

## Introduction to Gynecologic Oncology

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## Objectives Endometrial Neoplasia

- **Endometrial hyperplasia and cancer:**
- Discuss the epidemiology and risk factors for endometrial neoplasia.
- Discuss the clinical presentation and investigation of women presenting with
- symptoms of endometrial neoplasia.
- Discuss the different pathologies and prognostic factors in endometrial
- neoplasia.
- Discuss the principles and options for treatment of women with endometrial
- neoplasia.

## Objectives Pelvic Mass and Ovarian Cancer

- Discuss the differential diagnosis for a woman presenting with a pelvic mass.
- Discuss the diagnostic work up of a woman presenting with a pelvic mass.
- Discuss risk factors and possible prevention strategies for ovarian cancer.
- Discuss the classification of ovarian cancers based on a woman's age, and the prognosis for different ovarian tumors.
- Discuss the signs and symptoms of ovarian cancer.
- Discuss the therapeutic management of women with pelvic masses and ovarian cancer, including surgery and adjuvant therapy.

## Endometrial Neoplasia Case Discussion

- A 61 years old woman presents with post menopausal bleeding.
- What is your differential diagnosis?
- What history will you elicit?
- What physical examination will you perform?
- What investigations will you order?
- What treatment options would be available based on the diagnosis?

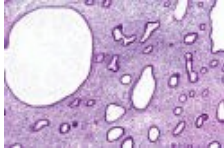
## Postmenopausal bleeding

- Atrophy (50%)
- Hyperplasia (15%)
- Polyps (15%)
- Endometrial cancer (10%)
- Cervix, vulva (10%)
- Consider non-gynecologic causes (urinary tract, GI)

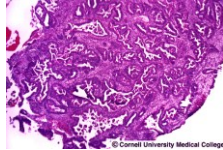
## Endometrial hyperplasia

- Abnormal proliferation of glands → can progress to cancer
- Characterized by architecture of glands (simple or complex) and cellularity (atypia or no atypia)

## Endometrial hyperplasia



Simple hyperplasia  
-uniform glands



Complex hyperplasia  
- branching glands

## Treatment of endometrial hyperplasia

- Presence of cellular atypia is the more important prognostic factor
- If atypia – higher risk of cancer (30% for complex hyperplasia with atypia)  
∴ surgery (HBSO)
- If no atypia – lower risk of cancer (1-3%)  
∴ progestins (Provera)

## Endometrial cancer

- Estrogen-related
  - Exogenous estrogen
    - HRT without progestins
    - SERM (e.g. Tamoxifen)
  - Endogenous estrogen
    - Obesity
    - PCOS (anovulatory ∴ no progesterone)
- 20% premenopausal, obese, low grade tumour, good prognosis
- Non-estrogen related
  - High risk histology
    - uterine papillary serous carcinoma
    - clear cell carcinoma
    - leiomyosarcoma, carcinosarcoma
- Postmenopausal, Caucasian, slim, high grade tumour, poor prognosis

## Investigations / work-up

- History and physical
  - R/O other sources of PMB
- Endometrial biopsy / D&C
- Ultrasound – *not* necessary investigation for PMB
  - Increased double layer thickness (anterior and posterior walls opposed to each other)

## Transvaginal ultrasound



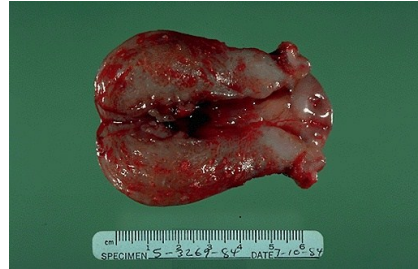
## Endometrial cancer

- Most common gynecologic malignancy
- ~ 3500 cases per year in Canada (1400 in Ontario)
- Majority have Stage I disease
  - Early presentation with abnormal bleeding
  - Overall 5 year survival ~ 70%

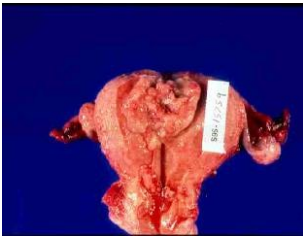
## Endometrial cancer

- Surgery
  - Total abdominal hysterectomy, bilateral salpingo-oophorectomy (+/- pelvic nodes)
- Radiation
  - as primary therapy (rare)
  - Adjuvant treatment (if high risk tumour factors)
    - To decrease risk of pelvic recurrence

## Endometrial cancer



## Endometrial cancer



## Summary

- The most common cause of PMB is atrophy
- Any postmenopausal bleeding requires a history, physical, and biopsy

## Ovarian Cyst Case Discussion

- A 41 years old woman comes to you after an ultrasound shows a 5 cm ovarian cyst
- What is your differential diagnosis?
- What history and physical examination will you obtain?
- What additional information do you want about the ultrasound?
- What investigations would you order?
- What treatment options will you discuss?

## Ovarian Cancer Case Discussion

- A 70 years old woman complains of early satiety and abdominal distension
- What is your differential diagnosis?
- What pertinent history will you elicit?
- What focused physical examination will you perform?
- What investigation will you order?
- What treatment options are recommended?

## Pelvic mass

- History
  - Onset
  - Symptoms
    - Changes in bowel and bladder function
    - Increase in abdominal girth
    - Early satiety, decreased appetite
    - Dyspnea
- Differential diagnosis
  - Gynecologic
  - Non-gynecologic (urinary tract, GI)

## Pelvic mass - differential

- Age at diagnosis
  - Childhood
    - Ovarian germ cell tumours, malignant
  - Reproductive age
    - Ovarian epithelial tumours, benign (endometrioma, serous cystadenoma)
    - Ovarian germ cell tumours (benign cystic teratoma)
  - Postmenopausal
    - Ovarian epithelial tumours, malignant and benign
    - Ovarian sex-cord/stromal tumours (granulosa cell)
    - GI tumours (cancer)

## Ovarian tumours

- Epithelial (80%)
- Germ cell (15%)
- Sex cord-stromal (5%)

## Germ cell tumours

- Classification
  - Dysgerminoma (most common)
  - Teratoma
    - Immature
    - mature (benign cystic teratoma, dermoid)  
\*reproductive age
  - Endodermal sinus tumour (yolk sac tumour)
  - Embryonal
  - Choriocarcinoma

## Characteristics of germ cell tumours

- Younger population (usually < 20 years)
- Usually diagnosed at Stage I
- Conservative surgery (fertility sparing)
- Curative with chemotherapy if metastatic

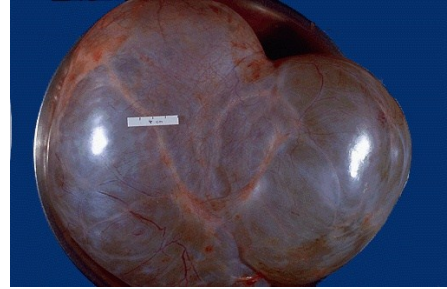
## Sex cord-stromal tumours

- Granulosa cell tumour
  - secretes estrogen → endometrial hyperplasia or cancer in 25%
- Sertoli-Leydig cell tumour
  - Secretes androgens → virilization

## Epithelial tumours

- Classification
  - Serous (cystadenoma)
  - Mucinous
  - Clear cell
  - Endometrioid (endometrioma)
  - Brenner (transitional cell)
  - undifferentiated

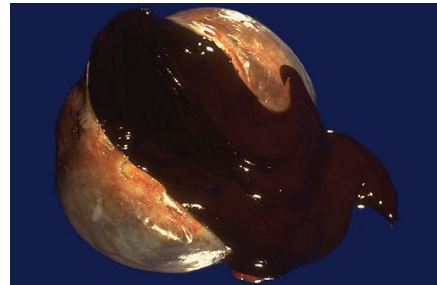
## Serous cystadenoma



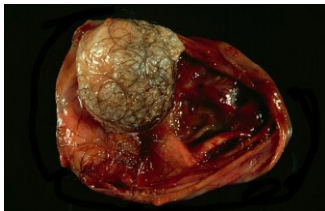
## Serous cystadenoma



## Endometrioma



## Mature cystic teratoma



## How to investigate a pelvic mass

- History and physical\*
- Ultrasound
  - Transvaginal is best
  - Features
    - Simple vs. complex
    - Cystic vs. solid
    - Excrescences, papillations
    - septations
    - ascites
- Other investigations
  - GI symptoms, bleeding or pencil-thin stools → barium enema or colonoscopy

## Ovarian cancer

- Symptoms
  - General
  - Appetite / N&V
  - Respiratory
  - Abdominal girth
  - Bladder
  - Bowel

## Ovarian cancer

- Lifetime risk ~ 1/70 (1.4%)
- Highest mortality rate of all gynecologic malignancies
- Usually presents as advanced stage
  - 70% will have Stage III/IV

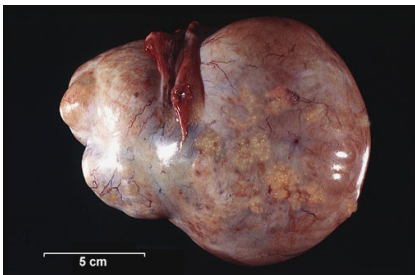
## Ovarian cancer

- Risk factors (“incessant ovulation”)
  - Early menarche
  - Late menopause
  - Nulliparity
  - Family history
- Protective factors (inhibit ovulation)
  - Oral contraceptive
  - Pregnancy / multiparity
  - breastfeeding

## Treatment of ovarian cancer

- Surgery
  - TAH BSO, omentectomy, debulking
- Chemotherapy (adjuvant, ie. after surgery)
  - Paclitaxel and Carboplatin
- Treatment goal
  - Prolongation of disease-free survival (not cure)
  - Overall 5-year survival 70-80% if Stage I, 10 % if Stage III/IV

## Ovarian cancer



## Ovarian cancer



## Is there a role for screening?

- Ultrasound
- CA125
  - Coelomic and mullerian epithelium

*These do NOT reduce the mortality from ovarian cancer*

## Role of screening - ultrasound

	N	# undergoing surgery	# cancers detected	# false positives	Positive predictive value
Andolf (1986)	805	39 (4.8%)	3	36	7.7%
Bourne (1993)	1000	52 (5.2%)	3	49	5.8%
Weiner (1993)	62	12 (19.4%)	3	9	25%
Van Nagell (2000)	3299	NR	6	NR	NR

## Screening with CA125

	% proceeding to U/S	Detection rate	PPV
2 U/mL	100%	100%	12.7%
10 U/mL	72.1%	86%	14%
20 U/mL	25.3%	71%	31.3%
30 U/mL	8.7%	43%	30%
35 U/mL	5.6%	43%	43%

## Elevated CA125

- Gynecologic
  - Endometriosis, fibroids, hemorrhagic ovarian cysts, menstruation, PID, pregnancy
- GI / hepatic conditions
  - Acute pancreatitis, colitis, hepatitis, cirrhosis, diverticulitis
- Other malignancies
  - Bladder, breast, endometrium, lung, liver, pancreas, NHL
- Miscellaneous
  - Pericarditis, PAN, renal disease, Sjogren's syndrome, SLE

## Role of screening – CA125 and ultrasound

	N	# having surgery	# cancers detected	# false positives	PPV
Akulenko (1992)	1003	1.4%	1	13	7.1%
Karlan (1993)	597	1.7%	1	9	10%
Muto (1993)	384	3.9%	0	15	0
Schwartz (1995)	247	0.4%	0	1	0
Belinson (1995)	137	1.5%	1	1	50%
Dorum (1996)	180	7.8%	7	7	50%

## Familial cancer phenotypes

- 1) Hereditary breast/ovarian cancer syndrome
  - BRCA 1 and 2
  - 3 or more relatives with breast and/or ovarian cancer
- 2) Hereditary non-polyposis colorectal cancer (HNPCC, Lynch II)
  - "3-2-1" rule (Amsterdam criteria): 3 affected individuals, 2 generations, 1 under age 50
  - Includes colorectal and endometrial cancer most commonly (ovarian cancer – less common)

## BRCA1 and BRCA2

- Tumor suppressor genes
- 90% of hereditary ovarian cancer
- Increased lifetime risk of breast and ovarian cancer

Population	Lifetime breast cancer risk	Lifetime ovarian cancer risk
General	11% (1 in 9)	1.4% (1 in 70)
BRCA1 carrier	50-85%	25-50%
BRCA2 carrier	50-85%	25%

- Variable frequency in different populations
  - e.g. Ashkenazi Jews, Mediterranean, French Canadian

## Features of BRCA mutation carriers

- Earlier age of diagnosis for BRCA1 carriers
  - Mean age ~ 53 years (10 years earlier than sporadic ovarian CA)
- (papillary) serous histology
- Increased risk of fallopian tube cancer
- Low penetrance for endometrial cancer
- Associated malignancies with BRCA2
  - Pancreas, gallbladder, gastric, melanoma, male breast and prostate

## Recommendations for BRCA mutation carriers

- Screening at early age for breast cancer
  - consider age of youngest family member diagnosed with breast cancer
- Prophylactic surgery for ovarian cancer (bilateral salpingo-oophorectomy)
  - Screening with ultrasound and CA125 not helpful in this high risk population
  - Prevents ovarian cancer
  - Reduces risk of breast cancer
  - Recommended ~ age 40 (after completed childbearing)

## Summary

- The diagnosis of a pelvic mass depends on the age of the patient and clinical features
- Ovarian cancer has the highest mortality rate of all gynecologic cancers
- There is no effective screening for ovarian cancer