Gynecologic Cancers

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What is Gynecologic Cancer?

- Any cancer that starts in a woman's reproductive organs
- Each GYN cancer is unique
- 5 main types
  - **Cervical**
  - **Ovarian**
  - Uterine
  - Vaginal
  - Vulvar

Who is at risk for GYN Cancer?

- All women are at risk
  - Risk generally increases with age
- Incidence - estimated
  - 107,470 new diagnosed cases
  - 31,600 deaths

Cervical Cancer - Facts

- 3rd most common GYN cancer in women in the U.S.
- Estimated Cases
  - New – 12,820
  - Deaths – 4,210 (ACS Facts and Figures 2017)
- Rates are decreasing in the U. S.
  - Incidence remains high among
    - Hispanic/Latino, Black, Asian women
- Persistent human papillomavirus (HPV) infection
  - most important factor in development of cervical cancer
- The only GYN cancer that can be prevented with screening tests and routine follow-up

Screening Recommendations

Organization	Age to initiate	Age to discontinue	Recommended screening test and frequency	
			Age 21 to 29	Age ≥ 30
ACS/ASCCP/ASCP (2012)	21	65	PAP test q 3 yrs (preferred)	Co-testing (pap test and HPV testing) q 5 yrs (preferred)
ASCCP/SGO (2015 interim guidelines)	21	NA	Can consider primary HPV testing q 3 yrs for women ≥ 25	Pap test q 3 yrs
USPSTF (2012)	21	65	PAP test q 3 yrs	Pap test q 3 yrs
				Alternative: Co-testing (pap + HPV testing) q 5 yrs
ACOG (2012)	21	65	PAP test q 3 yrs	Co-testing (pap test and HPV testing) q 5 yrs (preferred)
				PAP q 3 yrs

Screening Recommendations

- Guidelines intended for the general population
  - Not for women with a history of cervical cancer
  - High-grade cervical pre-cancer,
  - DES un utero exposure
  - Immunocompromised i.e. (HIV infection)
- Age to discontinue - 65
  - Adequate negative prior screening
    - 3 or more negative cytology tests
    - 2 consecutive negative co-tests in past 10 years – most recent within past 5 years

Cervical Cancer – Risk Factors

- Human Papilloma virus
- Smoking
  - Carcinogens concentrated in cervical mucus
- Immunosuppression
- STI's
  - Chlamydia
  - Genital herpes
- Multiple sexual partners
- Early age of onset of coitus
- Long term oral contraceptive use
- Multiple full term pregnancies
- Poverty

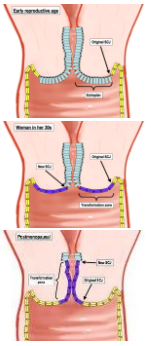
Human Papillomavirus (HPV) & Cervical Cancer

- Most significant risk factor
- Most common sexually transmitted disease
- > 100 types – most benign
  - About 40 affect the genital tract
    - Low-risk HPV – visible benign lesions/warts – condylomata accuminata
      - HPV 6 & 11
    - High-risk HPV – tend to persist – assoc. with precancerous lesions
      - HPV 16 & 18
- Virus enters through a break in the squamous epithelium
  - HPV proteins bind to p53 – interfere with cell growth
  - Allows damaged cells and HPV infection to thrive

HPV Vaccine

- 3 Vaccines
  - Gardasil (quadrivalent) – HPV 6, 11, 16 & 18
  - Gardasil 9 (9-valent) – also covers HPV 31, 33, 45, 52
- Quadrivalent HPV Vaccine (Gardasil)
  - Types 16 & 18
    - 70% of Cervical Cancer
  - Types 6 & 11
    - 90% genital warts
  - 9 y.o. – 26 y.o.
- CDC Advisory Committee on Immunization Practices
  - 9-10 yrs: per physician
  - 11-12 yrs: recommend immunization
  - 13-26 yrs who have not been previously vaccinated
  - Can receive if previous:
    - Abnormal PAP, HPV test positive, genital warts

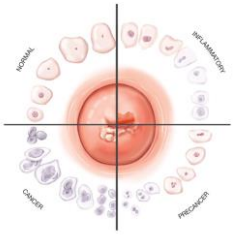
Cervical Cancer - Pathophysiology



- Two major parts
  - Endo and Exo cervix
- Main cell types
  - Columnar epithelium - Endocervix
  - Squamous epithelium - Exocervix
- Squamo-columnar junction (SCJ)
  - Transformation Zone (TZ)
  - Meeting point between endo & exo cervix
    - Glandular cells replaced by squamous cells
    - Response to hormonal changes - Metaplasia
- Cervical cancer
  - Culmination of progressive disease that begins as a series of events in the SCJ

Cervical Cancer - Pathophysiology

- Histology
  - 80-90% squamous
  - 10-20% adeno
- Pre-invasive or Premalignant changes
  - No invasion of cervical stroma
  - Squamous intraepithelial lesion
    - Low grade (LSIL) – CIN1
    - High grade (HSIL) – CIN2, 3
  - Glandular tissue
    - Adenocarcinoma in situ (AIS)



Cervical Cancer Presenting Signs/Symptoms

- Early signs / symptoms
  - Most are asymptomatic
  - Persistent vaginal discharge
  - Painless, intermittent, post-coital or intra-menstrual vaginal bleeding
  - Increase in menstrual length/flow
- Late signs / symptoms
  - Pelvic pain & referred pain to flank or leg; lower extremity edema
  - Urinary symptoms include: dysuria, urinary retention, urinary frequency or hematuria
  - Bowel symptoms may include: rectal bleeding, constipation or bowel obstruction
  - Weight loss

Diagnostic Testing

- HPV testing
- Pap test
  - Normal
  - Abnormal
- Colposcopy
  - Examination of the cervix
    - Evaluation of the transformation zone in its entirety
    - Any lesions noted are biopsied
- Endocervical curettage (ECC)
  - Tissue specimen from the endocervical canal

Cervical Intraepithelial Neoplasia (CIN)

- CIN 1 – low grade lesions
  - Mildly atypical cellular changes
    - Low-grade squamous intraepithelial lesions (LSIL)
    - Low potential for developing malignancy
- CIN 2 – high grade lesions
  - Moderately atypical cellular changes
    - High-grade squamous intraepithelial lesions (HSIL)
- CIN 3 – high grade lesions
  - Severely atypical cellular changes
    - High-grade squamous intraepithelial lesions (HSIL)

CIN Management

- Approaches
  - Continued observation - (cervical cytology HPV testing, colposcopy)
    - For most women with CIN 1
    - Persistent CIN 1 - LEEP
  - Treatment
    - Excision or ablation
    - Excisional treatments
      - Cone biopsies/cervical conization
      - Loop electrosurgical excision procedure – LEEP
      - Large loop excision of the transformation zone (LEEP/LLETZ)
      - Laser conization

CIN Management

- Ablative treatments
  - For patients with
    - CIN 2,3 if colposcopy is adequate
  - Cryotherapy (cold probe)
    - Refrigerant gas freezes tissue
  - CO_2 Laser
    - Causes vaporization of the lesion
  - Cold coagulation
    - Heat (at lower temperatures) to ablate cervix
  - Diathermy
    - Electrically induced heat

Staging Cervical Cancer

- Two systems in use
  - Federation of Gynecology and Obstetrics (FIGO)
    - Most commonly used
  - American Joint Committee on Cancer (AJCC)
    - TNM – Stage 0-IV
- Staging – FIGO based on
  - Physical exam
    - Pelvic exam
  - Cervical biopsy
  - Endoscopy

Staging Cervical Cancer

- Imaging studies
  - CT
  - MRI
    - Describe disease extent and guide treatment options
  - PET-CT
    - Detect and r/o metastasis
- Useful in treatment planning but not yet used for staging
  - Not universally available - yet
  - Rules for clinical staging not strictly followed – so difficult to compare results between clinicians and institutions

Cervical Cancer - Treatment

- Common types of treatment
  - Surgery
    - Cryosurgery
    - Laser surgery
    - Conization
    - Hysterectomy
      - Simple
      - Radical
    - Trachelectomy
    - Pelvic Exenteration

Cervical Cancer - Treatment

- Common types of treatment
  - Radiation therapy
    - Main treatment
    - Treat cancer that spread or recurred
  - Two main types
    - External beam
    - Brachytherapy
  - Long term effects
    - Vaginal stenosis
    - Vaginal dryness
    - Weakened bones
    - Leg swelling

Cervical Cancer - Treatment

- Common types of treatment
  - Chemotherapy
    - Depending on the stage concurrent therapy is preferred
      - Cisplatin weekly
      - Cisplatin + 5FU every 4 weeks
    - Recurrence
      - Cisplatin, Carboplatin
      - Paclitaxel
      - Topotecan
      - Gemcitabine

Cervical Cancer - Treatment

- Common types of treatment
  - Targeted therapy
    - Bevacizumab – can be used to treat advanced cancer
  - Side effects
    - High blood pressure
    - Bleeding
    - Proteinuria

Surveillance

- Survivorship Care Plan
- Follow-up physical exam
  - Every 3-6 mos for 2 yrs
  - Every 6-12 mos for 3-5 yrs
  - PAP test – yearly
  - Imaging as indicated based on symptoms
  - Lab work – CBC, BUN, creatinine as indicated
  - Patient education
    - Symptoms of potential recurrence, lifestyle, obesity, exercise and nutrition counseling
    - Regarding sexual health

References

- Fusco, E. (2010). Preinvasive Disease of the Cervix, Vulva, and Vagina. In L. Almadrones-Cassidy (Ed.) *Site-Specific Cancer Series: Gynecologic Cancers.* (pp. 37-43). Pittsburgh, PA: Oncology Nursing Society.
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- Tinari, M. A. (2008, November/December). Cervical Cancer. *Nursing Made Incredibly Easy,* pp. 32-41.
- NCCN Guidelines Version 1.2017. Cervical Cancer
- American Cancer Society Facts and Figures 2017
- American Cancer Society Statistics 2017

Ovarian Cancer

ACS Leading Sites of New Cancer Cases and Deaths in Females – 2017 Estimates

New Cases (852,630)	**Est. Deaths (282,500)**
Breast (30%)	Lung & Bronchus (26%)
Lung & Bronchus (12%)	Breast (14%)
Colon & rectum (8%)	Colon & rectum (8%)
Uterine Corpus (7%)	Pancreas (7%)
Thyroid (5%)	***Ovary (5%)***
Melanoma of the skin (4%)	Uterine Corpus (4%)
Non-Hodgkin's Lymphoma (4%)	Leukemia (4%)
Leukemia (3%)	Liver & intrahepatic bile duct (3%)
Pancreas (3%)	Non-Hodgkin's Lymphoma (3%)
Kidney & renal pelvis (3%)	Brain & other nervous system (2%)

ACS Facts and Figures 2017

Ovarian Cancer - Facts

- Leading cause of death from GYN cancer
- 5th most common cause of cancer mortality
- Lifetime risk 1 in 75
  - New Cases – 22,440
  - Deaths – 14,080
- < 40% are cured
- Incidence increases with age
- Median age at diagnosis – 63
- > 60% present with advanced disease
- Overall 5 yr survival is 46%

Ovarian Cancer Risk Factors

- **Patient Characteristics**
  - Age - >63
  - Personal Hx breast cancer
- **Reproductive factors**
  - Nulligravity
  - Early menarch
  - Late menopause
  - Infertility
  - Polycystic ovarian syndrome
  - Endometriosis
- **Genetic** – 5%
  - Family hx of ovarian cancer
  - BRCA 1 / 2 mutations
  - Lynch syndrome
- **Environmental factors**
  - Obesity & high-fat diet
  - Talc exposure
  - Cigarette smoking

Ovarian Cancer Decreased Risk

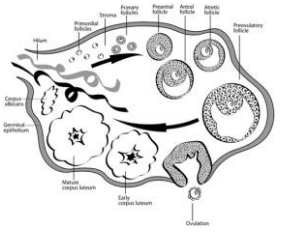
- Reproductive factors
  - Use of oral contraceptives
  - Pregnancy/multiparity
  - Breastfeeding
- Gynecologic surgery
  - Salpingo-oopherectomy
  - Tubal ligation

Ovarian Cancer - Screening

- Screening - Average risk
  - Routine screening NOT recommended
  - Several large RCTs – now completed
    - CA-125 and/or TVU
- Screening - High risk
  - Pelvic exams
  - CA-125
  - Transvaginal ultrasound (TVU)

Ovarian Cancer

- Epithelial tumors - (85-90%)
  - Papillary serous
  - Endometrioid cell
  - Mucinous cell
  - Clear cell
- Germ Cell tumors– 5%
  - Benign or malignant
- Stromal tumors – 7%



Ovarian Cancer Diagnosis & Evaluation

- Gastrointestinal
  - **Bloating**
  - **Urinary symptoms**
  - **Difficulty eating/early satiety**/dyspepsia
  - Nausea
  - Constipation/Diarrhea
  - Fatigue
  - Back pain
- Gynecologic
  - **Abdominal distention**/increased abdominal girth
  - **Pelvic pain**
  - Menstrual irregularities
  - Vaginal bleeding
  - Watery vaginal discharge
- 95% had symptoms prior to diagnosis
- 89% with early-stage disease

Goff, B et. al. (2007) Development of an ovarian cancer symptom index. Possibilities of earlier detection. Cancer. 109(2), 221-227.

Ovarian Cancer
Preoperative Workup

- History of present illness
  - Symptom index tool
- Family history
  - HBOC
  - Lynch syndrome
- GYN history
- Labwork
  - Full panels plus
    - CA-125 (consider HE4)
    - B-HCG
    - AFP
- Imaging
  - Transvaginal ultrasound
  - CT abd/pelvis
  - Chest x-ray

Ovarian Cancer
Surgical Treatment

- Laparotomy
  - En bloc TAH, BSO tumor removal
    - Comprehensive staging
    - Fluid sampling
    - Pathologic assessment of the abdomen
      - Diaphragm
      - Pericolic gutters
      - Serosal surfaces
  - Optimal debulking – remove visible disease to
    - < 1 cm tumors – small volume residual
      - improved response rate
      - longer disease free survival & overall survival

Ovarian Cancer – Treatment
Chemotherapy

- Chemotherapy
  - Neoadjuvant
    - Therapeutic benefit controversial
    - Stage III/IV not surgical candidates (dx by biopsy)
    - Pathologic dx should be confirmed prior to chemotherapy
  - Adjuvant
    - Combination of drugs
      - Platinum and a Taxane
  - Intraperitoneal (IP)
    - Chemotherapy directly into the abdominal cavity

Ovarian Cancer - Treatment
Intraperitoneal

- Rationale
  - Peritoneum the predominant site of tumor
    - receives sustained exposure to high concentrations of chemotherapy
    - Sparing normal tissues such as the bone marrow
  - Administered through an abdominal port
  - Different side effect profile than IV
    - Leukopenia, infection, fatigue, renal toxicity, abdominal discomfort and neurotoxicity

Ovarian Cancer – Treatment Intraperitoneal

- Intraperitoneal chemotherapy
  - Recommended regimen
    - Taxol 135 mg/m2 – continuous IV infusion over 3 or 24 hours Day 1
      - Published randomized trial used Taxol as a 24 hr infusion
      - 3 hour Taxol not proven to be equivalent
    - Cisplatin 75 – 100 mg/m2 IP on Day 2 after IV Taxol
    - Taxol 60 mg/m2 IP on Day 8
    - Every 3 weeks for 6 cycles
    - Initial studies only 42% able to complete all 6 cycles

Administration Considerations for IP Chemotherapy

- Type and location
  - Vascular or intraperitoneal
  - Implanted by rib or over abdominal muscle (instruct pt to "tense" abd muscle at time of access)
- Port access
  - Procedure similar to vascular port access
  - Non-coring needle
- Ensuring placement
  - Ability to flush
  - Aspirate?
  - Observe for infiltration
- Risk of dislodgement
  - Limit activity after access
  - Access IP port when ready to treat
- IP fluids
  - Warmed to body temperature
- Flushing
  - Heparin?
    - Fibrin sheath formation
  - 20 ml NS the 10 ml 100u/ml Heparin
- Rotation schedule
  - Side to side
  - Trendelenburg

Ovarian Cancer - Treatment Targeted Therapy

- Antiangiogenesis inhibitors
  - Bevacizumab
    - IV every 2-3 weeks
- PARP inhibitors
  - BRCA gene mutation
  - Typically used after 2 or more lines of therapy
  - Oral agents
    - Olaparib
    - Rucaparib
  - No BRCA gene mutation
    - Niraprib

Ovarian Cancer - Treatment

- Adjuvant chemotherapy
  - IV Regimens
    - Taxol 175 mg/m2 - over 3 hrs f/b Carboplatin AUC 5-6 - over 1 hr every 3 wks x 6 cycles
    - Dose dense Taxol 80 mg /m2 – over 1 hr days 1, 8, 15 + Carboplatin AUC 5-6 – over 1 hr every 3 wks x 6 cycles
    - Taxol 60 mg/m2 – over 1 hr f/b Carboplatin AUC 2 – over 30 min weekly x 18 wks
    - Docetaxel 60-75 mg/m2 – over 1 hr f/b Carboplatin AUC 5 or 6 – over 1 hr day 1, every 3 wks x 6 cycle

Surveillance

- Survivorship Care Plan
- Follow-up physical exam to include pelvic
  - Every 2-4 mos for 2 yrs
  - Every 3-6 mos for 3 yrs
  - Annually after 5 years
  - Other tests
    - Imaging as clinically indicated
    - Lab work – CBC, chemistry profile as indicated
    - CA125 or other tumor markers
  - Genetic risk evaluation – if not done before
  - Patient education
    - Symptoms of potential recurrence, lifestyle, obesity, exercise and nutrition counseling
    - Regarding sexual health

Surveillance

- Persistent treatment-associated effects at the completion of therapy
  - Physical Symptoms/treatment side effects
    - GI side effects
    - Neuropathy
    - Fatigue
    - Body image changes/problems with sexuality
  - Psychological issues
    - Depression/anxiety - guilt
    - Threat to the female image
  - Threat of recurrence
    - Preoccupation with lab values

Recurrence

- 50%-75% relapse with advanced disease
  - < 6 mos – Platinum resistant
    - Single agent non-platinum based
      - +/- Bevacizumab
  - > 6 mos - platinum sensitive
    - Carboplatin/Taxol
      - Hypersensitivity reactions to Carboplatin > after 7th dose
    - Carboplatin/ Liposomal doxorubicin
      - Equivalent to Carbo/Taxol
      - Different toxicity profiles
      - Easier to tolerate

Recurrence

- Non-platinum base drugs used in recurrence
  - Docetaxel, oral etoposide, gemcitabine, liposomal doxorubicin,
  - Weekly taxol, topotecan

Resources

- National Comprehensive Cancer Network
  - www.nccn.org
  - Practice guidelines for clinicians
  - Patient education
- National Cancer Institute
  - www.cancer.gov
  - Patient education pamphlets “What you need to know about…….”
  - Gynecologic Oncology Group (GOG)
    - www.gog.org