

Perimenopausal Age Group

- ❑ DUB due to increased ovarian resistance to LH and FSH

Mid-Cycle Spotting

- ❑ may be physiologic due to mid-cycle fall of estradiol

Premenstrual Spotting

- ❑ may be due to progesterone deficiency, endometriosis, adenomyosis and fibroids

Investigations/Management of DUB

- ❑ exclude organic (systemic/anatomic) causes first!
- ❑ ensure β-hCG is negative
- ❑ if anemic, supplement with iron
- ❑ mild DUB
  - OCP 1 tab tid for 10 days then 1 tab od for 4-6 months or
  - medroxyprogesterone acetate (Provera) 5-10 mg od on first 10-14 days of each month
- ❑ severe DUB
  - replace fluid losses
  - medroxyprogesterone acetate (Provera) 10 mg for next 7-10 days
  - acute, severe DUB: estrogen (Premarin) 25 mg IV q4-6h
- ❑ surgical
  - endometrial biopsy (for diagnosis)
  - D&C
  - endometrial ablation after pretreatment with danazol or GnRH agonists
  - hysterectomy

POLYCYSTIC OVARIAN SYNDROME

Clinical Presentation

- ❑ average age 15-35 years
- ❑ anovulation
- ❑ hirsutism
- ❑ infertility
- ❑ obesity
- ❑ virilization

Diagnosis

- ❑ most common pathologic finding: white, smooth, sclerotic ovary with a thick capsule; multiple follicular cysts in various stages of atresia; hyperplastic theca and stroma
- ❑ but ovarian pathology varies and none is pathognomonic
- ❑ diagnosis is biochemical/clinical
  - increased DHEAS, increased free testosterone, increased SHBG (sex hormone binding globulin)
  - increased LH, decreased or normal FSH (LH:FSH > 2)
  - clinically: presence of chronic anovulation with varying degrees of androgen excess

Pathogenesis

- ❑ fundamental defect = inappropriate signals to hypothalamic-pituitary axis (HPA) (see Figure 6)
- ❑ rarely, may be inherited in an X-linked manner

Associated Conditions

- ❑ insulin resistance
- ❑ acanthosis nigricans

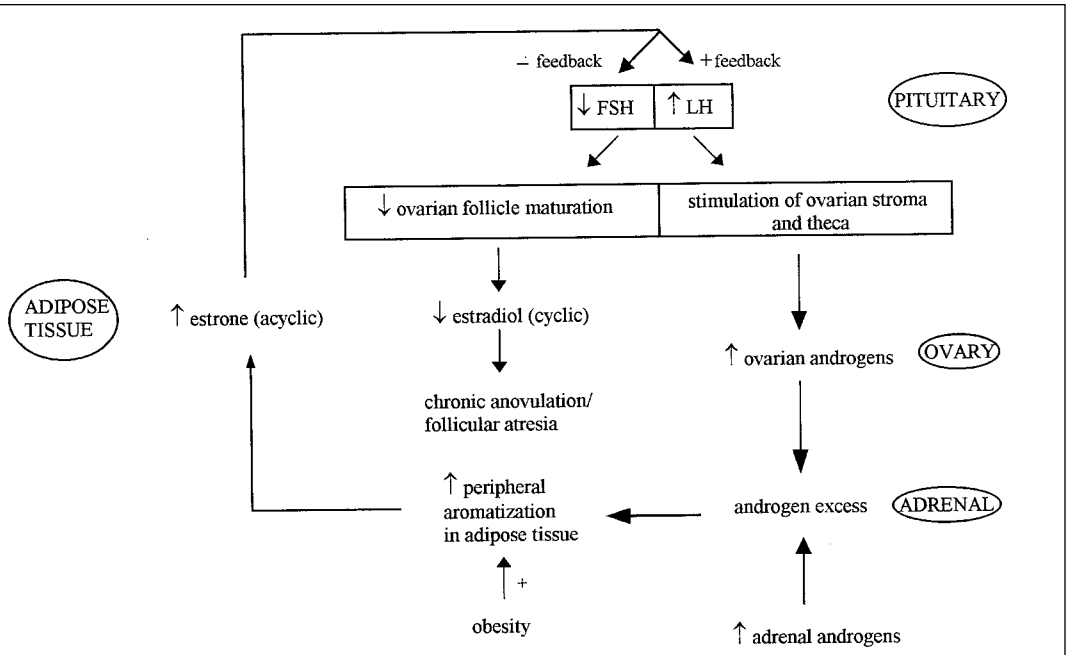

Figure 6. Mechanisms of Chronic Anovulation in Polycystic Ovarian Syndrome

Treatment
- ❑ interrupt the self-perpetuating cycle by
  - decreasing ovarian androgen secretion: OCP (wedge resections used in past)
  - decreasing peripheral estrone formation: weight reduction
  - enhancing FSH secretion: clomiphene, hMG (Pergonal), LHRH, purified FSH
- ❑ prevent endometrial hyperplasia from unopposed estrogen using progesterone (Provera) or OCP
- ❑ if pregnancy is desired, may need medical induction of ovulation
  - clomiphene citrate (Clomid) = drug of choice
  - human menopausal gonadotropin (Pergonal)

DYSMENORRHEA

Primary
- ❑ menstrual pain not caused by organic disease
- ❑ may be due to prostaglandin-induced uterine contractions and ischemia
- ❑ begins 6 months - 2 years after menarche (ovulatory cycles)
- ❑ colicky pain in abdomen, radiating to the lower back, labia and inner thighs
- ❑ begins hours before onset of bleeding and persists for hours or days (48 – 72 h)
- ❑ associated nausea, vomiting, altered bowel habits, headaches, fatigue
- ❑ treatment
  - PG synthetase inhibitors (e.g. naproxen)
    - must be started before/at onset of pain
  - OCP to suppress ovulation and reduce menstrual flow

Secondary
- ❑ menstrual pain due to organic disease
- ❑ begins in women who are in their 20s
- ❑ worsens with age
- ❑ associated dyspareunia, abnormal bleeding, infertility
- ❑ etiology
  - endometriosis
  - adenomyosis
  - fibroids
  - PID
  - ovarian cysts
  - IUD

ENDOMETRIOSIS

Definition
- ❑ the proliferation and functioning of endometrial tissue outside of the uterine cavity
- ❑ incidence: 15-30% of all premenopausal women
- ❑ mean age at presentation: 25-30 years

Etiology
- ❑ unknown
- ❑ theories
  - retrograde menstruation theory of Sampson
  - Mullerian metaplasia theory of Meyer
    - metaplastic transformation of peritoneal mesothelium under the influence of certain unidentified stimuli
  - lymphatic spread theory of Halban
  - surgical "transplantation"
  - deficiency of immune surveillance

Predisposing Factors
- ❑ nulliparity
- ❑ age > 25 years
- ❑ family history
- ❑ obstructive anomalies of the genital tract

Sites of Occurrence
- ❑ ovaries
  - most common location
  - 60% of patients have ovarian involvement
- ❑ broad ligament
- ❑ peritoneal surface of the cul-de-sac (uterosacral ligaments)
- ❑ rectosigmoid colon
- ❑ appendix

Symptoms
- ❑ there may be little correlation between the extent of disease and symptomatology
- ❑ pelvic pain
  - due to swelling and bleeding of ectopic endometrium
  - unilateral if due to endometrioma
- ❑ dysmenorrhea (secondary)
  - worsens with age
  - suprapubic and back pain often precede menstrual flow (24-48 hours) and continue throughout and after flow
- ❑ infertility
  - 30-40% of patients with endometriosis will be infertile
  - 15-30% of those who are infertile will have endometriosis
- ❑ deep dyspareunia
- ❑ premenstrual and postmenstrual spotting
- ❑ bladder symptoms
  - frequency, dysuria, hematuria
- ❑ bowel symptoms
  - direct and indirect involvement
  - diarrhea, constipation, pain and hematochezia

Diagnosis
- ❑ surgical diagnosis
- ❑ history
  - cyclic symptoms - pelvic pain, dysmenorrhea, dyschezia
- ❑ physical examination
  - tender nodularity of uterine ligaments and cul-de-sac
  - fixed retroversion of uterus
  - firm, fixed adnexal mass (endometrioma)
- ❑ laparoscopy **(see Colour Atlas GY1, GY2)**
  - dark blue or brownish-black implants (mulberry spots) on the uterosacral ligaments, cul-de-sac, or anywhere in the pelvis
  - chocolate cysts in the ovaries (endometrioma)
  - "powder-burn" lesions
  - early white lesions and blebs

Treatment
- ❑ medical
  - pseudopregnancy
    - cyclic estrogen-progesterone (OCP) or medroxyprogesterone (Provera)
  - pseudomenopause
    - danazol (Danocrine) = weak androgen
      side effects: weight gain, fluid retention, acne, hirsutism
    - leuprolide (Lupron) = GnRH agonist (suppresses pituitary GnRH)
      side effects: hot flashes, vaginal dryness, reduced libido
    - can only be used short term because of osteoporotic potential with prolonged use (> 6 months)
- ❑ surgical
  - laparoscopic resection and lasering of implants
  - lysis of adhesions
  - use of electrocautery
  - unilateral salpingo-oophorectomy
  - uterine suspension
  - rarely total pelvic clean-out
  - +/– follow-up with 3 months of medical treatment

ADENOMYOSIS

Definition
- ❑ extension of areas of endometrial glands and stroma into the myometrium **(see Colour Atlas GY4)**
- ❑ also known as "endometriosis interna"
- ❑ endometrium often remains unresponsive to ovarian hormones
- ❑ uterine wall may be diffusely involved

Incidence
- ❑ 15% of females > 35 years old
- ❑ older parous age group than seen in endometriosis: 40-50 yrs
- ❑ found in 20-40% of hysterectomy specimens

Symptoms
- ❑ menorrhagia
- ❑ secondary dysmenorrhea
- ❑ pelvic discomfort
- ❑ dyspareunia
- ❑ dyschezia

Diagnosis
- ❑ uterus symmetrically bulky
- ❑ uterus size is rarely greater than 2-3 times normal
- ❑ Halban sign: tender, softened uterus on premenstrual bimanual
- ❑ definitive diagnosis made at time of pathological examination

Treatment
- ❑ iron supplements as necessary
- ❑ diagnostic D&C to rule out other pathology
- ❑ analgesics/NSAIDs
- ❑ low dose danazol 100-200 mg daily for 4 months
- ❑ GnRH agonists (i.e. leuprolide)
- ❑ hysterectomy

INFERTILITY

DEFINTIONS
- ❑ infertility: failure to conceive after one year of regular unprotected intercourse
- ❑ primary infertility: no prior pregnancies
- ❑ secondary infertility: previous conception

INCIDENCE
- ❑ 10-15% of couples
- ❑ normally: 60% of couples achieve pregnancy within 6 months of trying, 80% within 1 year, 90% within 2 years

APPROACH TO THE INFERTILE COUPLE

History from Female
- ❑ age, occupation, length of time with current partner, use of contraception, previous sexual activity
- ❑ previous pregnancies, including abortions (therapeutic or spontaneous)
- ❑ menstrual history (age at menarche, cycle, duration of flow, dysmenorrhea, ovulation pain, recent change in cycle)
- ❑ vaginal discharge including character, amount, +/- irritation or soreness
- ❑ previous infections, operations (especially abdominal or pelvic)
- ❑ coitus frequency, difficulties, relation to fertile days
- ❑ previous investigations/treatment of infertility

Physical Examination of Female
- ❑ general (evidence of endocrine disorder?)
- ❑ abdominal scars, tenderness, guarding, masses
- ❑ vaginal exam: state of introitus, position/direction of cervix, position/size/mobility of uterus, uterine enlargement, enlargement or thickening of tubes/ovaries
- ❑ speculum exam: condition of cervix, cervical secretion in relation to time in menstrual cycle

History from Male
- ❑ age, occupation, length of time with current partner, duration of infertility
- ❑ sexual performance: frequency, ability to ejaculate in upper vagina
- ❑ previous relationships, fathering of any pregnancies
- ❑ history of mumps with orchitis, injury to genitalia, operations for hernia/varicocele, recent debilitating illness

Physical Examination of Male
- ❑ general build and appearance
- ❑ examination of genitalia, hypospadias
- ❑ palpation of testicles (size, consistency)

Possible Investigations
- ❑ see male/female factors for interpretation and explanation
- ❑ post-coital test
- ❑ seminal analysis
- ❑ sperm antibodies
- ❑ basal body temperature charts
- ❑ examination of endometrium
- ❑ tests for tubal patency
- ❑ hormonal tests
- ❑ ultrasound

ETIOLOGY
- ❑ male factors (40%)
- ❑ female factors (50%)
- ❑ multiple factors (30%)
- ❑ unknown factors (10-15%)
- ❑ note: even when fertilization occurs, > 50-70% of resulting embryos are non-viable

Male Factors
- ❑ inadequate or abnormal production of sperm
  - congenital (Kleinfelter's, cryptorchidism)
  - physical injury (trauma, heat, radiation)
  - varicocele (usually left sided due to anatomy)
  - infection (usually mumps or TB orchitis)
  - smoking, stress, alcohol
  - malignant disease
  - systemic/metabolic disease (endocrine, malnutrition, renal failure, cirrhosis)
- ❑ sperm delivery problems
  - bilateral obstruction of epididymis or ducts
  - ejaculatory dysfunction, e.g. retrograde ejaculation
  - erectile dysfunction
  - abnormal position of urethral orifice
- ❑ diagnosis
  - semen analysis after 2-3 days of abstinence (2 specimens several weeks apart)
  - normal ejaculate
    - volume: 2-5 mL
    - count: > 20 million sperm/mL
    - motility: > 50%
    - morphology: > 60% normal forms
    - liquefaction: complete in 20 minutes
    - pH: 7.2-7.8
    - WBC: < 10 per high power field
- ❑ oligospermia: count < 20 million/mL
- ❑ azoospermia: absence of living spermatozoa in the semen
- ❑ endocrine evaluation required if abnormal sperm (thyroid function, FSH, testosterone, prolactin)

Female Factors
- ❑ ovulatory dysfunction (15-20%)
  - etiology
    - hyperprolactinemia (e.g. pituitary adenoma, drugs including cimetidine and psychotropics, renal/hepatic failure)
    - polycystic ovarian syndrome
    - systemic diseases (e.g. thyroid, Cushing's syndrome)
    - congenital (Turner syndrome, androgen insensitivity syndrome, gonadal dysgenesis, or gonadotropin deficiency)
    - luteal phase defect
    - stress, poor nutrition, excessive exercise (even in absence of amenorrhea)
    - premature ovarian failure (e.g. autoimmune disease)
  - diagnosis
    - history of cycle patterns
    - basal body temperature (biphasic)
    - mucous quality (mid-cycle)
    - endometrial biopsy for luteal phase defect (day 24-26)
    - serum progesterone level (day 20-22)
    - serum prolactin, TSH, LH, FSH
    - if hirsute: serum free testosterone, DHEAS
    - ovulation predictor kits
    - karyotype, liver enzymes, renal function

- ❑ tubal factors (20-30%)
  - etiology
    - PID
    - adhesions (previous surgery, peritonitis, endometriosis)
    - tubal ligation
  - diagnosis
    - hysterosalpingogram, day 8-10: diagnostic and therapeutic (i.e. may open tube just prior to ovulation)
    - laparoscopy with dye injection of tubes
- ❑ cervical factors (5%)
  - etiology
    - hostile, acidic cervical mucous, glands unresponsive to estrogen (e.g. chlamydial infection)
    - anti-sperm antibodies
    - structural defects (cone biopsies, laser, or cryotherapy)
  - diagnosis
    - post-coital test (day 12-14, sperm motility in cervical mucous 2-6 hours after intercourse)
- ❑ uterine factors (< 5%)
  - etiology
    - congenital anomalies (prenatal DES exposure)
    - intrauterine adhesions (e.g. Asherman syndrome)
    - infection
    - leiomyomata
    - polyps
  - diagnosis
    - hysterosalpingogram
    - sonohysterogram
    - hysteroscopy

TREATMENT

- ❑ education
  - timing of intercourse (temperature charting)
- ❑ medical
  - ovulation induction
    - clomiphene citrate (Clomid): ovulation induction via increased pituitary gonadotropins
    - human menopausal gonadotropin (Pergonal): gonadotropins from post-menopausal women's urine
    - urofollitropin (Metrodin): FSH
    - followed by βhCG for stimulation of ovum release
  - may add
    - bromocriptine if increased prolactin: dopaminomimetic, which decreases prolactin
    - dexamethasone for women with hyperandrogenism (PCOS, DHEAS)
    - luteal phase progesterone supplementation for luteal phase defect
- ❑ surgical
  - tuboplasty
  - lysis of adhesions
  - artificial insemination
  - sperm washing
  - in vitro fertilization
  - intrafallopian transfers:
    - GIFT (gamete-immediate transfer with sperm after oocyte retrieval)
    - ZIFT (zygote-transfer after 24-hour culture of oocyte and sperm)
    - TET (tubal embryo transfer – transfer after > 24 hr culture)
  - ICSI (intracellular sperm injection)
  - can use oocyte or sperm donors

Table 5. Classification of Contraceptive Methods

Type	Description	Effectiveness
Surgical		
Sterilization (tubal ligation)		99.6%
Vasectomy		99.8%
Barrier Methods		
Condom Alone		90.0%
Condom with Spermicide		95.0%
Spermicide Alone		82.0%
Sponge		90.0%
Diaphragm with spermicide		81.0%
Female Condom		75.0%
Cervical Cap		64.0% Parous 82.0% Nulliparous
Lea's Shield with Spermicide		95.0%
Hormonal		
Oral contraceptives	• see below	98.0-99.5% (depending on compliance)
Norplant (levonorgestrel)	• six capsules inserted subdermally in arm • provides protection for up to 5 years • S/E: severe irregular menstrual bleeding, scar in arm, local infection, decreased effectiveness with anticonvulsants/rifampin	99.9%(per year), 96.0%(over 5 years)
Depo-Provera (medroxyprogesterone)	• 150 mg IM q 3 mths • restoration of fertility may take up to 1-2 yrs • S/E: irregular menstrual bleeding, weight gain, headache, breast tenderness, mood changes	99%
IUD	• see below	95.0%-97.0%
Physiological		
Withdrawal/Coitus interruptus		77.0%
Rhythm method/Calendar/Mucous/Symptothermal		76.0%
Chance – No method used		10.0%
Abstinence		100.0%
Emergency Postcoital Contraception (EPC)		
Yuzpe method	• see below	98%
'Plan B' Levonorgestrel only	• see below	98%
Postcoital IUD	• see below	99.9%

INTRAUTERINE DEVICE (IUD)

Mechanism of Action
- ❑ unclear
- ❑ spermicidal effect produced by local sterile inflammatory reaction caused by foreign body and copper
- ❑ breakdown products of leukocytes toxic to sperm and blastocysts and prevents delivery of sperm to egg
- ❑ possibly affects tubal motility

Absolute Contraindications
- ❑ current pregnancy
- ❑ undiagnosed vaginal bleeding
- ❑ acute or chronic PID
- ❑ suspected gynecologic malignancy
- ❑ copper allergy/Wilson's disease (alternative is to use copper-free IUD)

Relative Contraindications
- ❑ prior ectopic pregnancy
- ❑ menorrhagia, dysmenorrhea
- ❑ congenital abnormalities of uterus or fibroids
- ❑ valvular heart disease

Side Effects
- ❑ pregnancy: ectopic or septic abortion
- ❑ increased blood loss and duration of menses
- ❑ increased risk of PID especially in nulliparous women
- ❑ dysmenorrhea
- ❑ expulsion (5% in the first year)
- ❑ uterine wall perforation (1/5000)

ORAL CONTRACEPTIVES

❑ E + P or P alone (mini pill)

Mechanisms of Action

❑ ovulation suppression
❑ atrophic endometrium
❑ change in cervical mucous

Starting Oral Contraceptives

❑ before oral contraceptives are used, a thorough history and physical examination must be done
❑ be sure to address contraindications
❑ physical examination must include blood pressure determination, and examination of breast, liver, extremities and pelvic organs
❑ Pap smear should be taken if patient sexually active
❑ first follow-up visit should occur 3 months after oral contraceptives are prescribed, and at least annually thereafter
❑ at each annual visit, examination should include those procedures that were done at the initial visit as outlined above
❑ oral contraceptives should not be taken by pregnant women; if conception occurs despite oral contraceptive use, there is no conclusive evidence of fetal abnormalities
❑ in breastfeeding women, the use of oral contraceptives may reduce quantity and quality of breast milk; no evidence that low dose oral contraceptives are harmful to the nursing infant
❑ initial laboratory tests: CBC, PT/INR, PTT, liver enzymes
❑ instruct patient to start on a Sunday, with pills taken at same time each day
❑ if patient misses a dose, proceed as outlined below

Missed Pills

❑ miss 1 pill: patient to take 1 pill as soon as she remembers, and the next pill at the usual time; may result in taking 2 pills on one day
❑ miss 2 pills in a row during first 2 weeks of the cycle:
  - patient to take 2 pills the day she remembers, and 2 pills the next day
  - then 1 pill per day until finished the pack
  - back-up method of birth control required during the next 7 days of missing the pills
❑ miss 2 pills in a row during third week of the cycle:
  - continue to take 1 pill per day until Sunday
  - on Sunday, discard the rest of the pack and start a new pack that day
  - back-up method of birth control required during the next 7 days of missing the pills
❑ miss 3 or more pills in a row at any time during cycle:
  - continue to take 1 pill per day until Sunday
  - on Sunday, discard the rest of the pack and start a new pack that day
  - back-up method of birth control required during the next 7 days of missing the pills

Management of Breakthrough Bleeding/Spotting with Oral Contraceptive Use

❑ before switching patient to another formulation, need to discuss potential reasons for breakthrough bleeding
❑ address the following issues
  - missed pills?
  - other medications which interact with OCP?
  - gastrointestinal symptoms (vomiting, diarrhea)?
  - infection (chlamydia, gonorrhea, PID)?
  - any gynecologic issues (endometriosis, polyps, spontaneous abortion, pregnancy, leiomyomata, endometrial/cervical cancer)?
  - cigarette smokers shown to be 47% more likely than non-smokers to have spotting/breakthrough bleeding
❑ if above issues discussed and no positive findings, then change in formulation is warranted

Absolute Contraindications

❑ current pregnancy
❑ undiagnosed vaginal bleeding
❑ cardiovascular disorders
❑ thromboembolic events
❑ cerebrovascular disease
❑ coronary artery disease
❑ moderate-severe uncontrolled hypertension
❑ estrogen-dependent tumours
  - breast
  - uterus
❑ impaired liver function
❑ congenital hyperlipidemia
❑ age > 35 years and smoking
❑ diabetes mellitus/systemic lupus erythematosus with vascular disease
❑ migraine with significant neurological symptoms (hemiplegic, visual loss)

Relative Contraindications
- ❑ migraines with aura
- ❑ diabetes mellitus without vascular disease
- ❑ breastfeeding
- ❑ rifampin, phenytoin

Drug Interactions
- ❑ many drugs can decrease efficacy, requiring use of back-up method
- ❑ antibiotics, anticonvulsants, antacids, and others

Health Benefits
- ❑ reduces dysmenorrhea, anemia, and helps regulate cycles
- ❑ reduces likelihood of developing benign breast disease and ovarian cysts
- ❑ combined estrogen and progesterone OCP substantially reduces risk of ovarian carcinoma and endometrial carcinoma
- ❑ reduces risk of rheumatoid arthritis
- ❑ increases cervical mucous which decreases the risk of STDs
- ❑ decreases ectopic pregnancy rates

Table 6. Side Effects of the Oral Contraceptive Pill

Estrogen Excess	Progesterone Excess
❑ **general symptoms** chloasma recurrent monilial vaginitis UTIs ❑ **reproductive system** cystic breast changes breast enlargement uterine enlargement uterine fibroid growth dysmenorrhea cervical extrophy mucorrhea breast swelling ❑ **cardiovascular system** capillary fragility cerebral vascular accident (CVA) deep vein thrombosis (DVT) telangiectasia ❑ **pre-menstral symptoms** bloating dizziness, syncope edema headache (cyclic) irritability leg cramps nausea and vomiting visual changes (cyclic) weight gain (cyclic)	❑ **general symptoms** hypoglycemia increased appetite decreased libido neurodermatitis acne hirsutism non-cyclic weight gain ❑ **reproductive system** cervicitis moniliasis decreased flow length depression fatigue ❑ **cardiovascular system** hypertension dilated leg veins ❑ **miscellaneous** cholestatic jaundice
Estrogen Deficiency	**Progesterone Deficiency**
❑ **general symptoms** nervousness vasomotor instability ❑ **reproductive system** bleeding and spotting may be continuous or in first half of cycle no withdrawal bleed atrophic vaginitis ❑ **genitourinary system** pelvic relaxation symptoms e.g. incontinence, prolapse	❑ **reproductive system** breakthrough bleeding and spotting late: day 10-21 on OCP dysmenorrhea heavy flow and clots delayed withdrawal bleed ❑ **pre-menstral symptoms** bloating dizziness, syncope edema headache (cyclic) irritability leg cramps nausea and vomiting visual changes (cyclic) weight gain (cyclic)

Table 7. Commonly Used Oral Contraceptive Formulations

Product	Estrogen	Estrogen mcg/tablet	Progestin	Progestin mcg/tablet
Monophasic Estrogen				
MinEstrin	Ethinyl Estradiol	20	Norethindrone Acetate	1,000
MinOvral		30	Levonorgestrel	150
LoEstrin		30	Norethindrone Acetate	1,500
Orthocept/Marvelon		30	Desogestrel	150
Cyclen		35	Norgestimate	250
Brevicon (Ortho)1/35		35	Norethindrone	1,000
Brevicon (Ortho) 0.5/35		35	Norethindrone	500
Multiphasic – days for each dose in ( )				
Synphasic	Ethinyl Estradiol	35 (21)	Norethindrone	500 (7) 1,000 (9) 500 (5)
Ortho 10/11		35 (21)	Norethindrone	500 (10) 1,000 (11)
Ortho 7/7/7		35 (21)	Norethindrone	500 (7) 750 (7) 1,000 (7)
Triphasil/Triquilar		30 (6) 40 (5) 30 (10)	Levonorgestrel	50 (6) 75 (5) 125 (10)
Tricyclen		35 (21)	Norgestimate	180 (7) 215 (7) 250 (7)

EMERGENCY POSTCOITAL CONTRACEPTION (EPC)

- ❑ provides last chance to prevent pregnancy in case of failure to use contraception or contraception failure (e.g. broken condom)
- ❑ 3 methods: Yuzpe, 'Plan B' Levonorgestrel, Postcoital IUD

Yuzpe Method

- ❑ used within 72 h of intercourse
- ❑ Ovral 2 tablets then repeat in 12 h (ethinyl estradiol 100 mcg/levonorgestrel 500 mcg and repeat in 12 h)
- ❑ dedicated product packaged ready for this type of use: 'Preven'
- ❑ side effects: nausea (give with gravol), irregular spotting, bleeding
- ❑ mechanism of action
  - delays ovulation or causes deficient luteal phase
  - may alter endometrium to prevent implantation
  - may affect sperm/ova transport
- ❑ efficacy: 2% overall risk of pregnancy, but reduces the risk of pregnancy for the one act of intercourse by 75%
- ❑ risks/contraindications
  - preexisting pregnancy (although not teratogenic)
  - caution in women with contraindications to BCP (although no absolute contraindications)

Levonorgestrel Only

- ❑ recently approved for use in Canada (2000): 'Plan B'
- ❑ consists of Levonorgestrel 750 mcg q12h for 2 doses within 72 h of intercourse
- ❑ comparable efficacy to Yuzpe method
- ❑ less nausea
- ❑ no estrogen thus very few contraindications/side effects

Postcoital IUD

- ❑ insert 5 – 7 days postcoitus
- ❑ prevents implantation
- ❑ 0.1% failure rate
- ❑ usual contraindications/precautions to IUD

ECTOPIC PREGNANCY

Definition
❑ gestation that implants outside of the endometrial cavity

Incidence
❑ 1/200 clinically recognized pregnancies
❑ fourth leading cause of maternal mortality
❑ increase in incidence over the last 3 decades

Etiology
❑ obstruction or dysfunction of tubal transport mechanisms
❑ intrinsic abnormality of the fertilized ovum
❑ conception late in cycle
❑ transmigration of fertilized ovum to contralateral tube

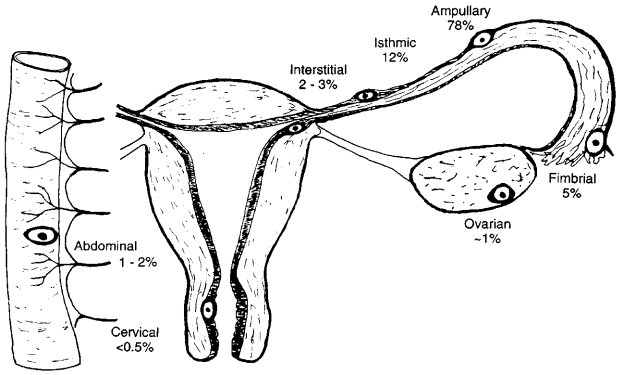

Figure 7. Sites of Implantation

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Risk Factors
❑ history of PID
❑ past or present IUD use
❑ previous lower abdominal surgery
❑ previous ectopic pregnancy
❑ endometriosis
❑ uterine or adnexal mass
❑ assisted reproductive techniques

Symptoms

Clinical Pearl
❑ **Think ectopic" in any female patient with triad of symptoms: amenorrhea, abdominal pain (usually unilateral), vaginal bleeding or spotting.**

❑ if ectopic pregnancy ruptures
- acute abdomen with increasing pain
- abdominal distension
- symptoms of shock

Physical Examination
❑ firm diagnosis is usually possible in 50% on clinical features alone
❑ hypovolemia/shock
❑ guarding and rebound tenderness
❑ bimanual examination
- cervical motion tenderness
- adnexal tenderness (unilateral vs bilateral in PID)
- palpable adnexal mass (< 30%)
- uterine enlargement (rarely increases beyond equivalent of 6-8 weeks gestation)

❑ other signs of pregnancy, i.e. Chadwick's sign, Hegar's sign

Diagnosis
❑ serial βhCG levels
- normal doubling time with intrauterine pregnancy is 1.4 - 2 days in early pregnancy which increases until 8 weeks, then decreases steadily until 16 weeks
- prolonged doubling time, plateau or decreasing levels before 8 weeks, implies non-viable gestation but does not provide information on the location of pregnancy

❑ ultrasound
- intrauterine sac should be visible when serum βhCG is
  - > 1,500 mIU/mL (transvaginal)
  - > 6,000 mIU/mL or 6 weeks gestational age (transabdominal)
- when βhCG is greater than the above values and neither a fetal heart beat nor a fetal pole is seen, it is suggestive of ectopic pregnancy

- ❑ culdocentesis (rarely done)
- ❑ laparoscopy (for definitive diagnosis)

Treatment
- ❑ goals of treatment
  - be conservative
  - try to save the tube
- ❑ surgical (laparoscopy)
  - linear salpingostomy or salpingectomy
  - if patient is Rh negative give anti-D gamma globulin (RhoGAM)
  - may require laparotomy
- ❑ medical
  - criteria (for increased success rate of medical treatment)
    - patient clinically stable
    - < 3.5 cm unruptured ectopic pregnancy
    - no fetal heart activity
    - βhCG < 1500 mIU/mL
    - no hepatic/renal/hematologic disease
    - compliance and follow-up ensured
  - methotrexate (considered standard of care)
    - use 50 mg/m^2; this is 1/5 to 1/6 chemotherapy dose, therefore minimal side effects
  - follow βhCG levels
    - plateau or rising levels are evidence of persisting trophoblastic tissue: requires further medical or surgical therapy
  - failure rate 5%
    - requires longer follow-up than surgical treatment in order to follow βhCG levels

Prognosis
- ❑ 5% of maternal deaths
- ❑ 40-60% of patients will become pregnant again after surgery
- ❑ 10-20% will have subsequent ectopic gestation
- ❑ prognosis for future pregnancy improves with more conservative treatment

GYNECOLOGICAL INFECTIONS

PHYSIOLOGICAL DISCHARGE
- ❑ clear or white discharge
- ❑ smear contains epithelial cells
- ❑ pH < 4.5
- ❑ increases with increased estrogen states: pregnancy, OCP, mid-cycle
- ❑ if increased in perimenopausal woman, investigate for other effects of excess estrogen (e.g. endometrial cancer)

NON-INFECTIOUS VULVOVAGINITIS

Prepubertal Vaginitis
- ❑ most common causes
  - foreign objects, trauma (consider child abuse)
  - poor hygiene (e.g. pinworm infection)

Postmenopausal Vaginitis/Atrophic Vaginitis
- ❑ symptoms
  - dyspareunia
  - post-coital spotting
  - mild pruritus
- ❑ treatment
  - rule out malignancy
  - estrogen creams
  - oral or transdermal hormone replacement therapy
  - good hygiene

Chemical Vulvovaginitis
- ❑ symptoms and signs of irritation present without infection
- ❑ irritants in vaginal contraceptives, bubble baths, soaps, genital deodorants, coloured or scented toilet paper, detergents, and fabric softeners
- ❑ frequent sanitary pad or tampon use
- ❑ tight synthetic clothing
- ❑ pools, hot tubs

INFECTIOUS VULVOVAGINITIS

Symptoms
- ❑ vaginal discharge
- ❑ odor
- ❑ pruritus
- ❑ lower genital tract pain
- ❑ dyspareunia
- ❑ dysuria

Pathophysiology
- ❑ normal vaginal flora contains a balance of many bacterial organisms
- ❑ flora may be altered by
  - a change in the environment
  - introduction of a new pathogen
- ❑ result is an imbalance in the relative number of organisms

Candidiasis (Moniliasis)
- ❑ *Candida albicans* (90%), *Candida tropicalis* (< 5%), *Torulopsis glabrata* (< 5%)
- ❑ 25% of vaginitis
- ❑ symptoms
  - begin in premenstrual phase
  - minimal whitish, curd-like, "cottage-cheese" vaginal discharge
  - intense itch
  - swollen, inflamed genitals
  - vulvar burning, dysuria, dyspareunia
  - asymptomatic (20%)
- ❑ predisposing factors
  - pregnancy
  - diabetes
  - OCP
  - antibiotic therapy
  - immunosuppression (primary or secondary)
  - if frequent recurrences, consider AIDS
- ❑ diagnosis
  - 10% KOH wet mount reveals hyphae and spores
  - pH < 5 (normal)
- ❑ treatment
  - advise regarding good hygiene (e.g. cotton underwear)
  - clotrimazole, butoconazole, miconazole, or terconazole suppositories and/or creams for 1-day, 3-day or 7-day treatments
  - oral fluconazole 150 mg single dose
  - symptomatic relief with douching, yogurt, acidophilus
  - treat partners only if symptomatic
  - treatment in pregnancy is nystatin

Bacterial Vaginosis
- ❑ *Gardnerella vaginalis* overgrowth in presence of vaginal anaerobes (*Bacteroides*, *Mobiluncus*) and scant lactobacilli
- ❑ especially susceptible when post-menstrual or post-coital, with IUD
- ❑ symptoms
  - fishy odour especially after coitus
  - profuse, thin greyish discharge
  - vulva rarely itchy or inflamed
  - not necessarily sexually transmitted, although can see "ping-pong" transmission
- ❑ diagnosis
  - saline wet mount
    - > 20% clue cells = squamous epithelial cells dotted with coccobacilli (Gardnerella)
    - paucity of WBC
    - paucity of lactobacilli
  - amine odour/ "whiff" test = fishy odour with addition of KOH to slide
  - pH 5-5.5
- ❑ treatment
  - no treatment required in non-pregnant, asymptomatic women unless scheduled for pelvic surgery or procedure
  - must treat all asymptomatic cases in pregnancy; higher incidence of pre-term labour, premature rupture of membranes, and miscarriage if left untreated
  - oral
    - metronidazole 500 mg bid for 7 days or 2 g once
    - clindamycin 300 mg bid for 7 days
  - topical
    - clindamycin 5g 2% vaginal cream qhs x 7 days
    - metronidazole 5g 0.75% vaginal gel qhs x 5d
  - ampicillin or amoxicillin if pregnant; may use metronidazole after first trimester
  - for repeated infection one capsule or tablet of lactobacillus acidophilus daily in vagina
  - controversy exists regarding treatment of partners

GYNECOLOGICAL SEXUALLY TRANSMITTED DISEASES (STD's)

Chlamydia

- ❑ *Chlamydia trachomatis*
- ❑ most common STD
- ❑ often associated with N. *gonorrhea*
- ❑ risk factors
  - sexually active youth < 25 years old
  - history of previous STD
  - new partner in last 3 months
  - multiple partners
  - not using barrier contraception
  - contact with infected person
- ❑ symptoms
  - asymptomatic
  - muco-prurulent endocervical discharge
  - urethral syndrome: dysuria, frequency, pyuria, no bacteria
  - pelvic pain
  - post-coital bleeding
- ❑ complications
  - acute salpingitis, PID
  - infertility - tubal obstruction from low grade salpingitis
  - perinatal infection - conjunctivitis, pneumonia
  - ectopic pregnancy
  - Fitz-Hugh Curtis syndrome (liver capsule infection)
  - arthritis, conjunctivitis, urethritis (Reiter's syndrome - male predominance)
- ❑ diagnosis
  - cervical culture or monoclonal antibody
  - obligate intracellular parasite - require tissue culture for diagnosis
- ❑ treatment
  - doxycycline 100 mg bid for 7 days or azithromycin 1 g orally in a single dose
  - amoxicillin or erythromycin if pregnant
  - treat partners
  - reportable disease
- ❑ screening
  - high risk groups
  - during pregnancy

Gonorrhea

- ❑ N*eisseria gonorrhea*
- ❑ symptoms and risk factors as with C*hlamydia*
- ❑ diagnosis
  - Gram stain shows gram-negative intracellular diplococci
  - cervical, rectal and throat culture
- ❑ treatment
  - single dose of ceftriaxone 125 mg IM or cefixime 400 mg PO or ciprofloxacin 500 mg PO
  - plus doxycycline or azithromycin to treat for concomitant chlamydial infection
  - amoxicillin or erythromycin if pregnant
  - treat partners
  - reportable disease
- ❑ screening as with Chlamydia

Trichomonas

- ❑ T*richomonas vaginalis*, a flagellated protozoan, anaerobic
- ❑ often co-exists with bacterial forms
- ❑ usually sexually transmitted (men asymptomatic)
- ❑ more frequent with multiple sexual partners
- ❑ possibly via hot tubs, whirlpools, saunas
- ❑ symptoms
  - profuse, thin, frothy yellow-green discharge
  - may be foul-smelling discharge
  - often seen post-menstrual
  - occasionally irritated, tender vulva
  - dysuria
  - petechiae on vagina and cervix (10%)
  - asymptomatic (up to 50%)
- ❑ diagnosis
  - saline wet mount
    - many WBC
    - motile flagellated organisms
    - inflammatory cells
  - pH 5 - 6.5
- ❑ treatment
  - metronidazole 500 mg bid for 7 days or 2 g once
  - treat partners

Condylomata Acuminata/Genital Warts (see Colour Atlas GY7)
- ❑ human papillomavirus (HPV)
- ❑ clinical presentation
  - latent infection
    - no visible lesions
    - detected by DNA hybridization tests
    - asymptomatic
  - subclinical infection
    - visible lesion only after 5% acetic acid applied and magnified
  - clinical infection
    - visible wartlike lesion without magnification
    - hyperkeratotic, verrucous or flat, macular lesions
    - vulvar edema
- ❑ lesions tend to get larger during pregnancy
- ❑ > 60 subtypes of which > 20 are genital subtypes
- ❑ classified according to risk of neoplasia and cancer
- ❑ types 16, 18, 45, 36 (and others) associated with increased incidence of cervical and vulvar intraepithelial hyperplasia and carcinoma
- ❑ diagnosis
  - cytology (Pap smear)
    - koilocytosis = nuclear enlargement and atypia with perinuclear halo
  - biopsy of visible and acetowhite lesions at colposcopy
  - detection of HPV DNA using nucleic acid probes not routinely done
- ❑ treatment
  - patient applied
    - podofilox 0.5% solution or gel
    - imiqimod 5% cream
  - provider administered
    - cryotheraphy with liquid nitrogen
    - podophyllin resin in tincture of benzoin
    - surgical removal/laser
    - intralesional interferon
- ❑ condyloma should be treated early during pregnancy; if not successful then C/S should be considered
- ❑ cannot be prevented by using condoms

Molluscum Contagiosum
- ❑ epithelial proliferation caused by a growth-stimulating poxvirus (Molluscipoxvirus)
  - mildly contagious
- ❑ symptoms
  - occasionally mild pruritis
- ❑ clinical presentation
  - multiple nodules up to 1 cm diameter on vulva and perineum with umbilicated center
- ❑ treatment
  - chemical
    - carbonic acid, TCA, or silver nitrate
  - physical
    - curette

Herpes Simplex
- ❑ Herpes Simplex virus type II (genital) (90%), type I (oral) (10%)
- ❑ initial symptoms
  - present 2-21 days following contact
  - prodromal symptoms: tingling, burning, pruritus
  - multiple, painful, shallow ulcerations with small vesicles
    - these lesions are infectious
    - appear 7-10 days after initial infection
  - inguinal lymphadenopathy, malaise, fever often with first infection
  - dysuria and urinary retention if urethral mucosa affected
  - may be asymptomatic
  - recurrent infections: less severe, less frequent and shorter in duration
- ❑ diagnosis
  - viral culture
  - cytologic smear
    - multinucleated giant cells
    - acidophilic intranuclear inclusion bodies
  - virus seen on electron microscopy
- ❑ treatment
  - first episode
    - acyclovir 400 mg PO tid for 7-10 d (also famciclovir, valacyclovir)
  - recurrent episode
    - acyclovir 400 mg PO tid for 5d
  - daily suppressive therapy
    - consider if 6-8 attacks per year
    - acyclovir 400 mg PO bid
  - severe disease:
    - consider IV therapy acyclovir 5-10 mg/Kg IV q8h x 5-7d
- ❑ education regarding transmission
    - avoid contact from prodrome until lesions have cleared
    - use barrier contraception

Syphilis
- ❑ *Treponema pallidum*
- ❑ primary syphilis
  - painless chancre on vulva, vagina or cervix
  - painless inguinal lymphadenopathy
  - 3-4 weeks after exposure
  - serological tests usually negative
- ❑ secondary syphilis
  - 2-6 months after initial infection
  - nonspecific symptoms: malaise, anorexia, headache, diffuse lymphadenopathy
  - generalized maculopapular rash: palms, soles, trunk, limbs
  - condylomata lata (anogenital, broad-based fleshy grey lesions)
  - serological tests usually positive
- ❑ tertiary syphilis
  - may involve any organ system
  - gumma of vulva
  - neurological: tabes dorsalis, general paresis
  - cardiovascular: aortic aneurysm, dilated aortic root
- ❑ congenital syphilis
  - may cause fetal anomalies, stillbirths or neonatal death
- ❑ latent syphilis
  - no symptoms, positive serology
- ❑ natural history
  - if untreated, 1/3 will experience late complications
- ❑ diagnosis
  - aspirate of ulcer serum or node
    - spirochetes on dark field microscopy
  - serology
    - VDRL is non-specific
    - MHA-TP is the confirmatory test
    - FTA-ABS is specific
    - TPI is the most specific test, most expensive
- ❑ treatment of primary, secondary, latent syphilis of < 1 year duration
  - benzathine penicillin G 2.4 million units IM
  - treat partners
  - reportable disease
- ❑ treatment of latent syphilis > 1 year duration
  - benzathine penicillin G 2.4 million units IM once per week x 3 weeks
- ❑ screening
  - high risk groups
  - in pregnancy

Chancroid
- ❑ H*emophilus ducreyi*
- ❑ symptoms
  - painful soft ulcer with or without pus
  - tender regional lymphadenopathy = buboe
- ❑ diagnosis
  - culture
  - Gram stain shows gram-negative bacilli in rows
- ❑ treatment
  - erythromycin 500 mg qid for 7 days OR
  - ceftriaxone 250 mg IM once OR
  - azithromycin 1g PO once
  - treat partners

Granuloma Inguinale (Donovanosis)
- ❑ C*alymmatobacterium granulomatis*
- ❑ symptoms
  - painless nodule —> ulcer —> intact pseudobuboes
- ❑ diagnosis
  - Donovan bodies with Giemsa stain
- ❑ treatment
  - tetracycline 500 mg qid for 14 days
  - erythromycin 500 mg qid for 14 days if pregnant

Lymphogranuloma Venereum
- ❑ C*hlamydia trachomatis* serotypes L-1, L-2, L-3
- ❑ symptoms
  - papule/vesicle —> painless vulvovaginal ulcer —> discharging buboe
  - rectal ulceration or stricture
  - inguinal lymphadenopathy
- ❑ diagnosis
  - microimmunofluorescent serology (Frei test) for antibodies to *chlamydia*
- ❑ treatment
  - doxycycline 100 mg bid for 21 days

Less Common STDs
- ❑ *Sarcoptes scabiei* - genital scabies
- ❑ Phthirus pubis - pediculosis pubis
- ❑ Mycoplasma - non-specific urethritis

BARTHOLINITIS
- ❑ inflammation of an obstructed Bartholin gland
- ❑ 5 and 7 o'clock positions at vaginal introitus
- ❑ usually sterile but causative organisms may include
  - S. *aureus*, S. *fecalis*, E. *coli*, N. *gonorrhea*, C. *trachomatis*
- ❑ treatment
  - sitz baths
  - antibiotics and heat (rarely help)
  - incision and drainage with placement of Word catheter for 2-3 weeks
  - marsupialization for recurrent abscesses

PELVIC INFLAMMATORY DISEASE (PID)

Definition
- ❑ inflammation of the endometrium, fallopian tubes, pelvic peritoneum, +/– contiguous structures
- ❑ acute febrile illness
- ❑ usually bilateral

Causative Organisms (in order of frequency)
- ❑ C. *trachomatis*
- ❑ N. *gonorrhea*
- ❑ GC and C*hlamydia* often co-exist
- ❑ endogenous flora
  - anaerobic organisms (e.g. Bacteroides)
  - a cause of recurrent PID
  - associated with instrumentation
- ❑ actinomyces
  - in 1-4 % of PID associated with IUDs
- ❑ others (TB, gram-negatives, etc.)

Risk Factors
- ❑ risk factors as for Chlamydia and GC
- ❑ history of salpingitis
- ❑ vaginal douching
- ❑ IUD (unilateral disease)
- ❑ infertility (instrumentation)

Clinical Presentation
- ❑ symptoms
  - low abdominal or pelvic pain
  - metrorrhagia
  - intermenstrual and/or post-coital bleeding
  - vaginal discharge
  - deep dyspareunia
  - exacerbated by menses and coitus
- ❑ signs
  - fever
  - abdominal tenderness
  - signs of peritoneal irritation
  - endocervical discharge
  - cervical motion tenderness
  - adnexal tenderness
  - adnexal mass
- ❑ acute disease
  - cervicitis, salpingitis, endometritis, myometritis, peritonitis
  - pelvic cellulitis
  - tubo-ovarian abscess
  - pelvic abscess
- ❑ chronic disease
  - constant pelvic pain
  - dyspareunia
  - palpable mass
  - often due to Chlamydia
  - very difficult to treat, may require surgery

Investigations
- ❑ Gram stain
  - Gram-negative intracellular diplococci (GC)
- ❑ cervical culture
  - aerobic and anaerobic bacteria as well as C*hlamydia* (obligate intracellular parasite)

- ❑ ultrasound
  - may be normal
  - fluid in cul-de-sac
  - pelvic or tubo-ovarian abscess
  - hydrosalpinx
- ❑ laparoscopy
  - for definitive diagnosis
  - for tubal cultures and endometrial biopsy

Diagnosis
- ❑ must have
  - lower abdominal pain
  - cervical motion tenderness
  - adnexal tenderness
- ❑ plus one or more of the following
  - temperature > 38ºC
  - WBC > 10.5
  - mucoprurulent cervical discharge
  - pelvic abscess or inflammatory mass on U/S or bimanual
  - positive culture for N. *gonorrhea*, C. *trachomatis*, E. *coli* or other vaginal flora
  - high risk partner
  - elevated ESR or C-reactive protein (not commonly used)

Consequences of Untreated PID
- ❑ chronic pelvic pain
- ❑ abscess, peritonitis
- ❑ adhesion formation
- ❑ ectopic pregnancy
- ❑ infertility
  - 1 episode of PID —> 13% infertility
  - 2 episodes of PID —> 36% infertility
- ❑ bacteremia
  - septic arthritis, endocarditis

Treatment
- ❑ must treat with polymicrobial coverage
- ❑ inpatient if:
  - atypical infection
  - adnexal mass, tubo-ovarian or pelvic abscess
  - moderate to severe illness
  - unable to tolerate oral antibiotics or failed oral therapy
  - immunocompromised
  - pregnant
  - surgical emergency cannot be excluded
  - PID is secondary to instrumentation
  - recommended treatment
    - cefoxitin 2 g IV q6h or cefotetan 2 g IV q12h + doxycycline 100 mg IV q12h, or
    - clindamycin 900 mg + gentamicin
    - continue IV antibiotics for at least 48 hours after symptoms have improved
    - then doxycycline 100 mg PO bid to complete 14 days
  - percutaneous drainage of abscess under U/S guidance
  - when no response to treatment, laparoscopic drainage
  - if failure, treatment is surgical (salpingectomy, TAH-BSO)
- ❑ outpatient if
  - typical findings
  - mild to moderate illness
  - oral antibiotics tolerated
  - compliance ensured
  - follow-up within 48-72 hours
  - recommended treatment: ceftriaxone 250 mg IM + doxycycline 100 mg bid for 14 days
- ❑ remove IUD after a minimum of 24 hours of treatment
- ❑ reportable disease
- ❑ treat partners
- ❑ re-culture for cure 2 weeks later

TOXIC SHOCK SYNDROME (TSS)
- ❑ multiple organ system failure due to S. *aureus* exotoxin
- ❑ rare
- ❑ associated with
  - tampon use
  - diaphragm, cervical cap or sponge use
  - wound infections
  - post-partum infections
- ❑ early recognition and treatment of syndrome is imperative as incorrect diagnosis can be fatal

Clinical Presentation
- ❑ sudden high fever
- ❑ sore throat, headache, diarrhea
- ❑ erythroderma
- ❑ signs of multisystem failure
- ❑ refractory hypotension
- ❑ exfoliation of palmar and plantar surfaces of the hands and feet 1-2 weeks after onset of illness

Management
- ❑ remove potential sources of infection
  - foreign objects and wound debris
- ❑ debridement of necrotic tissues
- ❑ adequate hydration
- ❑ penicillinase-resistant antibiotics - cloxacillin
- ❑ steroid use controversial but if started within 72 hours, may reduce severity of symptoms and duration of fever

SURGICAL INFECTIONS AND PROPHYLAXIS

Post Operative Infections in Gynecological Surgery (see General Surgery Chapter)
- ❑ urinary tract infections
- ❑ respiratory tract infections
- ❑ phlebitis
- ❑ wound infections
- ❑ necrotizing fasciitis
- ❑ pelvic cellulitis
  - common post hysterectomy
  - erythema, induration, tenderness, discharge involving vaginal cuff
  - treat if fever and leukocytosis with broad spectrum antibiotics, i.e. clindamycin and gentamycin
  - drain if excessive prurulence or large mass
  - intraabdominal and pelvic abscess

Prophylactic Antibiotics for Gynecologic Surgery
- ❑ aim to decrease numbers below critical level for infection
- ❑ benefit in: vaginal hysterectomy, TAH, D&C, and abortion
- ❑ cefazolin for most procedures (IV bolus 30 minutes before procedure and repeat if surgery > 2-3 hours long)
- ❑ bowel prep for procedures in which fecal contamination is possible
  - Go-Lytely, etc., to clear bowel
  - ampicillin + gentamicin IV or IM 30 minutes before procedure and q8h
  - vancomycin + gentamicin if penicillin-allergic
  - amoxicillin PO 1 hour before procedure if low-risk patient
  - cefoxitin IV pre-op and q4h if emergency
  - clindamycin, ampicillin, and cephalosporins are most often associated with C. *difficile* colitis

PELVIC RELAXATION/PROLAPSE

Definition
- ❑ protrusion of pelvic organs into or out of the vaginal canal

Etiology
- ❑ pelvic relaxation, weakness, or defect in the cardinal and uterosacral ligaments which normally assist in maintaining the uterus in an anteflexed position and prevent it from descending through the urogenital diaphragm (i.e. levator ani muscles)
- ❑ related to
  - trauma of childbirth
  - aging
  - decreased estrogen
  - following pelvic surgery
  - increased abdominal pressure, e.g. obesity, chronic coughing, and constipation
  - rarely congenital

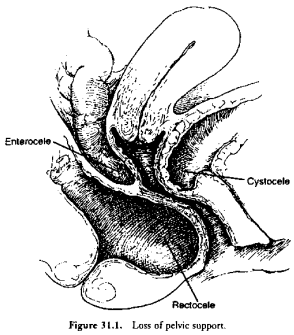

Figure 31.1. Loss of pelvic support.

Figure 8. Organ Prolapse

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UTERINE PROLAPSE

Symptoms
- ❑ mass or bulge at introitus
- ❑ back pain due to stretching of uterosacral ligaments
- ❑ feeling of heaviness in the pelvis
  - worse with standing, lifting
  - relieved by lying down

Classification
- ❑ 0 = no descent
- ❑ 1 = descent between normal position and ischial spines
- ❑ 2 = descent between ischial spines and hymen
- ❑ 3 = descent within hymen
- ❑ 4 = descent through hymen
- ❑ procidentia: failure of genital supports and complete prolapse of uterus

Treatment
- ❑ conservative
  - vaginal pessary
  - estrogen therapy
  - pelvic muscle exercises (Kegel)
- ❑ surgical
  - prosthetic slings in cases associated with urinary incontinence
  - vaginal hysterectomy ± anterior + posterior repair

VAULT PROLAPSE
- ❑ follows hysterectomy, vagina turns inside out

Treatment
- ❑ conservative
  - vaginal pessary
  - estrogen therapy
- ❑ surgical
  - colpopexy (vaginal vault suspension)

CYSTOCELE
- ❑ prolapse of bladder into the anterior vaginal wall

Symptoms
- ❑ frequency, urgency, nocturia
- ❑ stress incontinence
- ❑ incomplete bladder emptying
- ❑ increased incidence of UTIs

Treatment
- ❑ conservative
  - vaginal pessary, Kegel exercises
- ❑ surgical
  - anterior vaginal repair (colporrhaphy)
  - bladder suspension if symptomatic

RECTOCELE
- ❑ prolapse of rectum into posterior vaginal wall

Symptoms
- ❑ difficulty passing stool
  - constant straining may increase rectocele

Treatment
- ❑ conservative
  - laxatives and stool softeners
  - vaginal pessary usually not helpful
- ❑ surgical
  - posterior colporrhaphy (“posterior repair”)
    - plication of endopelvic fascia and perineal muscles approximated in midline to support rectum and perineum

ENTEROCELE
- ❑ prolapse of small bowel in upper posterior vaginal wall
- ❑ usually associated with rectocele

Treatment
- ❑ surgical
  - like hernia repair
  - contents reduced, neck of peritoneal sac ligated, uterosacral ligaments and levator ani muscles approximated

URINARY INCONTINENCE (see Urology Chapter)

❑ Canadian incidence of malignant lesions:
- endometrium > ovary > cervix > vulva > vagina > fallopian tube

UTERUS

Leiomyomata (fibroids) (see Colour Atlas GY5)

❑ benign uterine lesions

❑ epidemiology
- 20% of women > 35 years
- more common in blacks
- most common indication for major surgery in females
- minimal malignant potential (1:1000)

❑ pathogenesis
- arise from smooth muscle
- estrogen-dependent benign tumour
- degenerative changes
  - red degeneration (hemorrhage into tumor, occurs in 1/2 of women with fibroid in pregnancy)
  - hyaline degeneration (most common degenerative change)
  - cystic degeneration
  - fatty degeneration
  - calcification
  - sarcomatous degeneration

❑ clinical presentation
- general symptoms
  - asymptomatic
  - dysmenorrhea, menorrhagia or abnormal bleeding pattern
  - pelvic pain especially with torsion of pedunculated leiomyomata
  - pelvic pressure and/or heaviness
  - increased abdominal girth
  - infertility, recurrent abortions
  - difficulty voiding (more common) or defecating (less common)
  - submucosal leiomyomata are most symptomatic
  - locations (see Figure 9)

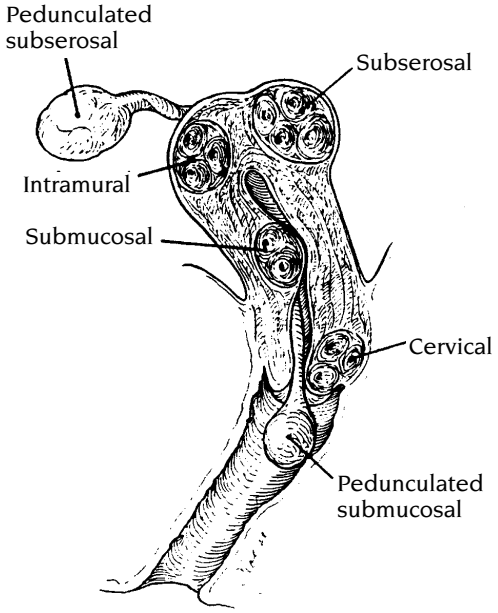

Figure 9. Possible Anatomic Locations of Uterine Leiomyomata

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❑ diagnosis
- physical examination: asymmetrically enlarged uterus, mass
- ultrasound
- hysteroscopy
- fractional D&C to rule out uterine cancer

❑ treatment
- only if symptomatic, rapidly enlarging, large blood loss
- treat anemia if present

- conservative approach advocated if
  - symptoms absent or minimal
  - tumours < 6-8 cm or stable in size
  - not submucosal (i.e. submucosal fibroids are more likely to be symptomatic)
  - virtually all postmenopausal patients would fall into this category
- medical approach
  - GnRH agonist e.g. leuprolide (Lupron), or androgen derivative e.g. danazol (Danocrine) to facilitate surgery (reduces menorrhagia and fibroid size); short-term use only
  - antiprostaglandin or OCP therapy for control of pain/bleeding in young patients or in those who do not want surgery
- surgical approach
  - myomectomy (hysteroscopic or transabdominal approach)
  - hysterectomy (abdominal or vaginal, depending on fibroid size)
- embolization of fibroid blood supply (new therapy)
- never operate on fibroids during pregnancy; expectant management only

MALIGNANT UTERINE LESIONS

Endometrial Carcinoma

❑ epidemiology
- most common gynecological malignancy (40%)
- 1 in 100 women
- mean age = 60 years
- majority are diagnosed early
- > 90% 5 year survival for stage I disease

❑ types
- adenocarcinoma (most common 75%)
- adenosquamous carcinoma
- papillary serous adenocarcinoma

❑ risk factors
- nulliparity
- unopposed estrogens
  - endogenous - PCOS, anovulation, obesity
  - exogenous – unopposed estrogen in HRT; better prognosis
- late menopause, early menarche
- history of breast, colon, or ovarian cancer
- diabetes mellitus, hypertension are cofactors

❑ OCP decreases risk

❑ clinical presentation
- postmenopausal bleeding in 90% (= endometrial carcinoma until proven otherwise!)
- abnormal uterine bleeding (menorrhagia, intermenstrual bleeding)

Table 8. Staging of Endometrial Cancer (Surgical Staging)

Stage	Description
0	atypical adenomatous hyperplasia
I	confined to corpus
IA	tumour limited to the endometrium
IB	invades through < one half of myometrium
IC	invades through > one half of myometrium
2	involves corpus and cervix
2A	endocervical glandular involvement only
2B	cervical stromal invasion
3	outside of uterus but not beyond true pelvis
4	outside of true pelvis, involving bowel and bladder

❑ diagnosis
- office endometrial biopsy
- D&C

❑ treatment
- based on tumour grade and depth of myometrial invasion
- surgical: TAH-BSO and pelvic washings
- adjuvant radiotherapy: to selected patients based on depth of myometrial invasion, tumour grade, and/or lymph node involvement
- hormonal therapy: progestins for distant or recurrent disease
- chemotherapy: if disease progresses on, progestins

Uterine Sarcoma

- ❑ rare
- ❑ arise from stromal components (endometrial stroma, mesenchymal or myometrial tissues)
- ❑ greater tendency to disseminate hematogenously
- ❑ 5-year survival: 35%
- ❑ leiomyosarcoma (uncommon)
  - average age of presentation = 55 years
  - clinical presentation
    - abnormal uterine bleeding
    - feeling of pelvic fullness and/or pressure
    - rapidly enlarging uterus
  - spread
    - via local invasion, hematogenous and lymphatic
  - treatment
    - TAH-BSO
    - no adjuvant therapy given if disease confined to uterus and mitotic index is low
    - radiation if high mitotic index or tumour spread beyond uterus (not used in Toronto)
    - chemotherapy generally not useful
- ❑ endometrial stromal sarcoma
  - clinical presentation
    - menometrorrhagia
    - postmenopausal bleeding
    - pelvic pain
    - 50% have metastatic disease at presentation, especially liver/lung mets
  - treatment
    - TAH-BSO
    - hormonal therapy (progestogens)
    - rarely use radiotherapy
- ❑ mixed Müllerian sarcoma (most common uterine sarcoma)

OVARY

Table 9. Characteristics of Benign vs. Malignant Ovarian Tumours

Benign	Malignant
• reproductive age group (epithelial cell) • very large tumours • unilateral • freely mobile • capsule intact, smooth surface, cystic, unilocular • no ascitic fluid • smooth peritoneal surfaces	• very young (germinal cell) or older (epithelial cell) age groups • bilateral • fixed, adherent to adjacent organs • multiloculation, thick septa, disruption of solid areas • ascites • peritoneal seeding e.g. cul-de-sac and bowel serosa

Benign Ovarian Tumours

Table 10. Benign Ovarian Tumours

Type	Description	Presentation	Ultrasound/Cytology	Treatment
Functional Tumours				
Follicular cyst	• follicle fails to rupture during ovulation	• usually asymptomatic • may rupture, bleed, twist, and infarct causing pain	• seldom measures greater than 6-8 cm • usually unilocular, lined by granulosa cells	• if < 6 cm, wait 6 weeks then re-examine as cyst may regress with next cycle • BCP (ovarian suppression) • aspiration via laparoscopy
Lutein cyst	• corpus luteum fails to regress after day 14, becoming cystic or hemorrhagic	• may rupture, bleed, twist, and infarct • may cause mild to severe pain • may delay onset of next period	• usually slightly larger and firmer than follicular cyst	• same as for follicular cyst
Theca-lutein cyst	• due to atretic follicles stimulated by abnormally high blood levels of βhCG	• classically associated with molar pregnancy • also occurs with PCOS, DM, ovulation induction , multiple pregnancy		• conservative • cyst will regress as βhCG level falls
Endometrioma	• see Endometriosis section			
Germ-Cell Tumours				
Cystic teratoma (dermoid cyst) **see Colour Atlas GY3**	• single most common solid ovarian neoplasm • elements of all 3 cell lines present • most commonly contains dermal appendages (sweat and sebaceous glands, hair follicles and teeth)	• may rupture or twist and infarct • may cause pelvic discomfort/pressure if large enough • 20% bilateral • 20% occur outside reproductive years	• usually 5-10 cm (seldom > 20 cm) • smooth-walled, mobile, often unilocular • often anterior to broad ligament • ultrasound may show calcification	• cystectomy • may recur
Epithelial Ovarian Tumours				
General	• believed to be derived from the mesothelial cells lining the peritoneal cavity • most common group of benign ovarian tumours	• increasing frequency after age 20-25	• varies depending on subtype (see below)	• cyst aspiration • cystectomy • unilateral salpingo-oophorectomy
Serous	• most common cystic tumour of ovary	• often occurs on OCP	• often multilocular • lining similar to fallopian tube epithelium	
Mucinous	• less common	• may occur on OCP	• often multilocular • may reach enormous size • resembles endocervical epithelium	
Endometrioid	• rare		• cytologically resembles endometrium but non-invasive (vs. endometriosis)	
Brenner tumour			• solid neoplasm with large fibrotic component • associated with mucinous epithelial elements in 1/3 of cases	
Sex Cord-Stromal Ovarian Tumours				
Fibromas		• non-functioning • occasionally associated with ascites and right pleural effusion (Meig syndrome)	• firm, smooth, rounded tumour with interlacing fibrocytes	• surgical resection of tumour
Granulosa-theca cell tumours		• occur in any age group • estrogen-producing —> feminizing effects (precocious puberty, menorrhagia, post-menopausal bleeding)		
Sertoli-Leydig cell tumours		• androgen-producing —> virilizing effects (hirsutism,deep voice, clitoromegaly, recession of frontal hairline)		

Malignant Ovarian Tumours

- ❑ epidemiology
  - 15% of all ovarian tumours are malignant
  - lifetime risk 1/100
  - in women > 45 years, 1 in 2,500/year will develop ovarian ca
  - in women > 50 years, more than 50% of ovarian tumours are malignant
  - highest mortality rate of all gynecological carcinomas due to late detection
  - fourth leading cause of cancer death in women
- ❑ risk factors
  - family history (BRCA-1)
  - Caucasian
  - age > 40
  - late menopause
  - nulliparity
  - delayed child-bearing
  - OCP is protective
- ❑ clinical features
  - asymptomatic since grows insidiously and painlessly
  - abnormal vaginal bleeding (30%)
  - post-menopausal bleeding
  - urinary frequency
  - constipation
  - dyspareunia
  - abdominal pain, swelling, or fullness
  - ascites
  - coughing, secondary to pleural effusions
- ❑ diagnosis
  - pelvic exam
    - painless adnexal mass
    - enlarged uterus
  - lab
    - CA-125
  - radiology
    - chest x-ray
    - abdominal and pelvic U/S
    - +/– CT or MRI for investigation of nodal involvement
  - laparotomy
    - for staging and treatment
- ❑ screening
  - no effective method of mass screening
  - routine CA-125 level measurements not recommended
  - in high risk groups:
    - familial ovarian cancer (> 1 first degree relative affected, BRCA-1)
    - other cancers (i.e. endometrial, breast, colon)
    - yearly pelvic exam, CA-125, pelvic U/S
    - may recommend prophylactic bilateral oophorectomy after age 35 or when child-bearing is completed
- ❑ types of malignant ovarian tumours
  - epithelial tumours
    - 80%-85% of all ovarian tumours (includes benign, malignant or low malignant potential)
    - histological classification of epithelial malignancies
      - serous type (50%)
      - endometrioid (10%)
      - mucinous types (10%)
      - clear cell type (5%)
      - undifferentiated (10-15%)
  - germ cell tumours
    - 2-3% of all ovarian malignancies
    - younger women
    - often produce hCG or AFP which serve as tumour markers
    - includes dysgerminomas and immature teratomas
  - sex cord-stromal tumours
    - granulosa cell tumours - estrogen-producing
    - associated with endometrial cancer in adult, pseudoprecocious puberty in child
    - Call-Exner bodies - histological hallmark
    - Sertoli-Leydig tumours - androgen-producing
  - metastatic ovarian tumours
    - 4-8% of ovarian malignancies
    - from GI tract, breast, endometrium, lymphoma
    - Krukenberg tumour = metastatic tumour from GI tract with “signet-ring” cells
    - most of these tumours originate from stomach
    - often bilateral

Table 11. FIGO Staging for Primary Carcinoma of the Ovary (Surgical Staging)

Stage I	Growth limited to the ovaries
Stage IA	1 ovary
Stage IB	2 ovaries
Stage IC	1 or 2 ovaries with ascites
Stage II	Growth involving one or both ovaries with pelvic extension
Stage IIA	Extension to uterus/tubes
Stage IIB	Extension to other pelvic structures
Stage III	Tumour involving one or both ovaries with peritoneal implants outside the pelvis and/or positive retroperitoneal or inguinal nodes Superficial liver metastasis equals stage III Tumour is limited to the true pelvis, but with histologically proven malignant extension to small bowel or omentum
Stage IV	Distant metastasis

Table 12. Treatment According to Stage

Stage IA & B surgical	TAH-BSO (consider alternatives if wish to child-bear) • peritoneal washings • staging laparotomy

Stage IC & II surgical	TAH-BSO
	• peritoneal washings
	• staging laparotomy + adjuvant therapy
	• radiotherapy
	• limited to small subset of patients without evidence of residual disease
	• effectiveness is controversial
	• chemotherapy
	  • cisplatinum
	  • carboplatinum
	  • cyclophosphamide
	• follow-up with serial U/S and CA-125

Stage III, IV surgical	TAH-BSO • peritoneal washings • staging laparotomy with omentectomy • debulking + chemotherapy 3-6 months

❑ prognosis
- 5-year survival
  - Stage I: 80-90%
  - Stage II: 60-70%
  - Stage III: 15-30%
  - Stage IV: 5-15%
- overall 5 year survival: 30-35%
- majority present late as Stage III
  - death from ovarian cancer usually results from progressive encasement of abdominal organs (i.e. bowel obstruction)

CERVIX

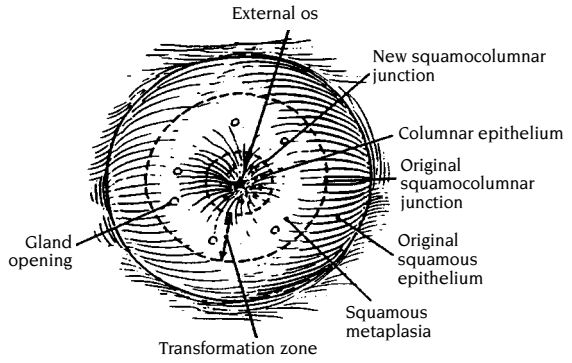

Figure 9. The Cervix

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Benign Cervical Lesions

- ❑ endocervical polyps
  - common post-menopause
  - treatment is polypectomy

Malignant Cervical Lesions

- ❑ squamous cell carcinoma (95%), adenocarcinoma (5%)
- ❑ 8,000 deaths annually in North America
- ❑ annual Pap test reduces a woman's chances of dying from cervical cancer from 4/1,000 to 5/10,000
- ❑ average age 52 years old
- ❑ etiology
  - at birth the vagina is covered with squamous epithelium, and the columnar epithelium covers only the endocervix and the central area of the ectocervix (original squamocolumnar junction)
  - during puberty, estrogen causes a single columnar layer to become everted (ectopy) thus exposing it to the acid pH of the vagina, leading to metaplasia (columnar to squamous)
  - since the metaplastic squamous epithelium covers the columnar epithelium, a new squamocolumnar junction is formed closer to the external os
  - the transformation zone (TZ) is an area of squamous metaplasia located between the original and the new squamocolumnar junction (Figure 10)
  - the majority of dysplasias and cancers arise in the TZ of the cervix
  - epithelium may also become susceptible to mutagenic agents leading to dysplasia
  - must have active metaplasia + inducing agent to get dysplasia
  - TZ is higher up in the endocervical canal in postmenopausal women
- ❑ risk factors
  - HPV infection
    - see Gynecological Infections section
    - high risk associated with types 16, 18
    - low risk associated with types 6, 11
    - 90% of cervical cancers contain one of the high risk HPV types
  - smoking
  - high risk behaviour
    - multiple partners
    - other STDs (HSV, trichomonas)
    - early age first intercourse
    - high risk male partner
- ❑ clinical presentation
  - squamous cell carcinoma
    - exophytic, fungating tumour
  - adenocarcinoma
    - endophytic, with barrel-shaped cervix
- ❑ symptoms
  - early
    - asymptomatic
    - discharge, initially watery, becoming brown or red
    - post-coital bleeding
  - late
    - spontaneous irregular bleeding
    - pelvic or back pain
    - bladder symptoms/bowel symptoms
- ❑ signs
  - friable, raised, reddened area
- ❑ pathogenesis
  - dysplasia —> carcinoma in situ (CIS) —> invasion
  - slow process (years)
  - growth is by local extension
  - metastasis uncommon and occurs late
- ❑ screening (Pap smear)
  - endocervical and exocervical cell sampling, TZ sampling
  - false positives 5-10%, false negatives 10-40%
  - identifies squamous cell carcinoma, less reliable for adenocarcinoma
  - yearly, starting when sexually active (after three consecutive negative smears, screening intervals may be increased to every three years at the physician's discretion (The Walton Report)
  - can stop after age 69 if she has at least 3 consecutive negative smears

Table13. Cytological Classification

Bethesda Grading System	Classic System/CIN Grading System
• within normal limits	• normal
• infection	• inflammatory atypia (organism)
• reactive and reparative changes	
• squamous cell abnormalities	
• atypical squamous cells of undetermined significance (ASCUS)	• squamous atypia of uncertain significance
• low grade squamous intraepithelial lesion (LSIL)	• HPV atypia or mild dysplasia — CIN I
• high grade squamous intraepithelial lesion (HSIL)	moderate dysplasia — CIN II severe dysplasia — CIN III carcinoma in situ (CIS)
• squamous cell carcinoma (SCC)	• squamous cell carcinoma (SCC)
• glandular cell abnormalities	
• atypical glandular cells of undetermined significance (AGUS)	• glandular atypia of uncertain significance
• endocervical adenocarcinoma • endometrial adenocarcinoma • extrauterine adenocarcinoma • adenocarcinoma, NOS	• adenocarcinoma

- ❑ diagnosis (colposcopy) **(see Colour Atlas GY6)**
  - apply acetic acid and identify white lesions
  - endocervical curettage (ECC) if entire lesion is not visible or no lesion visible
  - cervical biopsy
- ❑ cone biopsy if
  - unsatisfactory colposcopy
  - abnormal endocervical curettage
  - discrepancy between Pap smear results and punch biopsy
  - Pap smear shows adenocarcinoma in situ
  - microinvasive carcinoma
- ❑ complications (low incidence)
  - hemorrhage
  - infection
  - cervical stenosis or incompetence
  - infertility

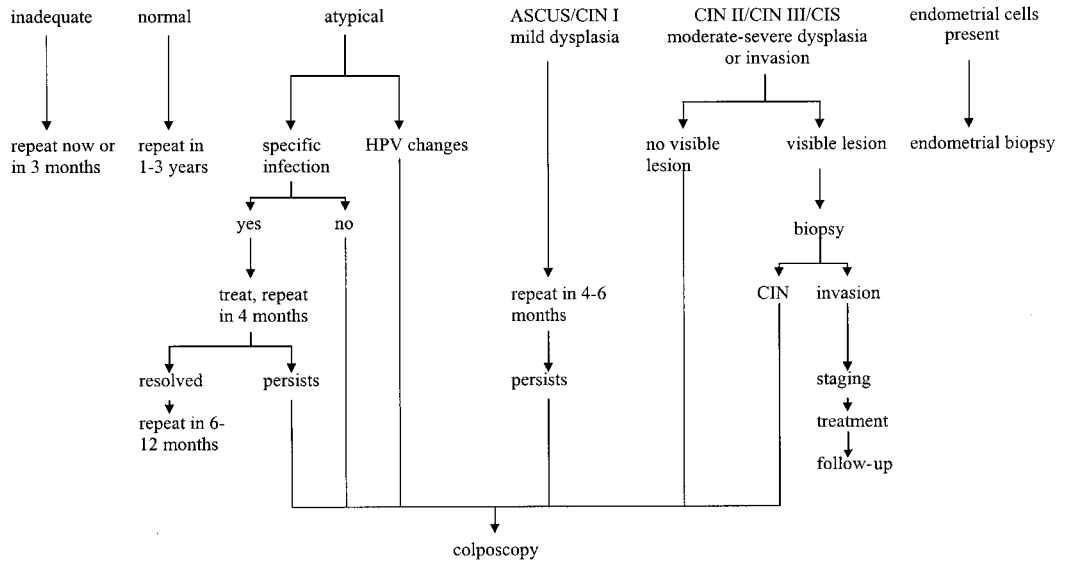

Figure 11. Decision Making Chart for Pap Smear

Table 14. Staging Classification of Cervical Cancer (Clinical Staging)

Stage	Description
0	carcinoma in situ (CIS)
1 **1A** **1B**	confined to cervix microinvasive all others
2	beyond cervix but not to the pelvic wall, does not involve lower 1/3 of vagina
3	extends to pelvic wall, involves lower 1/3 of vagina
4	beyond true pelvis +/– distant spread, bladder, and/or rectum involved

Table 15. Treatment of Abnormal Pap Smear and Cervical Cancer

CIN I (LGSIL)	• observe with regular cytology (every 6 months) • many lesions will regress or disappear (60%) • colposcopy if positive on 2 consecutive smears • lesions which progress should have area excised by either LEEP, laser, cryotherapy or cone biopsy (with LEEP tissues obtained for histological evaluation)
CIN II and CIN III (HGSIL)	• LEEP, laser, cryotherapy, cone excision • hysterectomy: only for CIN III with no desire for future childbearing
Stage 1A	• cervical conization if future fertility desired • simple abdominal hysterectomy if fertility is not an issue
Stage 1B	• radical (Wertheim) hysterectomy and pelvic lymphadenectomy • ovaries can be spared • radiotherapy if lesion expanded beyond 4 cm
Stages 2,3,4	• radiotherapy

❑ prognosis
- 5 year survival figures
  - Stage 0: 99%
  - Stage 1: 75%
  - Stage 2: 55%
  - Stage 3: 30%
  - Stage 4: 7%
  - Overall: 50-60%

Abnormal Pap Smears in Pregnancy

❑ incidence: 1/2,200
❑ Pap test and biopsy of any suspicious lesion should be performed at initial prenatal visit (refer to colposcopy)
❑ if a diagnostic conization is required it should be deferred until second trimester (T2) to prevent complications (abortion)
❑ microinvasive carcinoma
- followed to term and deliver vaginally or by C-section depending on degree of invasion

❑ stage 1B carcinoma
- depends on patient wishes
- recommendations in T1: external beam radiation with the expectation of spontaneous abortion
- recommendations in T2: delay of therapy until viable fetus and delivery

❑ follow-up with appropriate treatment

VULVA

❑ any suspicious lesion of the vulva should be biopsied
❑ multiple biopsies are needed

Benign Vulvar Lesions

- ❑ malignant potential (< 5%); greatest risk when cellular atypia on biopsy
- ❑ squamous cell hyperplasia (hyperplastic dystrophy)
  - post-menopausal
  - pruritus
  - thickened raised lesions with whitish plaques
  - treated with corticosteroid cream
- ❑ lichen sclerosis
  - mostly post-menopausal
  - pruritus, dyspareunia, burning
  - atrophic vulva with fusion of labia
  - not associated with increased incidence of malignancy
  - treated with high potency fluorinated steroids
- ❑ lichen sclerosis with epithelial hyperplasia (mixed dystrophy)
  - burning, pruritus, dyspareunia
  - increased incidence of cellular atypia
  - treated with corticosteroid cream
- ❑ papillary hidradenoma
  - sharply circumscribed nodule, usually on labia majora or interlabial folds
  - tendency to ulcerate (gets confused with carcinoma)
- ❑ HPV lesions (condylomata acuminatum) (see Gynecological Infections section)

Malignant Vulvar Lesions

- ❑ characteristics
  - 5% of genital tract malignancies
  - 90% squamous cell carcinoma; remainder Bartholin gland adenocarcinoma, Paget's
  - 50% of invasive lesions are associated with current or previous vulvar dystrophy
  - usually post-menopausal women
  - patient usually presents late or is biopsied late
  - worse prognosis when occurs at younger age
  - etiological association with HPV
    - VIN = precancerous change which presents as multicentric white or pigmented plaques on vulva
    - 90% of VIN contain HPV DNA, specifically types 16, 18
    - increased incidence associated with obesity, hypertension, diabetes, atherosclerosis, long-term steroid treatment
- ❑ sites of origin
  - labia minora (40-45%)
  - labia majora (35-40%)
  - clitoris (10-15%)
  - perineum, anus (3%); Bartholin gland (1%); multifocal (5%)
- ❑ spread
  - locally
  - ipsilateral groin nodes (superficial inguinal —> pelvic nodes)
- ❑ clinical features
  - localized pruritus, pain
  - raised red, white or pigmented plaque
  - ulcer, bleeding, discharge
  - dysuria
- ❑ diagnosis
  - physical examination
  - ALWAYS biopsy
  - +/– colposcopy

Table 16. Staging Classification and Treatments of Vulvar Cancer (Surgical Staging)

Stage	Description	Treatment
0	intraepithelial neoplasia (VIN) carcinoma in situ	local excision laser superficial vulvectomy
1	< 2 cm no suspicious groin nodes	wide local excision simple or radical vulvectomy nodal dissection
2	> 2 cm no suspicious groin nodes	individualized local surgery +/– radiation
3	local extension to adjacent structures suspicious or positive unilateral groin nodes	as for stage 2
4	fixed bilateral groin nodes distant spread	as for stage 2

❑ prognosis
- depends on nodal involvement and tumour size (node status is most important)
- lesions > 3 cm associated with poorer prognosis
- overall 5 year survival rate: 70%

VAGINA

Benign Vaginal Lesions

❑ VAIN (Vaginal Intra-Epithelial Neoplasia)
- pre-malignant
- grades: progression through VAIN1, VAIN2, VAIN3
- diagnosis
  - Pap smear
  - colposcopy
  - Schiller test (normal epithelium takes up iodine)
  - biopsy
- treatment
  - VAIN1: often regress and recur therefore manage conservatively with regular follow up
  - VAIN2: laser ablation, electrosurgical cautery
  - VAIN3: ablation, excisional biopsy should be considered to rule out invasion

Malignant Vaginal Lesions

❑ assessment
- cytology (Pap smear)
  - 10-20% false negative rate
  - increased incidence in patients with prior history of cervical and vulvar cancer
- colposcopy
- Schiller test
- biopsy, partial vaginectomy
- staging (see Table 16)

❑ squamous cell carcinoma
- 2% of gynecological malignancies
- most common site is upper 1/3 of posterior wall of vagina
- symptoms
  - asymptomatic
  - vaginal discharge (often foul-smelling)
  - vaginal bleeding especially during coitus
  - urinary symptoms secondary to compression
- treatment
  - radiotherapy if a primary
  - hysterectomy and vaginectomy

❑ adenocarcinoma
- most are metastatic, usually from the cervix, endometrium, ovary, or colon
- most primaries are clear cell adenocarcinomas
- 2 types: non-DES and DES syndrome
- management as for SCC

❑ diethylstilbestrol (DES) syndrome
- most existing cases have already been documented
- maternal use and fetal exposure to DES predisposes to cervical or vaginal clear cell carcinoma
- < 1 in 1,000 risk if exposed
- clinical presentation
- adenosis or the replacement of normal squamous epithelium of vagina by glandular epithelium
  - occurs in 30-95% of exposed females
- malformations of upper vagina, cervix, and interior of uterus (T-shaped); cockscomb or hooded cervix, cervical collar, pseudopolyps of cervix

Table 17. Staging Classification of Vaginal Cancer (Clinical Staging)

Staging	Description
0	intraepithelial neoplasia (VAIN) carcinoma in situ
1	limited to the vaginal wall
2	involves subvaginal tissue, but no pelvic wall extension
3	pelvic wall extension
4	extension beyond true pelvis or involvement of bladder or rectum

FALLOPIAN TUBES

- ❑ least common site for carcinoma of female reproductive system
- ❑ usually adenocarcinoma
- ❑ more common at extremes of age, < 20 or > 40
- ❑ 80% are benign
- ❑ clinical presentation
  - watery discharge (most important)= "hydrops tubae profluens"
  - vaginal bleeding
  - lower abdominal pain
- ❑ treatment
  - as for malignant ovarian tumours

GESTATIONAL TROPHOBLASTIC NEOPLASIA (GTN)

- ❑ refers to a spectrum of proliferative abnormalities of the trophoblast
- ❑ incidence
  - 1/1,200 pregnancies
  - marked geographic variation: in Asians (1/800)
  - more common in extremes of childbearing age
  - risk increases ten-fold following one GTN
- ❑ characteristics
  - 80% benign, 15% locally invasive, 5% metastatic
  - risk of malignant sequelae greater in women > 40 years, para > 3
- ❑ clinical and pathological classification (see Figure 12)

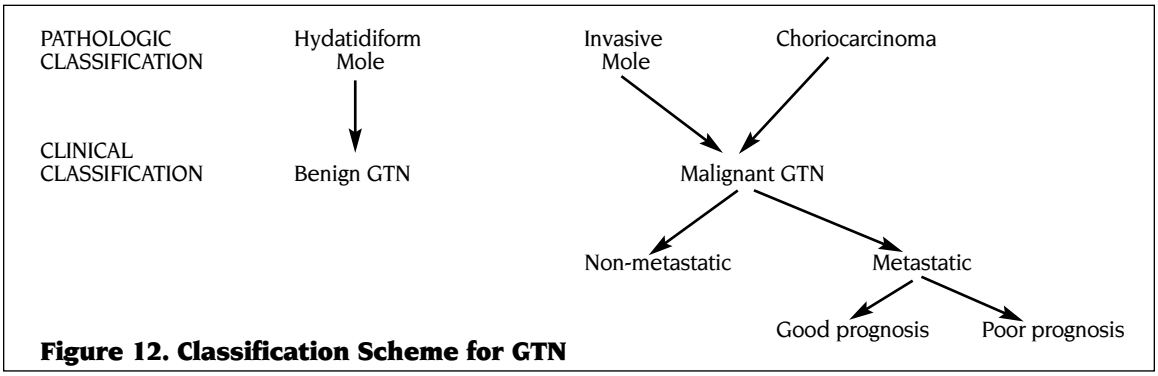

Figure 12. Classification Scheme for GTN

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Hydatidiform Mole (Benign GTN)

- ❑ complete mole
  - a proliferative or neoplastic trophoblast, hydropic swelling of chorionic villi, no fetal tissues or membranes
  - most common type of hydatidiform mole
  - 2 sperm fertilize empty egg or 1 sperm with reduplication
  - 46XX or 46XY of paternal origin
  - high malignant potential (15-20%)
  - marked edematous and enlarged villi
  - disappearance of villous blood vessels
- ❑ partial (or incomplete) mole
  - hydropic villi and focal trophoblastic hyperplasia are associated with a fetus or fetal parts
  - often triploid (XXY)
  - single ovum fertilized by two sperm
  - often associated with severe hypertension
  - low malignant potential (4%)
  - often associated with fetus that is clinically growth restricted and has multiple congenital malformations
- ❑ clinical presentation
  - vaginal bleeding (most common)
  - typically diagnosed as threatened abortion because of passage of tissue and vaginal bleeding (95%) and uterine cramps
  - uterus size large for dates (50-55%)
  - hyperemesis gravidarum (25-30%)
  - early hypertension (15-20%)
  - bilateral theca lutein cysts (10-20%)
  - hyperthyroidism (5-10%): due to elevated thyroid stimulating hormone (TSH)
  - anemia
  - anorexia
  - no fetal heart sound detectable
  - uterus may be tender and doughy
  - partial mole: similar presentation except less severe clinical features, later diagnosis, uterus usually small for dates

- ❑ diagnosis
  - clinical
  - U/S
    - vesicles seen
    - if complete: no fetus (see "snow storm")
    - if partial: molar degeneration of placenta with developing fetus/fetal parts
    - multiple echogenic regions corresponding to hydropic villi and focal intra-uterine hemorrhage
  - βhCG levels
    - abnormally high (> 80,000)
- ❑ treatment
  - suction D&C with sharp curettage + oxytocin
    - 2% risk of respiratory distress secondary to trophoblastic embolization
    - 80-85% have complete remission
    - 15% develop persistent disease or metastases
  - hysterectomy
    - for local control, does not prevent metastasis
  - oral contraception to prevent pregnancy for 1 year
- ❑ follow-up
  - serial βhCGs while patient on OCP
    - every 1-2 weeks until negative x 3
    - usually takes 3-10 weeks
    - then every two weeks for 2-3 months
    - then monthly until one year from D&C
    - partial moles need to be followed for six months
    - pregnancy should be avoided until follow-up completed
    - if βhCG plateaus or increases, patient needs chemotherapy

Malignant GTN

- ❑ malignant GTN can be metastatic or non-metastatic
  - metastatic disease refers to outside the uterus
- ❑ types
  - invasive mole or persistent GTN
    - extensive local invasion
    - excessive proliferation of trophoblastic tissue (can be variable)
    - morbidity and mortality related to tumour penetrating through myometrium into pelvic vessels resulting in hemorrhage
    - villous structures persist with metastases
    - metastases are rare
    - diagnosis made by rising or a plateau in βhCG, development of metastases after D&C for molar pregnancy
  - choriocarcinoma
    - highly anaplastic
    - no chorionic villi, just elements of syncytiotrophoblast and cytotrophoblast
    - may follow molar pregnancy, abortion, ectopic, or normal pregnancy
    - tumour is highly malignant
    - invades myometrium and local vasculature to disseminate hematogenously to lungs, liver, brain, vagina, kidneys, and GI tract
    - tumour is dark hemorrhagic mass on uterine wall, cervix, or vagina and leads to extensive ulceration with increasing spread on surface or myometrial penetration
    - uterine perforation and hemorrhage common
    - infrequent occurrence - 1:20,000 pregnancies (in U.S.)
- ❑ clinical presentation
  - vaginal bleeding (most common)
  - amenorrhea
  - metastases usually appear early
    - may present with respiratory symptoms, neurological symptoms, etc.
    - 1/3 cases choriocarcinoma presents with symptoms related to metastases
  - vagina and vulva mets appear as dark hemorrhagic nodules
  - increasing emaciation, weakness, and anemia as disease progresses
- ❑ diagnosis
  - as for benign GTN
  - metastatic work-up
    - pelvic exam
    - blood work (CBC, renal and liver function tests)
    - pre-evacuation βhCG
    - chest X-ray
    - CT head, thorax, abdomen

Table 18. Classification of Metastatic GTN

Good Prognosis	Poor Prognosis
• short duration • disease present < 4 months from the antecedent pregnancy • low pre-treatment βhCG titre • < 100 000 IU/24 hour urine or < 40 000 mIU/mL of blood • no metastases to brain or liver • no significant prior chemotherapy	• long duration • > 4 months from antecedent pregnancy • high pre-treatment βhCG titre • > 100,000 IU/24 hour urine or > 40,000 mIU/mL of blood • brain or liver metastases • significant prior chemotherapy • metastatic disease following term pregnancy

Table 19. Management and Outcome of Metastatic GTN

Type	Treatment	Outcome
• Good Prognosis	• medical treatment with methotrexate (course of 4 IM injections q48 hours with folinic acid rescue; repeated q2-3 weeks unless side effects; stop when βhCG is undetectable in blood on 3 consecutive weeks) • avoid pregnancy for 1-2 years • surgical treatment with hysterectomy considered if chemotherapy is unsuccessful or if childbearing not desired	• 90-95% cured
• Poor Prognosis	• combination chemotherapy with methotrexate, actinomycin, chlorambucil • radiation used in patients with brain or liver metastases • follow βhCG for 5 years • avoid pregnancy for 1-2 years	• 50-70% cured • death due to brain and liver metastases

SURGICAL PROCEDURES

ABDOMINAL HYSTERECTOMY

Subtotal Hysterectomy
- ❑ body of uterus removed
- ❑ cervix is left

Total Hysterectomy
- ❑ uterus and cervix removed
- ❑ indications
- ❑ fibroids
- ❑ adenomyosis
- ❑ menorrhagia
- ❑ dysfunctional uterine bleeding (DUB)
- ❑ cervical CIS

Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy (TAH-BSO)
- ❑ removal of uterus with both tubes and ovaries
- ❑ indications include malignant ovarian tumours

Extended Hysterectomy
- ❑ operation of choice for endometrial carcinoma
- ❑ total removal of uterus, both tubes and ovaries, and cuff of vagina
- ❑ regional lymph nodes may also be removed if growth is in the lower third of uterine cavity

Wertheim's Radical Abdominal Hysterectomy
- ❑ for cervical carcinoma
- ❑ removal of uterus, tubes, ovaries, broad ligaments, parametria, upper half of vagina, and regional lymph nodes

DILATATION AND CURETTAGE +/– HYSTEROSCOPY

General Approach

- ❑ D&C should always include examination of uterine cavity with hysteroscope
- ❑ patient placed in dorsal lithotomy position
- ❑ pelvic examination under anesthesia to confirm orientation and size of uterus
- ❑ cervix exposed and grasped on anterior lip with single-toothed tenaculum
- ❑ Kevorkian curet used to scrape endocervical canal and obtain specimen
- ❑ uterus sounded (measured); normal uterus size <8 cm along internal longitudinal axis
- ❑ cervix then dilated sequentially to 9 mm
- ❑ hysteroscope inserted at this point if hysteroscopy to be done; copious irrigation fluid (preferably glycine; also carbon dioxide, cytosol) is used to distend endometrial cavity; small biopsy forceps can be inserted into this port to sample tissue of interest under direct visualization
- ❑ after hysteroscopy completed, sharp curettage done by gently scraping all sides of uterus with curette
- ❑ all instruments removed and cervix inspected for bleeding

Indications

- ❑ diagnostic
  - DUB
  - sterility
  - amenorrhea/oligomenorrhea
  - malignant disease of uterus
- ❑ therapeutic
  - removal of retained products of conception following abortion
  - therapeutic termination of pregnancy
  - removal of polypi and small submucous fibroids
  - removal of IUD
  - drainage of pyometra/hematometra

Complications

- ❑ bleeding
- ❑ perforation
- ❑ infection
- ❑ absorption of excess distension medium

LAPAROSCOPY

General Approach

- ❑ bladder emptied with catheter, pelvic examination under anesthesia
- ❑ most common set-up
- ❑ laparoscope placed through 10 mm sheath placed just below umbilicus
- ❑ 5 mm sheath placed in midline at level of pubic hair line through which other probes may be placed
- ❑ if significant operative intervention, one or two 12 mm sheaths may be placed into abdomen lateral to either rectus muscle, approximately an inch below umbilicus
- ❑ Rubin cannula inserted into cervical canal to manipulate uterus
- ❑ Veress needle placed into abdomen in order to insufflate with 3-4 L of CO_2 (g)
- ❑ at the end of the procedure, probes and laparoscope are removed; gas allowed to escape through sheaths; then sheaths are removed followed by closure of the small incisions with simple interrupted sutures

Indications

- ❑ diagnostic
  - evaluation of infertility, pelvic pain, small pelvic masses, congenital anomalies, small hemoperitoneum, and endometriosis
- ❑ therapeutic
  - tubal ligation
  - lysis of adhesions
  - excision/vaporization of endometriosis
  - aspiration of small cysts
  - retrieval of lost IUDs
  - tuboplasty
  - lymphadenectomy
  - myomectomy
  - ectopic pregnancy removal
  - also increasingly used for major surgeries such as cystectomies, salpingo-oophorectomy, hysterectomy, and treatment for stress incontinence

SURGICAL PROCEDURES . . . CONT.

Contraindications
- ❑ bowel obstruction
- ❑ large hemoperitoneum
- ❑ clinically unstable patient

Complications
- ❑ general
- ❑ insufflation of the preperitoneal abdominal wall
- ❑ injury to vascular structures (e.g. aorta)
- ❑ injury to viscus (bowel, bladder, ureters)
- ❑ procedure-specific injury
- ❑ may need to convert to laparotomy

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