Roswell Park Cancer Institute

Gynecologic Oncology Resident Handbook 2015-2016

Revised 04/2016

ACKNOWLEDGEMENTS

This handbook would not have been possible without the contributions, inspirations, corrections and suggestions of many individuals, including:

Bonnie Blum

Peter Frederick

Kassondra Grzankowski

Shashi Lele

Joanne Masterson

Kunle Odunsi

Michelle Pelletier

Grazyna Riebandt

James Brian Szender

Emese Zsiros

"There are known knowns. These are things we know that we know. There are known unknowns. That is to say, there are things that we know we don't know. But there are also unknown unknowns. There are things we don't know we don't know".

Donald Rumsfeld

Gynecologic Oncology Handbook

Roswell Park Cancer Institute

Welcome to the Gynecologic Oncology service at Roswell Park Cancer Institute. Our goal is to provide first-rate, compassionate care for every patient. To accomplish this we must work as a team which includes physicians, nurses, pharmacists and support staff. Residents are a vital part of this team. To ensure the best experience for all involved everyone must know their role and expectations. The purpose of this handbook is to not only detail those expectations, but to provide you with some of the tools to attain them. Our hope is that in doing so we can allow for an educational and enjoyable rotation.

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PGY-2 & PGY-3 RESIDENT EDUCATIONAL OJECTIVES

The **educational objectives** of the RPCI Gynecologic Oncology Resident Program include the following:

I. Educational purpose-PGY-2-3 residents are trained to manage gynecologic nonmalignant and malignant tumors. They perform preoperative evaluations and major and minor surgical procedures. They manage uncomplicated and complicated postoperative and critical care patients.

II. Goals and Objectives

*By the end of the rotation, the resident will be able to:

1. Medical knowledge
    -Basic sciences
    -Describe indications for screening for BRCA1 and BRCA2
    -Describe the anatomy of the internal and external pelvic organs
    -Describe the vasculature and lymphatics to the internal and external pelvic organs
    -Describe the relationship between the bladder, ureter, bowels and uterus
    -Describe the histology of gynecologic malignancies
    -Describe chemotherapeutic agents used for gynecologic malignancies
    -Describe side effects of chemotherapeutic agents used for gynecologic malignancies

2. Patient care
-Perform comprehensive history and physical on patients with gynecologic malignancies
-Order and interpret appropriate diagnostic test for gynecologic malignancies
-Manage postoperative complications in patients with gynecologic malignancies
-Manage critical patients with gynecologic malignancies
-Describe the indications for radiation and chemotherapy in patients with gyn malignancies
-Describe the complications of radiation and chemotherapy
-Describe the principles of palliative care
-Describe the principles of pain management

3. Practice-based learning
-Maintain gynecologic oncology case mean numbers at the national average
-Attend grand rounds, chapter reviews and journal clubs
-Describe statistical test (Chi-square and t-test)
-Use information technology (PubMed literature, Cochrane Database)

4. Communication
-Communicate effectively with patients and family members
-Sustain a therapeutically sound relationship with patients and family members
-Maintain comprehensive, timely and legible medical records
-Present clear concise clinical presentations to attendings, residents and medical students

5. Professionalism
-Demonstrate respect for physicians, referring physicians, residents, medical students, nursing staff and clerical staff.
-Demonstrate responsibility for the care of all patients on labor and delivery
-Demonstrate accountability for all clinical decisions
-Advocate for all patients
-Demonstrate ability to teach medical students
-Demonstrate ability to interact with hospital staff

6. Systems-based practice
-Demonstrate interest in understanding the local health care system structure
-Demonstrate an understanding of the roles of the health care team members
-Effectively use ancillary service personnel

III. Types of clinical encounters
The PGY-2-3 resident will manage the following conditions:

-Describe the clinical presentation of VIN and VAIN
-Perform vulvar biopsies
-Describe the differential diagnosis of vulvar carcinoma
-Describe the FIGO staging of vulvar cancer
-Counsel a patient about treatment options including surgery, radiation and chemotherapy
-Describe the prognosis of vulvar cancer
-Describe the FIGO staging, treatment and prognosis of vaginal cancer
-Describe the classification of cervical dysplasia
-Describe the treatment options for cervical dysplasia
-Describe the FIGO staging, treatment and prognosis of vaginal cancer
-Describe the classification and management of endometrial hyperplasia
-Describe the FIGO staging, treatment and prognosis of endometrial cancer
-Describe the classification and management of ovarian tumors
-Describe screening methods to identify patients at risk of hereditary ovarian cancer
-Describe the histology of ovarian cancers
-Describe the FIGO staging, treatment and prognosis of ovarian cancer

-Diagnose and manage hydatidiform mole
-Describe the diagnostic approach to gestational trophoblastic disease (GTD)
-Classify metastatic GTD in low and high risk
-Counsel patients regarding treatment, prognosis and recurrence

The PGY-2 resident must understand and the PGY-3 must master the following procedures:
-Abdominal hysterectomy
-Staging laparotomy
-Washings, exploration and omentectomy
-Suction curettage of molar pregnancy
-Cervical conization (LEEP and cold knife cone)
-First assistant for robotic procedures (port placement, docking, uterine manipulation).

The PGY-2-3 resident must understand the following procedures:

-Radical hysterectomy
-Lymph node dissection
-Radical vulvectomy
-Vaginal reconstruction
-Radical vulvectomy
-Exenteration
-Bowel resection

IV. Rotation structure
Rotation Sites:
Roswell Park Cancer Center -2 modules
-0630 AM rounds with chief fellows (daily)
-0800 AM rounds with gyn-oncology attending (daily)
-The PGY-2-3 resident remains on the unit for 10-12 hours.

V. Resident supervision
-All gyn-oncology procedures performed by the PGY-2-3 resident on patients are performed under the supervising faculty member.

VI. Method of evaluation
-The PGY-2-3 resident receives daily feedback from fellows and attending faculty physicians
-Faculty physician evaluations are performed at the end of the rotation
-Global evaluations are performed semi-annually

VII. Reading list

1. Clinical Gynecologic Oncology, DiSaia, 7th Ed. (May 2007)
2. Practical Gynecologic Oncology, Berek, 5th Ed. (2009)
3. Atlas of Procedures in Gynecologic Oncology, Levine, 2nd Ed. (2007)
4. Principles and Practice of Gynecologic Oncology, Barakat, 6th Ed. (2013)
5. ACOG Compendium 2015

RESIDENT RESPONSIBILITIES

Prior to Day #1

- It has been arranged that residents will check in with the Department of Education Affairs, RSC Building (4th Floor, Room 408) for registration, attend the EMR training/ orientation to electronic medical records, obtaining passwords, dictation code, etc., and obtain an ID badge from The Parking and Transportation office (ground floor of the parking ramp, hours are 7am-5pm) the week prior to their start date to allow for maximum participation on their 1st day.

Day #1

- Please coordinate with the clinical fellows regarding where and when to report on Monday morning. Typically on the 1st and 3rd Monday of the month there is GYN Didactic Lecture held in the GYN Clinic Conference Room, Main Hospital, 2nd Floor, Room H2-128 at 6:45am-7:45am with rounds to follow. On opposite Monday's you should report to the floor for rounds.
- Parking: At this time, there is no reduced rate/dedicated parking for rotating residents. The parking ramp may be used on a daily basis. There is also an open lot next to the ramp that is privately owned, which may be available during the rotation.

Resident Responsibilities

- Round on inpatients
- Maintain *the list (Please contact Michelle Pelletier for access to the GYN Fellows Drive)*
- Operate in OR
- See patients in clinic
- Professional dress is encouraged
  - Women – Dress slacks or skirt
  - Men – Shirt and tie
- Resident: Give one PowerPoint presentation-topic to be discussed first week and scheduled with Michelle Pelletier.
- Dictate discharge summaries
- Discharge paperwork
- Discharge Prescriptions
- Residents do <u>not</u> take any home calls on this rotation

Daily Responsibilities

- Patients should be seen and have notes written by 6:45am each morning (time decided on the day prior depending on the patient load)

- Each resident will be responsible for a maximum of 5 inpatients in the morning. All ICU or IMCU patients should be seen by a fellow.
- Update *the list* (An electronic list is maintained and printed each morning. It provides a short "bio" of each patient, i.e. age, reason for admission, operation, medical co-morbidities, relevant diagnostic studies, significant in-hospital developments, etc. This list acts as a quick reference as well as allows for continuity of care as residents and fellows covering the service may periodically change.)
- A fellow and/or resident should be present and scrubbed for every case that goes to the OR. If there is more than one resident on service then the time spent covering the clinic and OR will be evenly divided amongst them.
- Follow-up on labs, radiology studies, call consults, etc.
- The first resident either out of the OR or out of clinic should go to the floor to pre-round and prepare for evening rounds; and report findings to the fellow. Find out vitals and I/O's for the day, know results of studies and labs, know what consultants recommended, talk with the patients to see how they are doing.
- Notes do <u>not</u> need to be written on evening rounds.
- During rounds, the fellow/ resident should pay attention and write down any new orders/plans.
- After rounds are over, all orders decided on rounds must be ordered.
- Patients that are going home will require the following items:
  - A dictated discharge summary (<u>Note</u>: Avoid writing the novel called "Discharge Summary." Brevity is the key. See Appendix 1 for discharge summary template. Make sure summary assigned to attending primarily managing patient's care.)
  - Discharge paperwork
  - Prescriptions for analgesia, constipation, etc.* (post op lovenox for high risk patients total 28 days and sent to tube #36 Anita-Social Work). See Appendix 2 for high-risk patients.
  - Schedule a follow-up appointment. Make sure you know where the patient will be following up (Buffalo campus, College Park, Niagara Falls, Jamestown)
  - Remove all drains, central lines, etc. when applicable—ideally the day before anticipated discharge unless told otherwise.
- Afternoon rounds: provide update of any patient issues that have come up during the day, e.g. results of any testing or imaging studies, any change in status?, etc.

Weekend Responsibilities

- There is always a fellow and attending on call.
- If two residents are on service, one resident will be responsible for rounding Saturday and Sunday, with weekend responsibilities to alternate between residents.

- If one resident is on service at a time, he/she is only responsible for rounding on Saturday morning

Clinic

- There are patients scheduled in clinic every weekday (see schedule)
- Clinic phone number: 845-5855
- Nurses will assess patients initially (vital signs, reason for visit, etc.) prior to putting them in a room
- Patients should be seen in the order in which they were placed in a room.
- Patient's last note will be placed in the chart as well as their medication list, chemotherapy sheet (if applicable); (any additional dictated reports, pathology reports, labs, etc. can be accessed in EMR)
- After seeing a patient, there are two sheets that need to be filled out (F10 and billing sheet). Most new patients are level 5. Most chemo and return patients are level 4. If it is a discussion-only visit, be sure to document it as such, with the amount of time spent in discussion, "with more than half that time spent in counselling and coordination of care."
- After completing the documentation, take the chart to the front desk (unless it is a chemotherapy patient; chemotherapy charts should be given to one of the chemotherapy providers.

Clinic Note Documentation: See Appendix 3 for instructions.

Operating Room

- The Operating Rooms are located on the 3rd floor
- Before being taken to the OR, patients are assessed in the pre-operative holding area (adjacent to the OR). After updating their H&P and undergoing pre-operative assessment and marking, patients are then wheeled back to the OR by the anesthesia team.

Clinic/OR Schedule (as of April 2016)

	Monday	**Tuesday**	**Wednesday**	**Thursday**	**Friday**
OR	Zsiros	Frederick	Lele	Odunsi /Akers	Open
CLINIC	(AM): Frederick **Niagara Falls** (PM): Frederick	(AM/PM): Lele **Amherst:** Akers	(AM): Odunsi (AM/PM): Zsiros	(AM/PM): Frederick **Amherst:** Lele/Zsiros Alternating weeks **BMG OP Clinic:** Lele/Zsiros Alternating weeks	(AM): Akers **Jamestown (4th Friday of the month):** Frederick

Note: Additional Activities:

- Fellow didactic lectures on Mondays at 6.45am and/or Fridays at 1:00pm.
- 1st and 3rd Wednesday @ 7:30am Multidisciplinary Tumor Board
- Every other Month on Tuesday @ 8:00am Familial Ovarian Cancer Registry meetings
- Tuesdays mornings at 8:45am weekly research meeting in the laboratory for lab fellows
- Every other month on Friday afternoons Morbidity and Mortality Conference
- Quarterly Surgical Services Quality Improvement meetings.
- Daily morning and evening rounds.
- Every Tuesday afternoon @ 4:00pm weekly chemotherapy review and planned surgical case review
- GYN Molecular Tumor Board 4th Tuesday of the month @ 4:00pm

Presentation

PGY-3 Residents on service are required to prepare and present a talk on a clinically relevant topic. The attendings and fellows can guide you in choosing a topic.

Past topics have included:

- Cancer in pregnancy
- Gestational trophoblastic disease
- Germ cell tumors
- Genetic predispositions to gynecologic malignancies
- Ureteral injuries in gynecologic surgery
- Molar pregnancy
- Post-operative bowel complications
- Necrotizing fasciitis
- Intraperitoneal chemotherapy
- Borderline ovarian tumors
- Venous thromboembolism

The presentation should last approximately 30 minutes. The use of primary sources with an in-depth analysis of available literature is encouraged.

Attendings and Fellows are available to assist with presentation suggestions. All topics should receive **final approval by Dr. Frederick**.

A projector will be provided as well as a laptop computer to facilitate a PowerPoint presentation.

Contact Michelle Pelletier at: Michelle.Pelletier@roswellpark.org with your topic and she will put you on the schedule to present near the end of your rotation.

An electronic copy of the presentation should be forwarded to Michelle Pelletier at: Michelle.Pelletier@roswellpark.org.

Conferences

- Every *other* Wednesday morning at 7:30 am there is Multidisciplinary Tumor Board where we review the pathology from the cases the weeks prior. It is coordinated by Dr. John Kazsnicka. Residents are excused if they have a conflicting lecture at CHOB, but expected to attend otherwise.
- Every Tuesday afternoon (04:00PM) we have Gyn Conference in which we review the OR schedule for the upcoming week, discuss chemotherapy patients, and have a learning topic/presentation (given by a fellow, resident, pharmacist, or guest speaker)

Order Entry

Roswell Park Cancer Institute utilizes a computerized physician order entry system. While this has streamlined order entry please do not let it be a substitute for communication with the nursing staff about the plan of care. The Gynecologic Oncology service has several order sets for use. Those orders may be access as below:

1. go to Roswell Park Cancer Institute internal web page
2. click on "EMR Citrix" on left side of web page
3. click on "EMR" icon
4. click on patient for whom orders are to be written
5. click on icon of clipboard with pen (upper left-hand corner of web page)
6. type in the word "gyn"
7. hit "enter" key
8. select desired order set

Common Sense Stuff

1. Always have a chaperone when doing a pelvic examination.
2. Ask if you don't know something.
3. The chemo nurse is an excellent resource. (Remember to give her chemo charts when done.)
4. When in doubt examine the patient.
5. Know what room the patients are in.

Welcome to Roswell from the Fellows

We are all very excited to have you on our team! Prior to your start date we would like to summarize some of our expectations to ensure we maximize your clinical experience and that you have a great time at Roswell.

We are a team and we expect everyone to help each other out on the floor, in the OR, and in clinic. This just makes for a more enjoyable work environment. If there are things that we are doing or not doing that you would like to see changed you please talk to us immediately in person, by email, or by phone (Kassondra 716-574-0571; Rachel 201-960-8148; Brian: 210-287-0836; Paul: 706-248-0797). As we are taking care of very sick and complex patients, we need to know everything about our patients and you are an essential part of our team looking after them and updating all of us. Your work and clinical judgement is very valuable to us, but we are also here to help you and teach you on how to manage them. If you think that you are in danger of violating work hours we need to be notified before anyone else, so we can fix your schedule and make sure you don't violate the work-hour rules.

Rounds in the AM:

Clinical notes need to be done prior to table rounds; however plans may change after we meet. Make sure you update your note after our discussion and rounding with the attending of the day, so before the attending signs off on your note the plan stated in your document reflects the correct assessment/plan for that day.

We will round as a team between 0615 and 0640 depending on the number of patients in house, when faculty are rounding, and other morning responsibilities, we'll meet in the conference room on 7E.

Please make sure that notes are assigned to the attending making rounds each morning, not the admitting attending. If people are away from the hospital there will be a different person rounding on their days. Please check with us if you have questions. We can also show you how to change the assignment if the appropriate attending is not initially chosen for your note. The general rule of thumb is as follows:

Monday: Dr. Zsiros
Tuesday: Dr. Lele
Wednesday: Dr. Odunsi
Thursday: Dr. Frederick
Friday: Dr. Akers

Weekends will be at the direction of the fellow/attending on call. The on call schedule is available on I2.

Clinic:

We expect everyone to help see patients, during fellowship our priority is working up new patients as well as managing patients undergoing chemotherapy, thus we will preferentially see new cancer patients (orange charts) and chemotherapy patients (purple charts).

You should preferentially see follow-up patients (especially post-ops whose surgeries you were involved with) and surveillance exams. If there are new patient referrals with abnormal Paps requiring colposcopy or conization, they are also good patients for you to see.

Every patient needs to be checked out with an attending. You cannot send home any patients without an attending seeing and examining them!

Providing high quality care and seeing patients in an efficient manner and reducing our clinic wait time are our top priority. This often means you have limited time to document between patients, especially as the clinic gets busy. In this case please start a blank note for them in their chart – as every patient need to have a note started on the day when they were seen – save it as incomplete and finish it at the end of clinic. It is unacceptable to spend time with documentation when patients are waiting to be seen.

You clinic notes need to be complete – including PMHx, PShx, Familyhx and Socialhx as well – every single time you see a patient. Please have your notes ready to be signed by the attending the latest 8 am the next morning.

OR:

Residents are expected to be on time for all OR cases. If you are late you may not be allowed to participate. First case starts as scheduled and you should arrive at least 15 mins before the start of the case to interview the patient and ensure pre-op paperwork is complete. For subsequent cases it is the resident's responsibility to monitor room turnover to know when the next case is to start.

If you pre-op a case we will try to let you come to the OR that day.

We are responsible for keeping track of all post-operative morbidity and mortality. We should already be aware of all fevers, surgical site infections, unexpected ICU admissions, or anything else; however, if you are aware of someone presenting and being discharged over the weekend please make sure it is brought to our attention. Criteria for and documentation of complications is also important as we are a NSQIP institution. Every other month morbidity and mortality cases are presented at conference.

We will write post-op orders on patients, preferably with you so that you can learn the way that we think about post-operative pain control, fluid management, and monitoring labs.

You will be responsible for writing the MD Brief Operative Note, this document is pretty straight forward in what it asks. It is very important that this is filled out correctly and on every patient

because operative dictations will often take a day or two to arrive into the system and the fellow on call will need to know the pertinent information for the patient if they receive any pages. These notes should be done after every case and not just at the end of the day, if one of us is in clinic and getting paged about a patient while the other of us is in surgery, it is helpful to at least know what surgery the patient had and what the EBL was.

If there are multiple residents on service we will leave it to you to divide up the cases between one another. It is important for you to try and work with all attendings both in the clinic and the operating room throughout your rotation. If you have concerns about case distribution, please speak to one or both of us and we will try to help make sure things are fair.

Rounds in the PM:

We will typically round after all OR cases are done and clinic patients are seen; however sometimes this will change based on schedules.

After rounds at Roswell are completed sometimes there are patients that need to be seen at BGH. Typically the fellows and attendings will head to BGH allowing you time to update the list and get orders ready for the AM. This is also a good time to call consults before other services have gone home for the day.

We will discuss what labs are required for individual patients while we are making our rounds, please take notes and make sure labs are ordered as AM LAB when you put them in for the next day.

After labs are ordered for the next day, this is a good time to get anticipated discharges for the next day squared away. Usually this involves cleaning up the electronic medical record/prescription writer, making sure that a Lovenox prescription or any other pre-auth prescription has been sent to Anita if appropriate (this should usually be done on post-op day #0, please ask if you have questions), and writing prescriptions for pain medications, stool softeners, and other home care needs.

Documentation:

Documentation is extremely important when taking care of our patients for a number of reasons: #1 it helps the next person who sees the patient know what was discussed and what the plan was, if you have questions please ask; #2 it helps the referring practitioner know about the status of their patient; #3 for billing purposes… if it isn't documented it didn't happen.

We have strict guidelines on clinical documentation, please follow that every single time for both inpatient and outpatient notes. Please see the attached document on how to write a structured note in EMR and follow that template for every single patient.

Information including diagnosis, stage, and list of prior therapies, including starting and ending dates should also be included on the daily checkout list. This will help on rounds when there are

questions about the patient's overall disease status and will help avoid losing the forest for the trees.

Discharge summaries should be assigned to the patient's clinic attending, not the attending that made rounds on the day of discharge. Sometimes the EMR has an attending listed as the admitting attending but the clinic attending who the patient belongs to is someone different.

Questions, Questions, Questions. We are a team and expect lots of questions, especially as you are starting out. When you have questions please ask, we are going to have a great rotation together!!

End of Rotation Presentation:

At the conclusion of your rotation, typically the last Tuesday of your rotation you will be expected to give a presentation. Discuss your topic choice with Dr. Frederick and receive his approval. Once you have received his approval please send your topic to michelle.pelletier@roswellpark.org and she will put you on the schedule. A copy of your presentation should also be saved on the fellows drive under the folder titled "Resident Papers and Lectures."

Thanks,

Kassy and Rachel

2015-2016 GYN Clinical Fellows

If you have additional questions, problems or concerns please contact the one who keeps us in line:

GYN Clinic/Fellowship Office
Michelle Pelletier
Fellowship Coordinator
Phone 716-845-3497

CONTACT INFORMATION/PHONE NUMBERS

Use the I2 on call calendar to text page or search by name in I2 and text page

- Roswell Park Cancer Institute (operator/main number): 716-845-2300
- To page or call someone: Dial "0"; follow prompts for 'call' or 'page' or page them from I2
- Gyn Clinic (front desk): 716-845-5855
- (nurses' desk): 716-845-5753
- 7 East(Front Desk): x3590 (716-845-3590)
- Operating Room: x226X (X=room number)
- Dr. Lele: office phone: x1330
- Dr. Odunsi: office phone: x8455
- Dr. Akers: office phone: x8337
- Dr. Frederick: office phone: x1694
- Dr. Zsiros: office phone: x7855
- Bonnie Blum (Pharmacist): Office phone: x3208
- Deanna Phoenix (Pharmacist): GYN Office phone: x8567
- Sharon Jankowski (chemotherapy nurse): x1420
- Karen Larkin (Nurse Practitioner): x8428
- Kim Ferrucci (Nurse Practitioner): x8365
- Margaret Duffy (Physician Assistant):x3026
- Anita Alfieri (Case Manager): phone: x4975
- Rachel Korman (Social Worker): direct line: x8486; office number: x8022; pager: 0767
- Michelle Pelletier (Fellowship Coordinator & Drs. Lele, Akers, Frederick, and Zsiros' assistant): x5776 x3497
- Ashley Sedelmeyer (Dr. Odunsi's assistant): x8376
- Odunsi Lab: x4502
- Microbiology lab: x3267
- IT Helpdesk: x8465
- Health Information Training (EMR questions): x3472

APPENDIX 1-Discharge Summary

Discharge Summary
Date of admit:
Date of discharge:
Service:
Attending:
Admit diagnosis: (*e.g. FIGO Grade 1 endometrial cancer)*
Discharge diagnosis: (*e.g. Clinical stage IA endometrial cancer on frozen section)*
Brief HPI: (*Ms. Jones is a 65-year-old female with a medical history significant for morbid obesity (BMI 52) and Type 2 DM who presented with postmenopausal bleeding and was confirmed to have endometrial cancer.*
Procedures/Operations:
Consultations:
Brief description of hospital course: (e.g.*Ms. Jones underwent the above procedure without complications. Please refer to op-note for full details. Postoperatively, she was transferred to the floor. On POD#1, she was tolerating PO with adequate pain control and was noted to meet all discharge milestones. She was afebrile with stable vitals throughout her hospital stay.*
Discharge condition:
Discharged to: (home, rehab, hospice, etc.)
Discharge medications:
Follow-up plan:
(make sure to list referring physicians to send copy of discharge summary to)

APPENDIX 2-Difficult Patients

Indications for prolonged anticoagulation (i.e. home prophylactic Lovenox)

- Any laparotomy with a cancer diagnosis
- Any robotic or laparoscopic hysterectomy with a cancer diagnosis and BMI $\geq$ 40
- Patients with borderline ovarian tumor or endometrial hyperplasia are on a case-by-case basis per risk factors and attending discretion
- In general, patients with current or recent thrombo-embolic disease should resume therapeutic anticoagulation (warfarin may require Lovenox bridge)
- There may be exceptions to above guidelines depending on patient's risk for bleeding

APPENDIX 3-Structured Notes in Clinic

- Please use the **MD H&P/Clinic Note** for every single visit.
- Under the first tab "**Reason for visit**" please ONLY fill out two things:
    - -Select the **Type of visit** (new, return, post-op…etc.)
    - -Enter the **Chief Complaint** (one max two words) – it is a MUST for billing for every patient
- Please do not use the Outpatient Statement or Current Therapy tab – it is redundant, will make a note too long and hard to read and this will be in the HPI
- **History of Present Ilness :** Please state the **patient age, diagnosis and why she is here**. If she is getting chemotherapy please type the number of cycle and the dose (ex*: Cycle 5 Carboplatin AUC 5 + Taxol 175 mg/m2 every 21 days*). If on chemotherapy please comment on any **Delays and Toxicities** (*ex: Cycle #4 delayed by 2 weeks due to grade 4 thrombocytopenia*). These are essential information for every patient getting treated.
- For chemotherapy patients also comment on: -**Response to treatment is monitored by**: CA-125 + imaging (or whatever we use for that particular patient). Current tumor marker is: ….
- Put the prior tumor markers for this cycle under this – so one can see if she is responding or not.
- -**Last imaging was**: ….. and showed NED or enlarged retropertineal lymph nodes etc…
- For any return or new patients:
- For **Brief HPI at least 3 elements for Extended HPI (every new pt) at least 5 elements** for billing (location, severity, duration, timing, associated sxs, modifying factors…etc. related to the complaint)

  Under this tab also write the:

  Oncology History

  Use bullet points so easy to follow and keep it clear and simple.

  Information that must be included:

  Time of diagnosis, histology and all prior treatments with their outcomes and complications

  Ex: Patient was diagnosed with stage IIIC ovarian cancer in Jan 2005.

  2005 Jan: Optimal/Suboptimal cytoreduction that included Exlap, TAH, BSO....

  2005 March –Aug: Carboplatin AUC6+ Taxol 175 mg/m2 q 3 weeks – CR (complete response)

  2007 April – first recurrence; started chemotherapy – list all chemotherapy regiments with # of cycles, doses, dates, any severe complications/reactions with any of them and why was the treatment discontinued (disease progression, toxicity or patient requested)

Performance Status, Procedures, Significant events tabs – skip all of these please

Past Medical History and Past Surgical History tabs

-Please use the Free Text Box – not the one when you click on things, which is harder to read, update and carry forward. All this should be in the free texted, **font Ariel size 10**.
-Under PMH – please put **Past OBGYN hx** – there is an acronym for this **.ezobhx**
All of our patients should have this documented.

Family history

This will be filled out during intake. Besides that in the Free Text Box please comment on if there is **any family hx of breast, ovarian, colon or uterine cancer,** which should be documented regardless of the rest. Acronym for the negative one: **.ezfamhx**

Social history

Smoking will be filled out by RNs – but you do have click on Alcohol Consumption and if you want on Marital status and Occupation – the rest of that tab is useless and do not click on anything else
In this case you don't need to use the Free Text box – as clicking is faster
ROS –The acronym for the Free Text Box negative ROS is **.ezros**

If you use the Free Text Box and something is positive – please highlight that with BOLD.
Vital Signs – please click on them to be included in the note.

Physical Exam

It is faster and easier to read the Free Text Box - .**ezphysical** for a negative one
Staging, RPCI results, Clinical Instructions, Decision Aids – please skip these

Please do not click the pathology results or on a bunch of lab results under these tabs. The way how the pathology result is pulled is essentially unreadable. Also no need to pull whole set of labs into the note, will make it very long. If something is pertinent – low ANC, Hgb or Plt# - please comment on these in the HPI session and address it in the A/P (ex: chemotherapy will be delayed due to Plt# 40K and will hold anticoagulation or Patient will be transfused with 2UPRBCs for Hgb of 6.5 etc…)

MU2 required – you cannot save the started note without commenting on these even as an incomplete note – so I recommend starting with this all the time in case you have to save your note as incomplete.

-This will include – Sign off on Meds, Comment on Outside referral and commenting on Flu and Pneumococcal vaccination – which has to be done only once for that patient.
-Please do not type under the Problem List and in the boxes under that for now. Use the A/P instead. We will use these fields when we become MU2 compliant as these will be printed on the patient's after visit summary.
Assessment/Plan:

If patient is a post-op patient, please copy the summary of the pathology result here (do this by opening the report from the Result section
highlight the summary and paste it here). This way it is legible.
If you have done an endometrial biopsy or colposcopy - please put the brief procedure note here – as there is no other place to document it. There are acronyms for both in case you want to use that:
.ezembx
.ezcolpo

Please write a clear Assessment including **age, stage of the disease and type of disease and whatever is pertinent for this visi**t– this is often missing or incomplete by trainees. Such as: *Patient is a 56 year old female with stage IA endometrioid adenocarcinoma of the uterus 2 weeks s/p uncomplicated Robotic Assisted Hysterectomy, BSO, recovering well and here for a postoperative visit*
Please do not use RAH – for robotic hysterectomy – community physicians might not understand our lingo or others may use this for radical hysterectomy. To make life easier when writing structured notes I strongly encourage everyone to create acronyms for all you common abbreviations. (RAH="robotic hysterectomy" etc)
Under this type the plan – make it clear, precise and short – easy to follow and read for referring providers.

Op Note
Pre-op Diagnosis:
Post-op Diagnosis:
Operation:
Surgeon:
Assistant(s):
Anesthesia:
Complications:
EBL:
IVF:
UOP:
Intra-op Findings:
Frozen Section:
Drains/Packing?
Disposition:

DISEASE SITE

UTERINE CANCER (EPITHELIAL)

I. Incidence
- Estimated 47,130 new cases in U.S. in 2012 with 8,010 deaths
- (Source: Barakat, 6th Ed.)
- Most common gynecologic malignancy (in U.S.)
- 4th most common cancer in ♀s
- Average onset of 60 years old.
- Estimated that 75% to 85% of the cases occur in patients 50 years old and older, and 95% occur in patients over 40 years of age.
- Confined to uterine corpus 75% of time

II. Risk Factors
- Obesity, exogenous estrogen, PCOS, granulosa/theca cell tumors of ovary, nulliparity
- Endometrial cancer is the most common extra-colonic cancer in hereditary nonpolyposis colorectal cancer (HNPCC)
- Taxoxifen (selective estrogen receptor modulator (SERM) with antiestrogenic properties in breast and estrogenic effects in bone and CV system)
  - **Fisher et al**. *(J Natl Cancer Inst. 1994;86(7):527-37)*
  - 2,843 node-negative, ER+, invasive breast cancer patients
  - randomized to placebo vs. tamoxifen (20mg/d)
  - hazard rate for endo ca in placebo was 0.2/1,000 vs. 1.6/1,000 for tamoxifen group (<u>but</u>…6 of the endo CA cases within 9 months of starting therapy)
  - reduction in breast cancer relapse (227.8 cases in placebo group vs. 123.5 in tamoxifen group) and reduction in contralateral breast cancer
  - "the benefit of tamoxifen therapy for breast cancer outweighs the potential increase in endometrial cancer"

III. Signs/Symptom
- 90% of patients present with postmenopausal bleeding or abnormal uterine bleeding

IV. Diagnosis
- Endometrial sampling by endometrial pipelle biopsy or dilation and curettage

V. Primary Treatment
- TH/BSO
- Cytology (peritoneal washing)
- Pelvic lymphadenectomy
- Para-aortic lymphadenectomy
- (for intra-abdominal disease also attempt maximal debulking and omentectomy)

VI. Staging

Table 22.4 Corpus Cancer Surgical Staging, FIGO 2009

Stages/Grades	Characteristics
IA G123	No or less than half myometrial invasion
IB G123	Invasion equal to or more than half of the myometrium
II G123	Tumor invades the cervical stroma but does n extend beyond the uterus
IIIA G123	Tumor invades serosa of the corpus uteri and/ adnexae
IIIB G123	Vaginal and/or parametrial involvement
IIIC1 G123	Metastases to pelvic lymph nodes
IIIC2 G123	Metastases to paraaortic lymph nodes, with o without positive pelvic nodes
IVA G123	Tumor invades bladder and/or bowel mucosa
IVB	Distant metastases including intra-abdominal and/or inguinal lymph node

(Positive cytology should be reported separately without changing the stage)

VII. Cell Types

- Endometrioid Adenocarcinoma
  - Most common form (75-80%)
  - Glands are formed of tall columnar cells that share a common apical border
  - With decreasing differentiation there is a preponderance of solid growth rather than gland formation
- Serous Carcinoma
  - Usually found in advanced stage in older women
  - Fibrous papillary fronds lined by epithelial cells, which are almost devoid of cytoplasm
  - Lymphatic invasion is commonplace
  - Psammoma bodies are frequently observed
  - 10% of endometrial carcinomas
  - Advanced-stage disease common
  - about 60% of patients are upstaged following complete surgical staging
- Clear Cell Carcinoma
  - Clearing of the cytoplasm of the neoplastic cells (result of glycogen abundance)
  - *Hobnail cells*
  - Almost exclusively a disease of post-menopausal women (mean age=68 years)
  - Aggressive
  - 4% of endometrial adenocarcinomas
  - Less common cell types include: villoglandular, secretory, ciliated, squamous, mucinous, undifferentiated

VIII. Prognostic Factors

- FIGO stage (the single strongest predictor of outcome)
- Histologic Cell Types (serous and clear cell associated with poor outcomes)
- Grade (as the grade becomes less differentiated there is greater tendency for deep myometrial invasion
- Myometrial Invasion
- Isthmus-Cervix Extension (lower segment involvement doubles risk of pelvic node metastases (16% vs. 8% with fundal involvement))
- Intraperitoneal Spread
- Ploidy (higher survival rates and progression-free survival for women with diploid tumors)
- Steroid Receptors (estrogen receptor positivity predictive of low probability of recurrence and improved survival)

IX. Adjuvant Treatment

Adjuvant Treatment of Stage I Endometrial Carcinoma*				
		Grade 1	**Grade 2**	**Grade 3**
IA	**NO** adverse risk factors	Observe	Observe or Vaginal Brachytherapy	Observe or Vaginal Brachytherapy
	+ adverse risk factors	Observe or Vaginal Brachytherapy	Observe or Vaginal Brachytherapy and/or Pelvic RT (Category 2B for Pelvic RT)	Observe or Vaginal Brachytherapy and/or Pelvic RT
IB	**NO** adverse risk factors	Observe or Vaginal Brachytherapy	Observe or Vaginal Brachytherapy	Vaginal Brachytherapy and/or Pelvic RT or Observe (Category 2B for Observation)
	+ adverse risk factors	Observe or Vaginal Brachytherapy and/or Pelvic RT	Observe or Vaginal Brachytherapy and/or Pelvic RT	Pelvic RT and/or Vaginal Brachytherapy ± (Category 2B for Chemotherapy)

Histologic Grade and Depth of Invasion				
Depth	**G1**	**G2**	**G3**	**Total**
Endometrium only	24%	11%	7%	14%
Superficial	53%	45%	35%	45%
Middle	12%	24%	16%	19%
Deep	10%	20%	42%	22%

Adverse risk factors= >60 years old, lymphovascular invasion, tumor size, lower uterine involvement

*recommendations per NCCN (based on FIGO 2015 staging guidelines)

X. Surveillance
- Physical exam every 3-6 months for 2 years then 6 months or annually
- Chest x-ray annually
- Vaginal cytology every 3-6 months for 2 years then annually
- Patient education regarding symptoms

What is the significance of the depth of invasion of endometrial cancer?
- The grade and depth of invasion are related to the presence of extrauterine disease
- Creasman *et al*. Cancer 60:2035-2041,
- 1987 (GOG 33)
- 621 patients with *clinical* stage I carcinoma of the endometrium
- Depth of invasion was correlated with grade
- There is also a correlation between depth of invasion and nodal metastasis.

Grade, Depth of invasion and PELVIC node metas.			
Depth	**G1**	**G2**	**G3**
Endometrium only	0%	3%	0%
Inner	3%	5%	9%
Middle	0%	9%	4%
Deep	11%	19%	34%

What is the role of adjuvant external beam pelvic radiation in intermediate risk endometrial adenocarcinoma?

- Keys *et al*. Gynecol Oncol 92: 744-751, 2004. (**GOG99**)
- 392 women with either IB, IC or occult stage II disease
- Patients randomized to either external beam radiation therpy (IBRT) to pelvic or to 'no adjuvant therapy' (NAT)
- 58% decreased risk of recurrence in RT arm vs. NAT arm
- High-intermediate risk (HIR)

Any age and…	1. moderate to poorly differentiated 2. Lymph-vascular space invasion 3. over third myometrial invasion
>50 years and…	Any 2 of above
>70 years and…	Any 1 of above

- One-third of patients in this group were considered high intermediate risk (HIR) but account for 2/3s of recurrences and 2/3s of cancer-related deaths
- In the HIR group the 2 year cumulative incidence of recurrence was 26% in the NAT arm vs. 6% in the RT arm
- RT was associated with more hematologic, GI, GU and cutaneous toxicities
- 2 patients in RT arm died of RT complication
- No difference in overall survival between RT and NAT arm
- Half of deaths due to causes not related to endometrial cancer
- Conclusions: Local recurrences are significantly altered by the use of RT. A majority of patients (non-HIR group) are at very low risk of recurrence regardless of treatment.

What is the risk of concurrent endometrial carcinoma in a woman with a biopsy diagnosis of atypical endometrial hyperplasia?

- Reference: Trimble et al. (*Cancer 106: 812-9, 2006*)
- 289 patients
- Prospective cohort study
- Atypical endometrial hyperplasia (AEH) biopsy specimens reviewed by 3 different pathologists
- 123 of 289 (42.6%) hysterectomy patients with endometrial biopsy samples consistent with AEH had concurrent endometrial carcinoma

- Conclusions: Many patients with suspected AEH will ultimately be upstaged at time of surgery and will require lymphadenecomy if invasion is present, therefore a gynecologic oncologist should be available.

EPITHELIAL OVARIAN CANCER (EOC)

I. Incidence
   - In US, 22K cases annually with 15K deaths in 2012
   - Age: 50% over age 65
   - Majority of case are Stage III or IV
II. Risk Factors
   - Genetic predisposition (e.g. BRCA, Lynch syndrome)
   - Family history
   - Repeated ovulation
   - Infertility
   - nulligravity
III. Protective Factors
   - Oral contraceptive use
   - Breast feeding
   - Tubal ligation
IV. Signs/Symptoms
   - Vague, non-specific
   - Bloating, increased abdominal girth, urinary complaints, early satiety, abdominal/pelvic pain
V. Diagnosis
   - CT or U/S-guided biopsy
   - Paracentesis
   - Thoracentesis
   - Surgery
   - CA125
     - Not specific for ovarian cancer
     - May be elevated with benign conditions, e.g. endometriosis, pregnancy, infection
     - Elevated in a majority of patients with EOC

VI. Staging (Updated January 2014)

OVARIAN CANCER: FIGO STAGING	
Stage I	Tumor confined to ovaries or fallopian tube(s).
IA	Tumor limited to one ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings.
IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings.
IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following: IC1: Surgical spill intraoperatively. IC2: Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface. IC3: Malignant cells present in the ascites or peritoneal washings.
Stage II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer (Tp).
IIA	Extension and/or implants on the uterus and/or fallopian tubes and/or ovaries.
IIB	Extension to other pelvic intraperitoneal tissues.
Stage III	Tumor involves one or both ovaries, or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside of the pelvis and/or metastasis to the retroperitoneal lymph nodes.
IIIA	Metastasis to the retroperitoneal lymph nodes with or without microscopic peritoneal involvement beyond the pelvis.
IIIA(i)	Positive retroperitoneal lymph nodes only (cytologically or histologically proven).
IIIA(ii)	Metastasis >10 mm in greatest dimension.
IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes.
IIIB	Macroscopic peritoneal metastases beyond the pelvic brim ≤2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes.
IIIC	Macroscopic peritoneal metastases beyond the pelvic brim >2 cm in greatest dimension, with or without metastases to the retroperitoneal nodes.
Stage IV	Distant metastasis excluding peritoneal metastases.
IVA	Pleural effusion with positive cytology.
IVB	Metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity).

VII. Cell types

- Serous (75%)
- Mucinous (10%)

- Endometrioid (10%)
- Clear cell
- Transitional cell

VIII. Primary Treatment

- Cytoreductive surgery*
- The goal is to leave the patient with no visible tumor remaining at the end of surgery

  * Lele S, Kesterson J. In Pursuit of Optimal Cytoreduction in Ovarian Cancer Patients: The Role of Surgery and Surgeon. *J Obstet Gynecol India* 2009;59(3):209-216.

IX. Chemotherapy

- The most efficacious chemotherapy regimen has been determined by a series of randomized, prospective trials conducted by groups such as the GOG, SWOG, SCOTROC, AGO and ICON. Based on these trials, women with advanced stage epithelial ovarian cancer should be offered adjuvant platinum-based chemotherapy. Some of these sentinal papers are summaried below, including GOG172 which, in combination with GOG104 and GOG114, prompted the National Cancer Institute statement recommending that all women undergoing optimal cytoreduction be considered for intraperitoneal chemotherapy.
- **GOG 111**: A Phase III Randomized Study of Cyclophosphamide and Cisplatin versus Paclitaxel and Cisplatin in Patients with Suboptimal Stage III and IV Epithelial Ovarian Cancer. McGuire et al. N Engl J Med 334: 1-6, 1996.
  - Patients
    - 410 patients with advanced stage EOC
    - Residual disease > 1 cm
  - Regimen
    - Cisplatin 75 mg/m2 and Cyclophosphamide 750 mg/m2, OR:
    - Cisplatin 75 mg/m2 and Paclitaxel 135 m/m2 (over 24 hours)
  - Outcomes
    - PFS: cisp/cyclo=13 months VS. Cisp/taxol=18 months
    - OS: cisp/cyclo=24 months VS. Cisp/taxol=38 months
  - Toxicity
- **GOG 158**: Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol 21(17):3194-200, 2003.

- Patients
  - Stage III
  - Optimally debulked
- Regimen
  - Regimen: 1: Paclitaxel 135 mg/m^2/24 hr + Cisplatin 75 mg/m^2
  - Regimen 2: Paclitaxel 175 mg/m^2/3 hr + Carboplatin AUC 7.5
- Outcomes
  - PFS: carbo/3hr taxol=20.7 months VS. 19.4 months with cisp/24hr taxol
  - Overall survival: carbo/3hr taxol=57.4 months VS. 48.7 months with cisp/24hr taxol

- **GOG 172**: Intraperitoneal cisplatin and paclitaxel in ovarian cancer. Armstrong et al. N Engl J Med 354(1):34-43, 2006.
  - Patients
    - Stage III (residual disease <1cm)
  - Regimen
    - Regimen 1 (intravenous):
      - Day 1: Paclitaxel 135 mg/m^2
      - Day 2: Cisplatin 75 mg/m^2
    - Regimen 2 (intraperitoneal)
      - Day 1: Paclitaxel 135 mg/m^2 IV
      - Day 2: Cisplatin 100 mg/m^2 IP
      - Day 8: Paclitaxel 60 mg/m^2 IP
  - Outcomes
    - PFS: IV arm=18.3 months VS. IP arm=23.8 months
    - OS: IV arm=49.7 months VS. IP arm=65.6 months
  - Toxicity
    - In IP arm: only 42% completed all 6 cycles
    - 48% received 3 or fewer cycles of IP therapy
    - IP arm: Grade 3/4: leucopenia (76%), GI events (46%), metabolic events (27%)
- **GOG 218** and **GOG 252** are evaluating the role of bevacizumab, an anti-angiogenic agent, in combination with platinum-based therapy in the adjuvant setting

X. Surveillance
- Currently the NCCN (V.2.2011) recommends
  - Visits every 3-6 months for up to 5 years then annually
  - Physical exam, including pelvic exam
  - CA125 (or other tumor markers) every visit if initially elevated
  - CBC or CMP as indicated

XI. Outcomes
- 80-85% of patients with Stage III/IV disease will recur
- Overall survival at 5 years: IIIC=33%, IV=19%*
  (*Int J Gynaecol Obstet. 95:S161 (2006))

XII. Chemotherapy for Recurrent Disease
- Therapy for recurrent disease is based on patient being either 'platinum-sensitive' (>6m progression free interval) or 'platinum-resistant' (<6m progression free interval)
  - Platinum-sensitive: Carboplatin or cisplatin + paclitaxel; Carbo+Doxil; Carbo+Gemcitabine
  - Platinum-resistant: single agent therapy (e.g. paclitaxel, Doxil); (must balance treatment toxicity, ease of administration, and scheduling with goal of symptom palliation)

XIII. Surgery for Recurrent Disease
- Patients with recurrent EOC may be candidates for surgical cytoreduction if the following criteria are met:
  - Platinum-sensitive disease with a PFI ≥12 months
  - Good performance status
  - Disease location amenable to surgical resection of all gross tumor volume

Borderline Ovarian Tumors
- 4,000 cases annually in US
- Histo types:
  - Serous
    - 75% with stage I disease
    - 25-50% bilateral
    - Complete staging critical b/c 25-30% with extraovarian dz
    - 6-27% with FS dx of borderline will be upgraded to invasive CA

        - Micropapillary features in 10-15%...micropapillations increases probability of invasive implants (6 to 49%) and of recurrence
    - Mucinous
        - 90% are stage I
        - <10% bilateral (except endocervical type' in which bilateral 40% of time)
    - Other: endometrioid, clear-cell, Brenner (transitional cell)
- Clinical
    - Most are asymptomatic
    - 49% with normal CA125 and <25% with CA125>100 U/mL
    - Staging is same as FIGO criteria for ovarian cancer
    - 70% are stage I
    - Need for staging is controversial…upstaging with complete staging in 12-47% with presumed stage I serous (but not mucinous); survival is high regardless of staging (meta-analysis with 98% survival at 6.5 years WITH lymph node involvement)
    - Goal of staging: discover areas of occult invasion, prognostic counseling, obtain info about biologic behavior of these patients
- Surgery:
    - Fertility sparing:
        - unilateral salping-oophorectomy
        - resect all macroscopic disease
        - risk of recurrence after conservative surgery=7-30% (recurrences typically borderline histology; not invasive CA);
            - Ref. Gynecol Oncol. 2006 Dec;103(3):841-7.of 1066 pts: 142 recurrences (13%) with 134 borderline and 8 malignant
    - Hysterectomy +BSO: lower tumor recurrence rate (6%);

Chemotherapy: **NO** advantage in treatment of women with early stage dz;

CERVICAL CANCER

I. Incidence
- In US, 12,170 cases diagnosed annually with 4,220 deaths in 2012
- Incidence highest in Hispanics and African-Americans
- Globally, 500,000 cases annually with 250,000 deaths
- 3rd most common cancer in women worldwide
- Majority (78-83%) of cases in developing countries

II. Risk Factors

- Persistent HPV infection
- Multiple sexual partners
- Early age of sexual debut
- Smoking
- Immunosuppression (AIDS patients, transplant recipients)

III. Signs/Symptoms

- Abnormal vaginal bleeding
- Post-coital bleeding
- Abnormal vaginal discharge
- (Early cervical cancer may not have symptoms)

IV. Diagnosis

- Approved procedures for staging
  - Colposcopy
  - Biopsy
  - Cervical conization
  - Cystoscopy
  - Proctosigmoidoscopy
  - CXR
  - IVP
  - Barium enema

V. Staging

CERVICAL CANCER: FIGO STAGING	
Stage I	Carcinoma is confined to the cervix
IA	Microscopic
IA1	Stromal invasion ≤ 3 mm in depth and extension ≤ 7 mm
IA2	Stromal invasion 3-5 mm with extension ≤ 7 mm
IB	Macroscopic/clinically visible
IB1	Lesion ≤ 4 cm
IB2	Lesion >4 cm
Stage II	Carcinoma extends beyond the uterus, but not to the pelvic wall or lower 1/3rd of vagina

IIA	No obvious parametrial involvement
IIB	Obvious parametrial involvement
Stage III	Carcinoma extends to pelvic side wall or lower 1/3rd of vagina
IIIA	Tumor involves lower 1/3rd of vagina, with no extension to pelvic wall
IIIB	Tumor extends to the pelvic wall or hydronephrosis or nonfunctioning kidney
Stage IV	Extends beyond the true pelvis or involves the bladder or rectum
IVA	Spread of the growth to adjacent organs
IVB	Spread to distant organs

VI. Primary Treatment

1. **IA1**: extrafascial hysterectomy
2. **IA2** & **IB1**: Radical hysterectomy with pelvic LND +/- para-aortic LND

   OR

   Brachytherapy + pelvic RT

   OR

   Radical trachelectomy with LND (if desires fertility)

3. **IB2**: Radical hysterectomy + pelvic and para-aortic LND

   OR

   Pelvic RT + cisplatin + brachy

   OR

   Pelvic RT + cisplatin + adjuvant hyst
4. **IB2-IVA**: surgical vs. radiographic evaluation of LNs ⇒ RT (tailored to LNs +/- for metastatic disease) + concurrent cisplatin
5. **IVB**: systemic chemotherapy + individualized RT (JCO 2009.21.8909)

VII. Cell types

- Squamous cell (80%)
- Adenocarcinoma
- Adenosquamous
- Less common: neuroendocrine, small cell, sarcomas

VIII. Prognostic factors-See page 76-81

IX. Surveillance

- 1st year: Pap & exam every 3 months
- 2nd year: Pap & exam every 4 months
- 3rd-5th year: pap & exam every 6 months
- >5 years: Pap and exam annually
- CXR annually

X. Prevention

- The implementation of routine Pap smears has decreased the incidence and mortality of cervical cancer by 70% over the last half-century
- HPV vaccines
  - *Cervarix* (targets HPV types 16 and 18)
  - *Gardasil* (targets HPV types 16, 18, 6, 11)
    - Gardasil efficacy of preventing CIN2 or worse ≥97% if HPV naïve (44% when combining those with/without HPV)
    - FDA approved 2006
    - Target population: 11-12 year old girls (can be given as early as 9 years of age); 'catch up' vaccination recommended for females 13-26 years of age
    - Administration: 3 doses given at 0, 2, & 6 months

XI. Radical trachelectomy criteria *(References: Roy and Plante. Am J Obstet Gynecol 1998;179:1491-6. & D'Argent et al. Cancer 2000;88:1877-82.)*

- Desire to preserve fertility
- No evidence of impaired fertility
- Stage IA2 or IB
- Lesion size < 2cm
- Absence of adenocarcinoma
- Absence of capillary space involvement
- Limited endocervical involvement on colposcopic examination
- No evidence of pelvic lymph node metastasis

More recently some have proposed a list of 3 essential criteria *(Ref: Burnett A. Curr Opin Obstet Gynecol 18:8-13)*:

- Can the cancer be safely and completely removed?
- Does the woman wish to retain her uterus?
- Is she informed of the risks, benefits, and alternatives to this procedure?

The Role of Radiation Therapy in Treatment of Early Stage Cervical Cancer

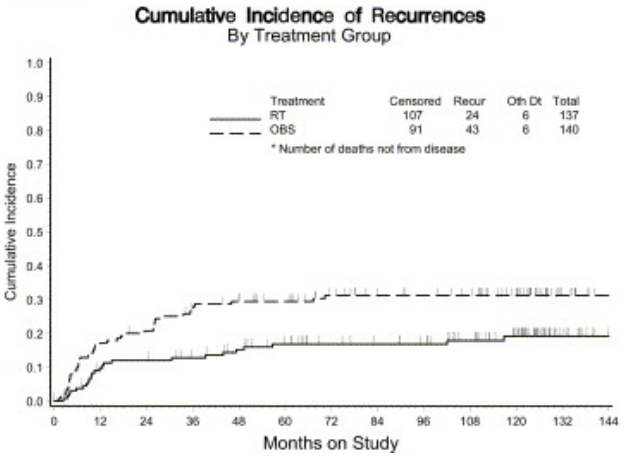
Randomized study of radical surgery verses radiotherapy for stage IB-IIA cervical cancer. *(Landoni et al.The Lancet, Vol 350, Issue 9077, August 1997, p. 535.)*

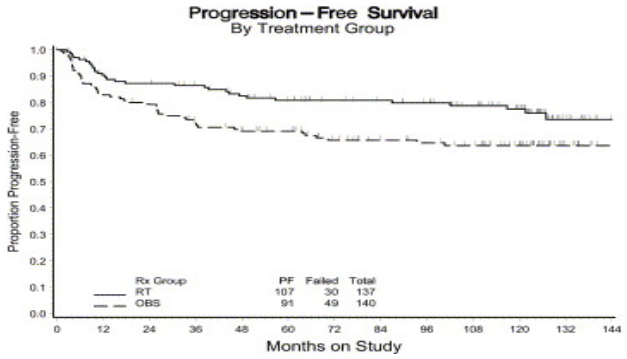
- Study dates: 1986-1991
- 343 women with stage Ib and IIa cervical cancer
- Mean follow up of 87 months
- 5 year overall survival and DFS were identical (83% and 74%)

  Conclusion: "There is no treatment of choice for early-stage cervical carcinoma in terms of overall or disease free survival. The combination of surgery and radiotherapy has the worst morbidity, especially urological complications."

GOG 92: *A Phase III Randomized Trial of Post-operative Pelvic Irradiation in Stage IB Cervical Carcinoma with Poor Prognostic Features: A GOG Study*

- Rotman et al. *Int J Radiation Oncology Biol Phys*, Vol 65, No. 1, pp. 169-176 (2006)
- Sedlis et al. Gynecol Oncol 1999;73:177-183
- 277 pts with Stage IB cervical cancer (218 squamous, 27 adeno, 32 adenosquamous) with negative LN's but with 2 or more of following features:
  - >1/3rd stromal invasion
  - Capillary lymphatic space involvement
  - Tumor diameter of >4cm
- Pelvic RT=46 Gy (23 fx) to 50.4 Gy (28 fx) VS. observation





Recurrence by cell type and treatment regimen:

	RT	**Observation**
Adenocarcinoma	0% (0/16)	36% (4/11)
Adenosquamous	17% (3/18)	50% (7/14)
Squamous	20%(21/103)	28%(32/115)

…newer trials looking at the role of RT alone in cervical cancer are limited…

See April 1999 NEJM…

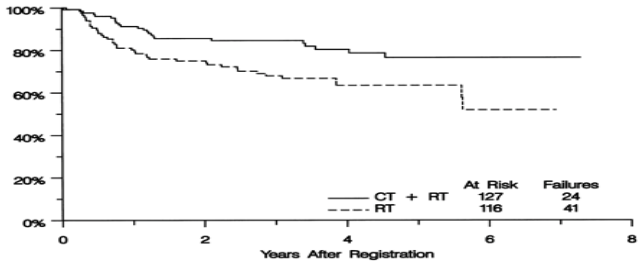
Study	**FIGO stage**	**Control group**	**Comparison group**	**RR of death in comparison group**
Keys et al. p.1154-61	IB2	RT	RT + weekly cisplatin	0.54
Rose et al. p.1144-53	IIB-IVA	RT + hydroxyl urea	⇒RT + weekly cisplatin ⇒RT+ cisplatin,5FU, hydroxyurea	0.61 0.58
Morris et al. p. 1137	IB2-IVA	Extended-field RT	RT plus cisp and 5FU	0.52

GOG 109/SWOG8797/RTOG91-12: *Concurrent chemotherapy and pelvic irradiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early stage cancer of the cervix*

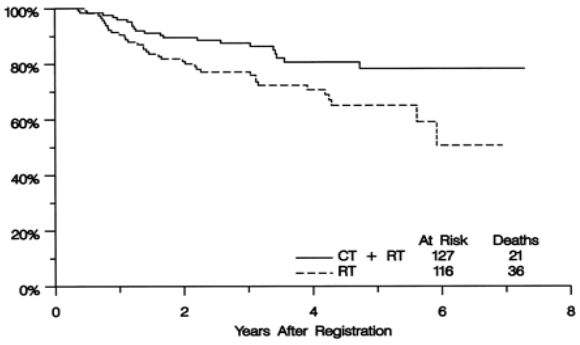
- Peters et al. J Clin Oncol 2000;18(8):1606-13.
- Stage IA2, IB, IIA initially treated with rad hyst + pelvic LND
- 243 patients: Path: squamous=193 pts; adeno=31
- Enrolled those with + pelvic LN's and/or microscopic involvement of the parametrium and/or + surgical margins
- Randomized to either:
  - Pelvic RT alone (49 Gy in 29 fx)

    OR
  - Pelvic RT in combo with cisplatin 70 mg/m^2 and a 96-hr infusion of fluororacil 1000 mg/m^2 every 3 wks x 4 cycles
- RT + CT improved the PFS and OS (statis significant)

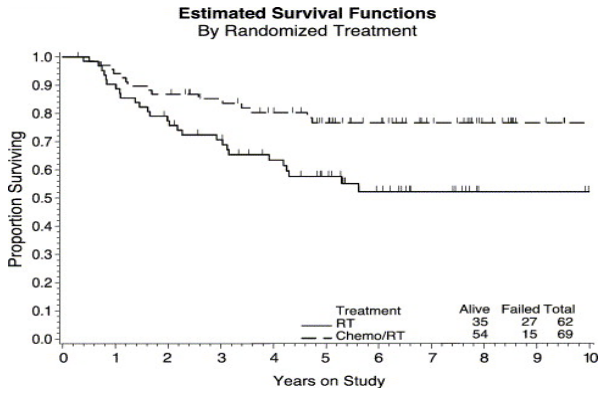
PROGRESSION FREE SURVIVAL



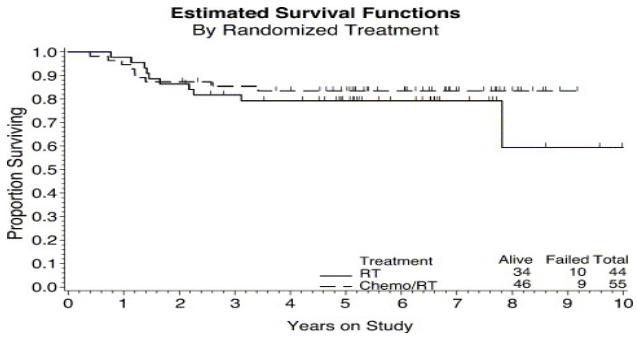
OVERALL SURVIAL



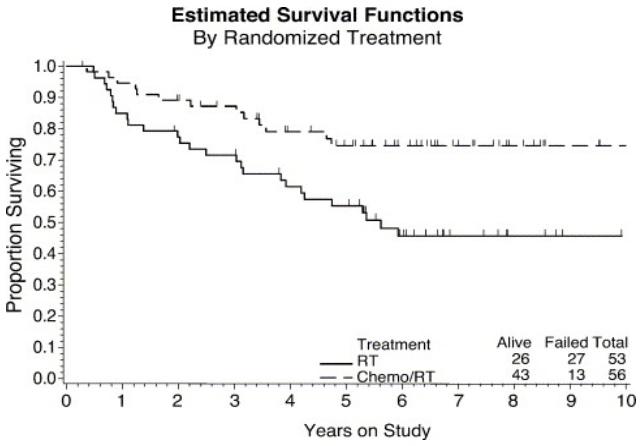
Conclusion: "Regardless of the mechanism of action, we conclude that the addition of CT to RT significantly improves progression-free and overall survival for high-risk early-stage patients who undergo a radical hysterectomy and pelvic lymphadenectomy for carcinoma of the cervix."



Rethinking the use of radiation and chemotherapy after radical hysterectomy: a clinic-pathologic analysis of a GOG/SWOG/RTOG trial. Monk et al.Gynecol Oncol 96(2005): 721-728.



Survival of women with 1 nodal metas



Survival of women with tumors >2cm *(no difference btw RT and RT/CT for tumors >2cm)*

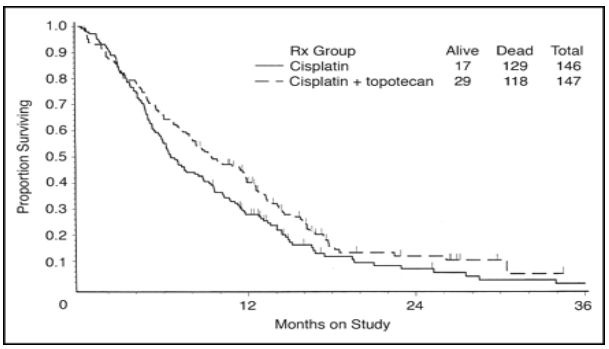
What is the current standard of care for advanced stage (IVB), recurrent or persistent cervical cancer?

GOG 179: "Randomized Phase III Trial of Cisplatin With or Without Topotecan in Carcinoma of the Uterine Cervix: A GOG Study" **(**Long *et al*. JCO Vol 23 (no. 21): 4626-4633)

Why? • Cisplatin 50mg/m2 every 3 wks as standard of care (GOG 43) • What can be added to Cisplatin to improve outcomes?...Topotecan (*Gyn Onc* 85:89-94(2002))
Who? • Advanced stage (IVB), recurrent, or persistent cervical cancer • 364 women entered • 57% received prior chemoradiotherapy
What? • Cisplatin 50mg/m2 IV Q 21 days VS. topotecan 0.75mg/m2 IV D#1, 2, 3 with Cisplatin 50mg/m2 on Day 1 repeated every 21 days VS. MVAC (MVAC arm d/c'd) [x 6 cycles or dz progression]
When? o Btw June 1999 and Sept 2002 o Neutropenia (G3, 4): 70% with C+T vs. 1.4% with Cisplatin o Thrombocytopenia (G3, 4): 31% with C+T vs. 3.4% with Cisplatin o PFS: 2.9 months for Cisp….vs….4.6 months for C+T (adding topotecan days 1-3 gets you 1.7 months at the expense of increased toxicity, e.g. febrile neutropenia, thrombocytopenia, etc) o Median survival: Cisp+Topotecan = **9.4** months VS. **6.5** months for Cisplatin alone

Although only 3 months, this is the 1st randomized clinical trial to demonstrate a significant survival advantage for combination chemo in cervical cancer.

- Survival of recurrent pts by interval from dx to recurrence



The addition of topotecan has a separation of 2 months that is sustained until 18 months

VULVAR CANCER

I. Incidence (Source: Barakat, 6th Ed.)
- 4,490 new cases in United States annually as of 2012
- accounted for 950 deaths in 2012
- 4th most common gyn malignancy

II. Risk Factors *(Int J Cancer. 2008; 122(12): 2822-34*)
- older age (mean age: 65)
- cigarette smoking
- vulvar dystrophy
- vulvar and cervical intraepithelial neoplasia
- HPV
- Immunodeficiency
- History of cervical cancer

III. Pathogenesis
- chronic inflammation (older women)
- HPV infection (younger women)

IV. Presentation
- Symptoms: pruritis, dysuria, vulvar bleeding

- Exam: warty lesion, plaque, ulcer, abnormal vasculature on colposcopy

V. Diagnosis

- **Biopsy**!!!

VI. Histologic Subtypes

- Squamous (90%)
- Melanoma (5-10%)
- Basal Cell (2%)
- Sarcoma (rare)
- Paget Disease
  - look for synchronous primary malignancy (Ref. Gynecol Oncol 1990;38(1):81-9)
- Bartholin gland adenocarcinoma

VII. Staging

VULVAR CANCER: FIGO STAGING 2009	
Stage I	Tumor confined to the vulva
IA	Lesions ≤ 2cm in size; confined to the vulva or perineum and with stromal invasion ≤ 1mm*, no nodal metastsis
IB	Lesion > 2cm in size or with stromal invasion > 1mm*, confined to the vulva or perineum, with negative nodes
Stage II	Tumor of any size with extension to adjacent perineal structures (lower 1/3 of urethra, lower 1/3 of vagina, anus) with negative nodes
Stage III	Tumor of any size with or without extension to adjacent perineal structures with positive inguino-femoral lymph nodes
IIIA	i. with 1 lymph node metas (≥5mm), or ii. 1-2 lymph node metas (<5mm)
IIIB	i. with 2 or more lymph node metastasis (≥5mm), or ii. 3 or more lymph node metastases

	(>5mm)
IIIC	With positive nodes with extracapsular spread
Stage IV	Tumor invades other regional (upper 2/3 of urethra, upper 2/3 of vagina) or distant structures
IVA	Tumor invades any of the following: i upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or ii. fixed or ulcerated inguino-femoral lymph nodes
IVB	Any distant metastasis including pelvic lymph nodes

* the depth of invasion is defined as the measurement of the tumor from the epithelial-stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion

VIII. Patterns of Spread

- local growth and extension
- emobilization to regional lymph nodes
- hematogenous spread to distant sites

IX. Treatment

- Microinvasive tumors (<1mm invasion)
  - minimal risk for LN metastasis and can therefore treat with wide local excision with 1cm margin (Ref: *Gynecol Oncol 1994;53(1):55-8*)
- Stage IB
  - increased risk of inguinal LN metas. (≥8%) thus must perform radical local excision with…
    - **unilateral** inguinal LN dissection if:
      - unifocal lesion
      - lesion >1cm from midline
      - lesion not located on anterior portion of labia minora
      - no palpable lymphadenopathy
      - ipsilateral LN dissection negative for metastatic dz.
    - **bilateral** inguinal LN dissection if:
      - stage II disease

- centrally located lesion
- ipsilateral LN dissection + for malignant dz.

- Stage II
  - primary surgical resection (with negative margins) plus bilateral inguinofemoral LND
  - ? adjuvant RT for high risk features?
- Stage III / IV
  - surgical excision with bilateral inguinofemoral LND with adjuvant radiation therapy for ≥2 positive LNs
  - may use chemoradiation for inoperable patients

X. Prognosis

Stage	1 yr survival	5 yr survival
I	96%	79%
II	88%	59%
III	75%	43%
IV	35%	13%

*(Ref: *Int J Gyn Ob 2006;95:57*)

PRE-INVASIVE LESIONS

Endometrial Hyperplasia

I. Definition
- The proliferation of endometrial glands resulting in a greater gland-to-stroma ratio than seen in the normal endometrium
  - Glands vary in size and shape
  - Glands may develop cytologic atypia

II. Classification (World Health Organization)
- Glandular/Stromal architectural pattern
  - Simple
  - Complex
- Nuclear Atypia
  - Presence
  - Absence

III. Etiology
- Estrogen (unopposed by progesterone)

- Chronic anovulation
- Obesity
  - Peripheral conversion of androstenedione to estrone
  - Aromatization of androgens to estradiol
  - Low circulating levels of SHBG
- Sex cord-stromal tumor of ovary
- Exogenous estrogens (HRT)

IV. Presentation

- Abnormal uterine bleeding is most common clinical symptom

V. Evaluation for Endometrial Hyperplasia if:

- >40 yrs old with AUB
- <40 with abnormal uterine bleeding and risk factors
- Failure to respond to medical therapy for AUB
- Exogenous unopposed estrogen with in situ uterus
- Atypical glandular cells on cervical cytology
- Endometrial cells on cervical cytology in woman >40 yrs old
- Hereditary nonpolyposis colorectal cancer (HNPCC)

VI. Diagnosis/Evaluation

- Endometrial sampling (Endometrial bx vs. D&C)

VII. Risk of Endometrial Cancer[1]

	Risk of Progression to Endometrial Cancer
Simple hyperplasia withOUT atypia	1 %
Simple hyperplasia WITH atypia	3 %
Complex hyperplasia withOUT atypia	8 %
Complex hyperplasia WITH atypia	29 %

VIII. Treatment

- Tx decisions based on:
  - Risk of progression to / presence of coexistent malignancy
  - Menopausal status
  - Desire for uterine preservation
- Endometrial hyperplasia **WITHOUT** atypia

- Risk of progression to cancer low
- Goal: control abnormal uterine bleeding
- Treatment: Progestin therapy
  - Medroxyprogesterone acetate 5-10 mg
  - Norethindrone acetate 5-15 mg
  - Levonorgestrel IUD (*Mirena*)

- Endometrial hyperplasia **WITH** atypia
  - Should be considered a potential harbinger of malignancy
  - Goal: to prevent &/or diagnose and treat endometrial cancer
  - Treatment: hysterectomy +/- staging
- Endometrial hyperplasia **WITH** atypia (desires childbearing potential)
  - Significant risk of progression to / coexistence of endometrial cancer
  - Goal: preserve fertility while minimizing risk of endometrial cancer
  - Treatment:
    - D & C
    - Progestin therapy:
    - Megestrol acetate 40 mg PO BID
    - Levonorgestrel IUD (*Mirena*)

IX. What is the risk of "Concurrent Endometrial Carcinoma in Women with a Biopsy Diagnosis of Atypical Endometrial Hyperplasia"[2]

- 289 women with community dx of AEH
  - 108 with D & C
  - 181 with endometrial biopsy
  - Hysterectomy within 12 wks of diagnosis
  - Review of AEH bx specimen by 3 gynecologic pathologists
- Concurrent Endometrial Cancer in Hysterectomy Specimen
  - 123 of 289 specimens (42%); (including 11% deeply myo-invasive tumors)

X. Conclusions

- Endometrial hyperplasia represents a continuum of histologic abnormalities resulting from persistent stimulation of the endometrium with estrogen
- The presence of atypia is a marker for progression to, or coexistence of endometrial carcinoma

- Treatment should be based on the risk of endometrial cancer and the patient's desire for uterine preservation

CRITICAL CARE MEDICINE

"You don't have to be that smart to be an intensivist. Most of the time it's either sepsis, a PE or an MI."

- Larry Cohen, RPCI intensivist

Sepsis and Systemic Inflammatory Response Syndrome (SIRS)

(ref. Hoskins and "The Intensive Care Unit Manual" ed by P. Lanken; ICU, Marino)

- Goal of inflammation is to enhance the movement of nutrients and phagocytic cells to the injury site; beneficial as a local response but harmful if an exaggerated, systemic response, i.e. SIRS
- Sepsis accounts for 1/4th of all ICU admits
- Four phases:
  - Induction
  - Triggering of cytokine synthesis
  - Evolution of cytokine cascade
  - Elaboration of secondary mediators leading to cellular injury
- Most important mediators in SIRS: tumor necrosis factor-α (TNF-α), interleukin-1(IL-1), interleukin-6 (IL-6)

Definitions of SIRS and Sepsis	
SIRS	Two or more of the following in the setting of a known cause of inflammation: T>38 degrees C or <36 degrees C Pulse >90 Respirations >20 or PaCO2<32mmHg WBC count >12,000 or <4,000 or >10%bands
Sepsis	SIRS due to known infection
Severe Sepsis	Sepsis with evidence of organ dysfunction, hypoperfusion, or hypotension
Septic shock	Sepsis with hypotension despite adequate fluid resuscitation

- Severe sepsis has mortality of 28-50%

- Septic shock has 2 phases:
  - Hyperdynamic state (*early*) aka "warm shock"
    - Low systemic vascular resistance (via TNFα ⇒inducible nitric oxide synthase in vascular endothelium⇒nitric oxide⇒loss of vascular tone)
    - Splanchnic vasoconstriction
    - Increased cardiac output
    - This phase best managed in the ICU with:
      - aggressive volume resuscitation
        - ♦ Must balance maintenance of adequate preload with risk of cardiogenic and non-cardiogenic pulmonary edema
        - ♦ IVFs to maintain PAWP at 10-12 mmHg
      - broad-spectrum antibiotics,
      - ABG, labs, cultures, oxygenation,
      - pressors or inotropes
        - ♦ **Phenylephrine**
          - ❖ Only vasoconstrictor withOUT direct cardiac effects
          - ❖ Vasoconstrictive effects can actually decrease C.O. secondary to increased afterload
          - ❖ Epinepherine: β_1 stimulation of heart and β_2 of periph vasculature
          - ❖ Norepinephrine: <u>no</u> β_2 stimulation so more potent vasoconstrictor
        - ♦ **Dopamine**
          - ❖ Cardiac $\beta_1$and peripheral α
          - ❖ Low dose (<5μg/kg/min)⇒regional vasodilation
          - ❖ Mod dose (5-10 μg/kg/min)⇒stimulate β_1 receptors⇒increased C.O.
          - ❖ High dose (>10 μg/kg/min)⇒ stimulate $\beta_1$and α1 in vasculatur⇒increased C.O. and vasoconstriction
        - ♦ **Dobutamine**
          - ❖ Activates both β_1 in heart and β_2 in periph vasculature⇒inotropic effect and systemic vasodilation (so must watch use in volume underresuscitated pt b/c of risk for hypotension)
  - Hypodynamic state (*late*) aka "cold shock"
    - Hypotension resulting from cardiac output deterioration
    - Pt is cool, mottled, oliguric, diaphoretic and confused

- Etiology of this phase: inadequate volume resuscitation, cardiac dz, myocardial dysfunction
- A state of gross decompensation

Myocardial Infarction (MI)

- Diagnosis
  - Requires two of following:
    - Chest pain, dyspnea, nausea, emesis, fatigue, diaphoresis
    - May occur without pain in post-op patient
    - Physical exam: hemodynamic instability, pulmonary congestion, and systolic murmurs, elevated JVD if right heart failure
- EKG – Look at every EKG (learn to recognized pattern)
  - Convex ST segment elevation with either peaked upright or inverted T waves
  - New Q waves
  - Changes may mimic those seen in PE, COPD, cardiomyopathy
- Cardiac Enzymes
  - Troponins
    - more specific and sensitive than CK-MB
    - increase 3-12 hrs after MI, peak at 24-48 hrs, return to baseline over 5-14 days
- Creatine Kinase (CK)
  - CK-MB levels increase within 3-12 hrs, peak in 24 hours
- Acute Management*
  - Continuous cardiac monitoring
  - Oxygen
  - IV access
  - Relief of ischemic pain
  - Assess hemodynamic status and correct abnormalities
  - Initiation of reperfusion (percutaneous coronary intervention or fibrinolysis)
  - Antithrombotic therapy
  - Beta-blockade

*Ref. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction. Circulation 2004; 110 (9):e82

Venous Thromboembolism (VTE)*

- Venous thromboembolism (VTE) includes both deep venous thrombosis (DVT) and pulmonary embolism (PE).
- VTE is the most common cause of death at 30-day follow-up for cancer patients undergoing surgery.
- Cancer increases the risk of VTE by 4- to 7-fold.
- The occurrence of VTE increases the risk of death for cancer patients by 2- to 8-fold.
- **The NCCN recommends that all adult, hospitalized patients with cancer receive anticoagulation therapy in the absence of contraindications.**
- Risk Factors:
  - age
  - prior VTE
  - familial &/or acquired thrombophilia
  - cancer
  - trauma
  - surgery
  - prolonged immobility
  - central venous catheter
  - CHF
  - Pregnancy
  - Bulky lymphadenopathy with extrinsic vascular disorders
  - Smoking
  - Obesity
  - Chemotherapy
  - Estrogen compounds (e.g. HRT, OCPs, tamoxifen)
  - EPO
  - Growth factors
- Prophylaxis
  - Who? Cancer diagnosis, Inpatient
  - Initial work-up: H&P, CBC, PT, aPTT, serum creatinine
  - Prohylactic anticoagulation (if no contraindications)
    - +/- SCDs
    - Enoxaparin 40 mg SC QD (30mg SC BID if BSA >2)

- May also use: Unfractionated heparin (5,000 units SC q 8 hours)

Deep Vein Thrombosis (DVT)

- Symptoms
  - swelling of unilateral extremity
  - heaviness or pain in extremity
  - swelling in supraclavicular space
  - catheter dysfunction
- Diagnosis/Work-up
  - history and physical
  - CBC
  - PT, aPTT
  - Serum creatinine
  - Venous ultrasound
- Treatment
  - Enoxaparin 1 mg/kg SC every 12 hours or 1.5 mg/kg SC QD
  - Anticoagulation to continue for minimum of 3-6 months

Pulmonary Embolism

- Signs/Symptoms
  - Current DVT or recent DVT
  - Unexplained shortness of breath, chest pain, tachycardia, apprehension, tachypnea
  - Syncope
  - Oxygen desaturation
- Work-up
  - H&P
  - CBC, PT, aPTT, serum creatinine, CXR, EKG
- Diagnosis
  - CT angiography
  - VQ scan (if patient has renal insufficiency or uncorrectable allergy to contrast)
- Treatment
  - if contraindication to anticoagualation → mechanical IVC device

- if no contraindication to anticoagulation → check Troponin and for evidence of right ventricular enlargement (CT or ECHO)
  - if normal troponin and no RV compromise then anticoagulate (Refer to 'DVT Treatment' above);
    - anticoagulation to continue for minimum of 6-12 months
  - if suggestion of massive PE &/or right heart compromise then consider thrombolytic therapy, IVC filter, embolectomy

- Anticoagulation Contraindications
  - CNS bleed
  - Intracranial or spinal lesion at risk for bleeding
  - Active bleeding
  - Platelets <50K
  - Platelet dysfunction
  - Recent major operation at high risk for bleeding
  - Coagulopathy
  - Spinal anesthesia
  - Lumbar puncture
  - High risk for falls
- Consider placement of mechanical IVC device if:
  - contraindication to anticoagulation
  - Failure of anticoagulation
  - Non-compliance with prescribed anticoagulation
  - Baseline cardiac or pulmonary dysfunction severe enough to make any new or recurrent PE life threatening
  - Patient with documented multiple PE and chronic pulmonary hypertension

Notes:
- D-dimer is not recommended for the diagnosis of DVT in cancer patients because of its low specificity in that particular population
- VTE prophylaxis is not recommended for patients with central venous catheters

*Recommendations adapted from NCCN Practice Guidelines in Oncology-v.2.2008 "Venous Thromboembolic Disease"

Acute Tubular Necrosis

Acute tubular necrosis (ATN) describes a situation in which blood flow is sufficient to maintain tubular integrity but not to sustain glomerular filtration.

RIFLE Criteria for Acute Kidney Injury

Risk	Increased Cr x 1.5 or GFR decrease >25%	UOP<0.5ml/kg/hr x 6 hrs
Injury	Increased Cr x 2 or GFR decrease >50%	UOP<0.5ml/kg/hr x 12 hrs
Failure	Increased Cr x 3 or GFR decrease >75% or Cr ≥4mg/dl	UOP<0.3ml/kg/hr x 24 hrs or Anuria x 12 hrs
Loss	Persistent ARF=complete loss of renal function >4 wks	
ESRD	End Stage Renal Disease	

Ref. Kellum JA. Crit Care Med 2008 Vol. 36, No. 4 (Suppl)

Common Infections and their Treatment

Infection	Treatment	Note
Community Acquired Pneumonia (CAP)	Levofloxacin 500mg QD x 7-14 d Or Levofloxacin 750 mg QD x 5 d	listed are initial treatment choices; treatment should ultimately be based on culture sensitivity and response to therapy
Nosocomial pneumonia	Zosyn 4.5 gm IV q 6 hrs	
Febrile neutropenia	Zosyn 4.5 gm IV q 6 hrs	
C. Diff	Metronidazole 500 mg PO TID x 10-14 days	
UTI* Uncomplicated Complicated	Levaquin 500mg PO/IV q 24 hrs Cipro 250 mg PO BID x 3 days Cipro 100 mg/day x 7-14 days	

***** use Levaquin as in-patient and Ciprofloxacin as out-patient

Clostridium difficile infection

- **Background**
  - Clostridium difficile can cause colitis after the normal gut flora has been altered by antibiotics.
- **Incidence**
  - most frequent cause of nosocomial diarrhea

- **Risk Factors**:
  - The antibiotics most commonly associated with C. diff colitis include: clindamycin, fluoroquinolones, penicillins, and cephalosporins.
- **Signs/Symptoms**
  - Watery diarrhea
  - Lower abdominal/pelvic pain and cramping
  - Low grade fever
  - Leukocytosis
  - Sigmoidoscopy findings: pseudomembranes (scattered, raised plaques on colonic mucosa)
- **Diagnosis**
  - Stool C. diff toxin assay
- **Treatment**
  - Stop causative antibiotic
  - Contact precautions
  - Supportive care (fluid replacement, correct electrolyte imbalances)
  - Oral metronidazole (500 mg TID or 250 mg QID)

Remember! Alcohol hand wash does NOT kill C. diff spores. Must wash hands with soap and water.

Neutropenic Fever

- Fever: single oral temperature ≥ 38^{o} C (101.4^{o} F)
- Neutropenia: neutrophil count < $500/mm^3$
- Initial Evaluation
  - Blood culture from 2 different sites
  - Urine culture
  - CBC with diff
  - CMP
  - CXR
- Initial Treatment
  - Piperacillin/Tazobactam 4.5 gm IV Q 6 hours

- If PCN allergic: Ceftazidime 2 gm IV Q 8 hours
- If PCN and Cephalosporin allergic:
  - Aztreonam 2gm IV Q 8 hours + Vancomycin 1 gm Q 12 hours (Add Metronidazole 500 mg IV Q 8 hrs if anaerobic infxn suspected)

- Add vancomycin to empiric therapy if
  - Catheter-assc soft tissue infxn
  - Hypotension or cardiovascular compromise
  - Gram + blood culture
  - MRSA colonization
- Notes
  - At least 3 days of antibiotic treatment required to determine efficacy of regimen
  - 2-7 days (median=5) for defervescence in febrile neutropenic cancer patient

COMMONLY USED CHEMOTHERAPEUTIC AGENTS IN GYNECOLOGIC ONCOLOGY

BEVACIZUMAB

Tumor growth is dependent on angiogenesis. Vascular endothelial growth factor (VEGF) is a potent mitogen for vascular endothelial cells. Bevacizumab (Avastin) is a humanized monoclonal antibody directed against VEGF. It binds to vascular endothelial growth factor (VEGF) and inhibits the interaction of VEGF to Flt1 and KDR receptors on the surface of endothelial cells. In the process, it prevents the proliferation of endothelial cells and formation of new blood vessels.

In phase II trials, single agent bevacizumab has been shown to be active in the setting of persistent, recurrent, and platinum-resistant ovarian cancer. Monk *et al*. observed a 16% response rate with single-agent bevacizumabin in patients with advanced refractory epithelial ovarian cancer. Cohn and colleagues reported an improvement in cancer-related symptoms in patients with refractory epithelial ovarian cancer treated with biweekly bevacizumab and weekly taxane chemotherapy. Gynecologic Oncology Group Study 218 sought to evaluate whether the addition of bevacizumab to standard chemotherapy concurrently and as consolidation therapy improves overall survival in patients with Stage III or IV epithelial ovarian or primary peritoneal cancer.

Dosing: 15mg/kg q 3 weeks

Adverse Effects: GI perforation, impaired wound healing, hypertension, proteinuria, minor bleeding (e.g. epistaxis), thromboembolic events, fatigue, headache

Recommended reading regarding Bevacizumab in ovarian cancer

1. Perren TJ, A Phase III trial of bevacizumab in epithelial ovarian cancer. NEJM 2011;2484-96. (GOG **218)**

2. Han ES, Monk BJ. What is the risk of bowel perforation associated with bevacizumab therapy in ovarian cancer? Gyn Oncol 2007;105:3-6

3. Burger RA, Sill MW, Monk BJ, Greer BE, Sorosky JI. Phase II trial of bevacizumab in persistent or recurrent epithelial ovarian cancer or primary peritoneal cancer: A gynecologic oncology group study. J Clin Oncol 2007;25(33):5165-71.

4. Cannistra SA, Matulonis UA, Penson RT, Hambleton J, Dupont J, Mackey H, Douglas J, Burger RA, Armstrong D, Wenham R, McGuire W. Phase II study of bevacizumab in patients with platinum-resistant ovarian cancer or peritoneal serous cancer. J Clin Oncol 2007;25(33):5180-86.

5. Monk BJ, Han E, Josephs-Cowan CA, Pugmire G, Burger RA. Salvage bevacizumab (rhuMAB VEGF)-based therapy after multiple prior cytotoxic regimens in advanced refractory epithelial ovarian cancer. Gyn Oncol 2006;102:140-44.

6. Cohn DE, Valmadre S, Resnick KE, Eaton LA, Copeland LJ, Fowler JM. Bevacizumab and weekly taxane chemotherapy demonstrates activity in refractory ovarian cancer. Gyn Oncol 2006;102:134-39.

CARBOPLATIN

- Carboplatin is an alkylating-like agent.
- Exact mechanism of action is unknown, action is thought to be similar to that of the bifunctional alkylating agents, that is, possible cross-linking and interference with the function of DNA .
- It is cell cycle–phase nonspecific.

Adverse Effects: Nausea, vomiting, and diarrhea are common. Myelosuppression (dose-limiting toxicity), nephrotoxicity, ototoxicity, peripheral neuropathy and CNS toxicity

CISPLATIN

Cisplatin is an alkylating-like agent.

- Exact mechanism of action is unknown, action is thought to be similar to that of the bifunctional alkylating agents, that is, possible cross-linking and interference with the function of DNA and a small effect on RNA.
- It is cell cycle phase–nonspecific. Stimulation of the host immune system is also possible.

Adverse Effects: myelosuppression, nephrotoxicity, ototoxicity, neuropathy, nausea/vomiting

CYCLOPHOSPHAMIDE

Cyclophosphamide (*Cytoxan*) is an alkylating agent of the nitrogen mustard type.

- An activated form of cyclophosphamide, phosphoramide mustard, alkylates or binds with intracellular molecular structures, including nucleic acids. Its cytotoxic action is primarily due to cross-linking of strands of DNA and RNA, as well as to inhibition of protein synthesis.
- Cyclophosphamide is a potent immunosuppressant.
- Marked and persistent inhibition of cholinesterase activity.

Adverse Effects: myelosuppression (neutropenia > anemia, thrombocytopenia), nausea, alopecia, hemorrhagic cystitis, secondary neoplasia

DOCETAXEL

- Docetaxel (*Taxotere*) is a semisynthetic analogue of paclitaxel currently approved for the treatment of breast cancer in patients who failed prior chemotherapy and in patients with non-small cell lung cancer.
- Docetaxel has antitumor activity against ovarian cancer.
- Prepared from a noncytotoxic precursor, 10-deacetyl baccatin III, which is extracted from the needles of the European yew tree (Taxus baccata L).
- Structurally, docetaxel is identical to paclitaxel except for replacement of the benzamide phenyl group on the C-13 side-chain of paclitaxel by an OC(CH3)3 moiety, and substitution of a hydroxy group for the acetyl group at position 10 of paclitaxel.
- These changes slightly increase the water solubility of docetaxel compared to paclitaxel.
- The cytotoxic mechanism of action of docetaxel is like that of paclitaxel. Both agents bind to microtubules, promote their assembly, and inhibit depolymerization of tubulin.

Adverse Effects: neutropenia, anemia, thrombocytopenia, alopecia, stomatitis, nausea/vomiting, neuropathy, elevated liver enzymes

DOXORUBICIN

Doxorubicin hydrochloride (*Adriamycin*) is a cytotoxic anthracycline antibiotic thought to act on malignant cells by intercalating the cell nucleotide base and binding the cell membrane lipid.

- Intercalation blocks replication of nucleotide and action of DNA and RNA polymerases.
- It also interacts with topoisomerase II to form DNA-cleavable complexes, which is believed to be an important mechanism of its cytocidal activity.

Adverse Effects: myelosuppression (dose-limiting), nausea/vomiting, alopecia, radiation recall, extravasation injury, cardiomyopathy, red urine.

DOXIL (DOXORUBICIN HCL LIPOSOME)

- Compared to conventional liposomal doxorubicin, sterically-stabilized liposomal doxorubicin (doxorubicin hydrochloride liposome) has a longer elimination half-life and reduced affinity for cells of the RES, and may provide superior antitumor efficacy and reduced toxicity.
- Encapsulation of doxorubicin in these liposomes (Stealth(R) liposomes) confers a prolonged circulation time (elimination half life, 45 to 55 hours), which is considered essential for efficacy, and a slower plasma clearance and smaller volume of distribution compared to conventional liposomal doxorubicin or free doxorubicin.

Adverse Effects: palmar-plantar erythrodysesthesia (Hand-foot syndrome), stomatitis, rash, myelosuppression, edema

ETOPOSIDE

Etoposide (*Toposar*) is a topoisomerase II inhibitor . It seems to act at the premitotic stage of cell division to inhibit DNA synthesis; it is cell cycle–dependent and phase-specific, with maximum effect on the S and G2 phases of cell division.

Adverse effects: myelosuppression, alopecia, nausea/emesis, **extravasation injury,** hypotension (with rapid infusion).

GEMCITABINE

- Gemcitabine (Gemzar) is a nucleoside analogue that exhibits antitumor activity which is cell phase-specific for the S-phase and for the G1/S-phase boundary of cell division.
- Metabolized intracellularly by nucleoside kinases to the active diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleosides.
- Cytotoxic effect of gemcitabine is due to a combination of 2 actions of the dFdCDP and dFdCTP nucleosides, which leads to inhibition of DNA synthesis.

Adverse Effects: myelosuppression, nausea, diarrhea, constipation, transient elevations of LFTs

IFOSFAMIDE

Ifosfamide (Ifex) is classified as an alkylating agent of the nitrogen mustard type. After metabolic activation, active metabolites of ifosfamide alkylate or bind with many intracellular molecular structures, including nucleic acids.

- The cytotoxic action is primarily due to cross-linking of strands of DNA and RNA, as well as inhibition of protein synthesis.

Adverse Effects: myelosuppression, nausea/vomiting, alopecia, hemorrhagic cystitis, CNS toxicity (somnolence, confusion, disorientation)

METHOTREXATE

- Methotrexate sodium (MTX) reversibly inhibits dihydrofolate reductase.
- Dihydrofolates are reduced to tetrahydrofolates by this enzyme before they are used in the synthesis of purine nucleotides and thymidylate. Via this mechanism, methotrexate sodium arrests DNA and inhibits protein synthesis.

Adverse Effects: myelosuppression (nadir 6-10 days with rapid recovery), nausea/vomiting, stomatitis, mild alopecia

Note: In patients with increased risk for methotrexate toxicity (eg, pleural effusion, ascites, gastrointestinal tract obstruction, previous cisplatin therapy, dehydration, aciduria, and renal dysfunction) it is recommended to measure serum methotrexate levels at 24, 48, or 72 hours.

OXALIPLATIN

Oxaliplatin (*Eloxatin*) undergoes nonenzymatic conversion in physiologic solutions to active derivatives via displacement of the labile oxalate ligand.

- Several transient reactive species are formed, including monoaquo and diaquo diaminocyclohexane (DACH) platinum, which covalently bind with macromolecules. Both inter- and intra-strand Pt-DNA crosslinks are formed. Crosslinks are formed between the N7positions of two adjacent guanines (GG), adjacent adenine-guanines (AG), and guanines separated by an intervening nucleotide (GNG). These crosslinks inhibit DNA replication and transcription.

Adverse Effects: anemia, thrombocytopenia, peripheral neuropathy, nausea, fatigue, diarrhea, vomiting, elevated liver enzymes

PACLITAXEL

- Paclitaxel (Taxol) is an antimicrotubule agent.
- Promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This stability results in the inhibition of the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions.
- Paclitaxel induces abnormal arrays or 'bundles' of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis.

Adverse Effects: neutropenia, thrombocytopenia, flushing, hypotension, alopecia, elevated liver enzymes, peripheral neuropathy, myalgia/arthralgia, hypersensitivity reaction

TOPOTECAN

Topotecan (Hycamtin) is an anti-neoplastic agent that inhibits topoisomerase I from causing reversible single strand breaks in deoxyribonucleic acid (DNA) by attaching to the topoisomerase I-DNA complex.

- Cytotoxic effects when it forms a ternary complex with topoisomerase I and DNA that interacts with replication enzymes, causing double stranded DNA damage during DNA synthesis.

Adverse Effects: neutropenia, anemia, thrombocytopenia fatigue, pain, alopecia, rash, nausea/vomiting, diarrhea, constipation, anorexia, stomatitis

Chemotherapy Extravasation

Definition: escape of chemotherapy agent into extravascular space (e.g. leakage from vessel or by direct infiltration)

Agents are divided into 'vesicants' or 'irritants' based on their ability to induce local toxicity

- **Irritant**: inflammatory reaction with burning, pain, phlebitis
- **Vesicant**: can cause skin necrosis as well as underlying tissues

Vesicant	**Irritant**
Cisplatin (if large volume and high concentration) Docetaxel (rare) Doxorubicin Oxaliplatin (rare) Paclitaxel (rare) Vinblastine* Vinorelbine* *No ice packs	Bleomycin Carboplatin Cisplatin Cyclophosphamide Docetaxel Etoposide* Gemcitabine Liposomal doxorubicin Oxaliplatin Paclitaxel Topotecan

MISCELLANEOUS

Intraoperative Ureteral Injury

A majority of all operative ureteral injuries occur during gynecologic surgery.
A ureteral injury is more common during an abdominal hysterectomy versus a vaginal hysterectomy (2.2% vs. .03%, respectively).
The key to avoiding ureteral injures intraoperatively is to know your anatomy. This can only be accomplished with a knowledge of the ureter's anatomical course.
→ The ureter exits the kidney at the renal hilum.
→ It travels inferiorly in the retroperitoneum, along the psoas muscle.
→ At the level of the pelvic brim, the ovarian vein crosses the ureter.
→ The ureter then crosses anterior to the common iliac, then lateral to the internal iliac vessels before turning medially until passing under the uterine artery.
→ It ultimately enters the posterior wall of the bladder.

The ureter is most often injured where it crosses under the uterine artery. The most important aspect of an intraoperative ureteral injury is recognizing it at the time of surgery. Up to 87.5% of ureteral injuries are not recognized intraoperatively. The recognition of a ureteral injury during a TAH, can be done with close visual inspection of the suspected compromised area and/or the administration of methylene blue with observation for leakage of dye. During a vaginal hysterectomy, cystoscopy can easily be performed with observation for efflux of intravenously administered dye from the ureteral orifices. If an injury is suspected it should be further inspected and corrected via an abdominal approach.

The type of repair should be dictated by the site of injury and the length of functional ureter remaining. A majority of operative ureteral injures occur distally. These are best repaired with a ureteroneocystostomy. If there is loss of more of the distal ureter a vesico-psoas hitch can be performed. Regardless of the type of repair, care must be taken to ensure adequate mobilization with preservation of the ureteric blood supply, removal of nonviable tissue, and a tension-free anastomosis over a ureteral stent.

The patient with a ureteral injury not recognized intraoperatively may present with fever, flank pain, nausea, urosepsis, hydronephoris, a ureteral fistula, or an urinoma.
Note: A thermal injury to the ureter may result in an area of devitalized tissue which extends beyond the original site of injury.
For an excellent review of ureteral injuries, their recognition and management please refer to Elliott and McAninch's article (Urol Clin N Am 33 (2006): 55-66).

Instructions for removing a central venous catheter:

- Request suture removal kit and antibiotic ointment to bedside
- Make sure patient is in supine position
- Make sure patient is adequately hydrated
- Cut sutures
- Cover the area with an antibiotic ointment (this helps create and airtight seal over defect upon catheter removal)
- Have patient valsalva with removal of catheter (or if patient can't valsalva, remove catheter while patient exhales); patient should not be talking or laughing while catheter is being removed
- Place sterile finger immediately on site of catheter removal
- Place a sterile occlusive dressing over the site for 24 hours
- Direct digital pressure should be applied to site of catheter removal for several minutes
- Patient is to remain supine for 30 minutes following catheter removal

"PIMP" QUESTIONS

What is the most painful vulvar tumor?
Adenoid cystic carcinoma of the Bartholin gland

What is the main dose limiting toxicity of pegylated liposomal doxorubicin (Doxil)?
PPE

What is the Will Rogers Effect?

Who was Armand Trousseau?

How long is the small bowel?

How much small bowel is necessary for life (to not require TPN)?

What are some common side-effects of TPN?

When does CA125 peak during pregnancy?

What is the half-life of CA125?
14 days

What are the 5 hysterectomy types?

What metabolic derangement is seen in patients with an ileal conduit? Why?
Answer: hyperchloremic metabolic acidosis (up to 80% of patients)

> 2 reasons: (1) the colon has an anion exchange pump with luminal chloride being reabsorbed as bicarbonate is secreted. Thus when chloride enters the colon (in the case of a conduit, from the urine) it will be absorbed and traded for bicarb…bicarb loss…acidosis); (2) the colon absorbs ammonium (from the urine and from the urea-splitting bacteria in the colon)…the ammonium is converted to ammonia and hydrogen ion in the liver…acidosis

What happens if you cut the obturator nerve?

How much gastric juice is produced in a day?

What are the insensible losses of post op patients?

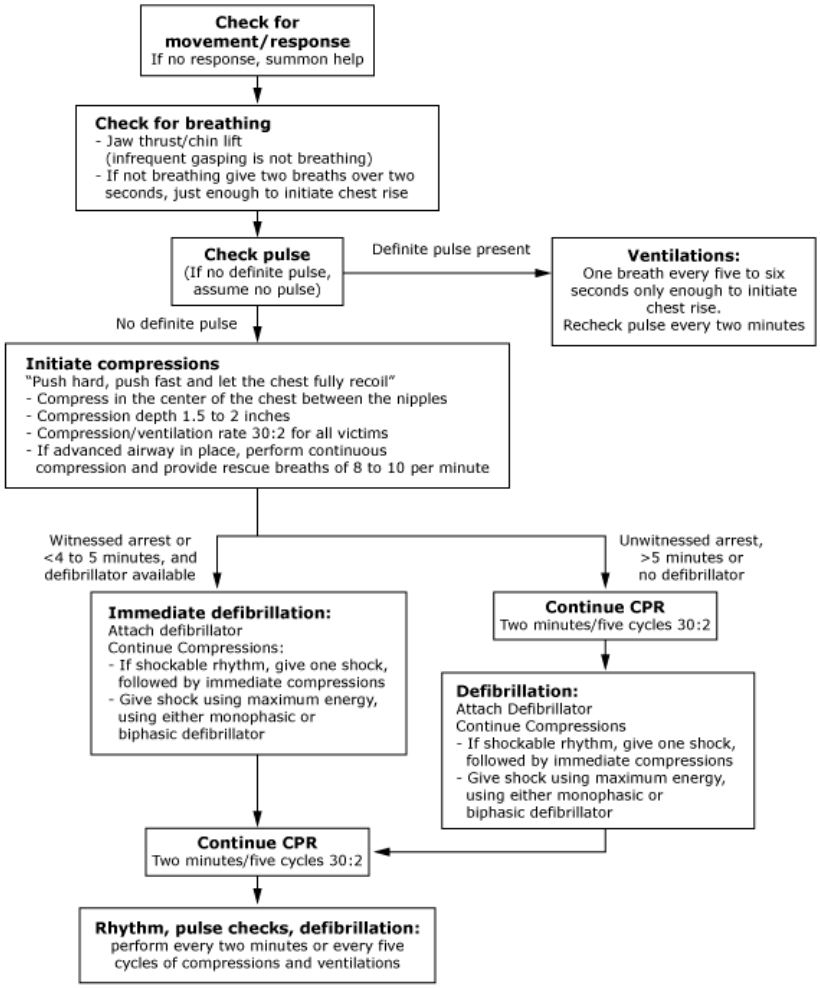
Why would you give chemo to Stage I uterine cancer?

What meds do you give to patients with Ifex toxicity?

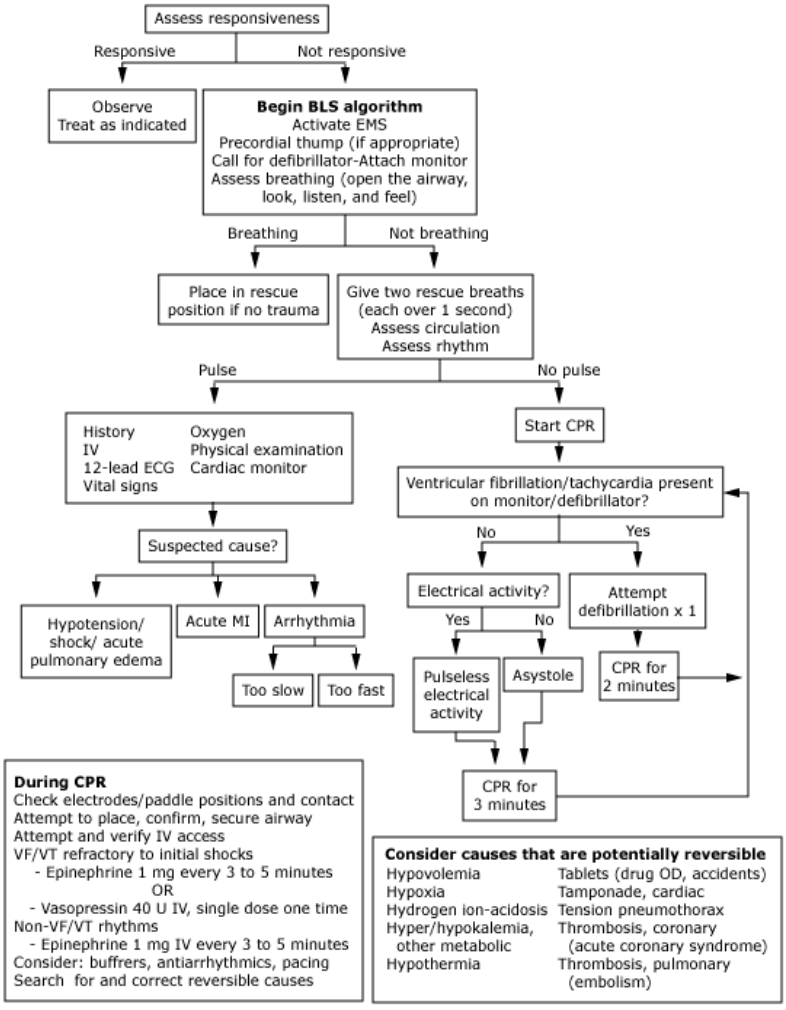
What is DLCO?

BLS Algorithm

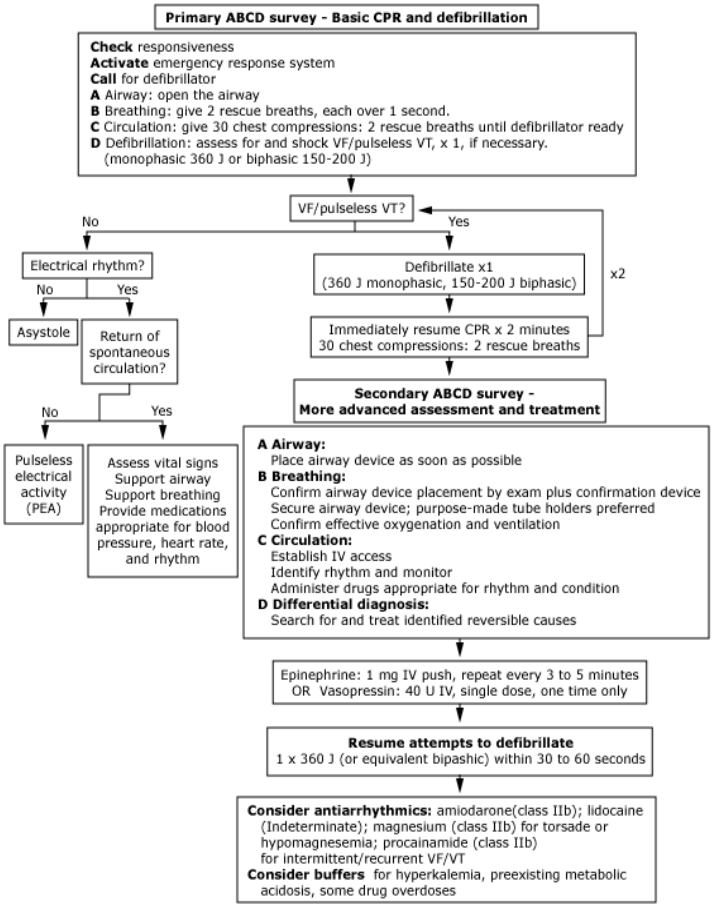
(Note: algorithms per Circulation 2005; 112:III-25.)



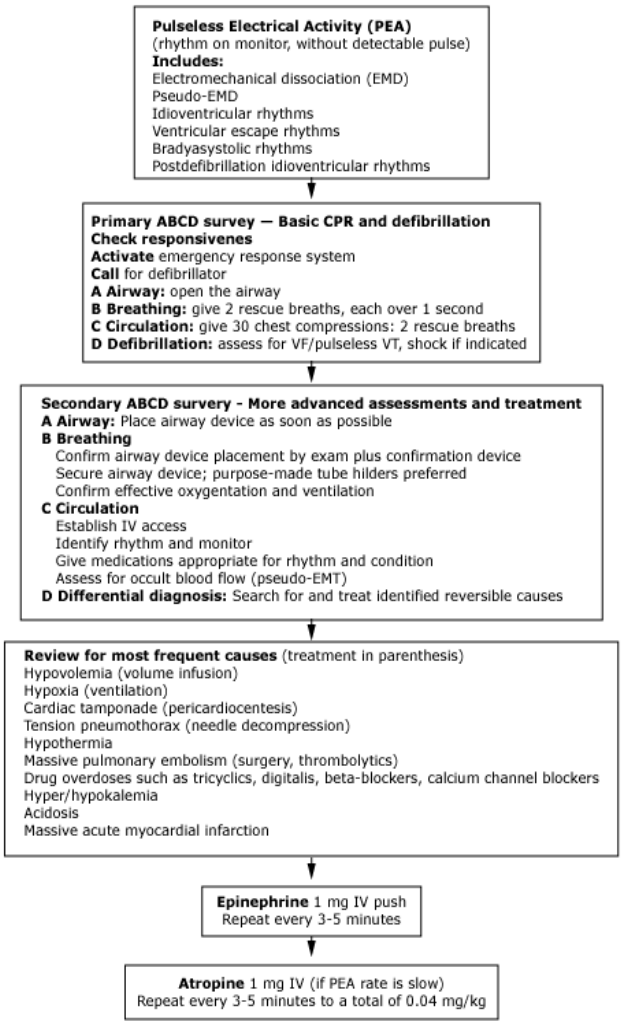
Advanced Cardiopulmonary Life Support in Adults



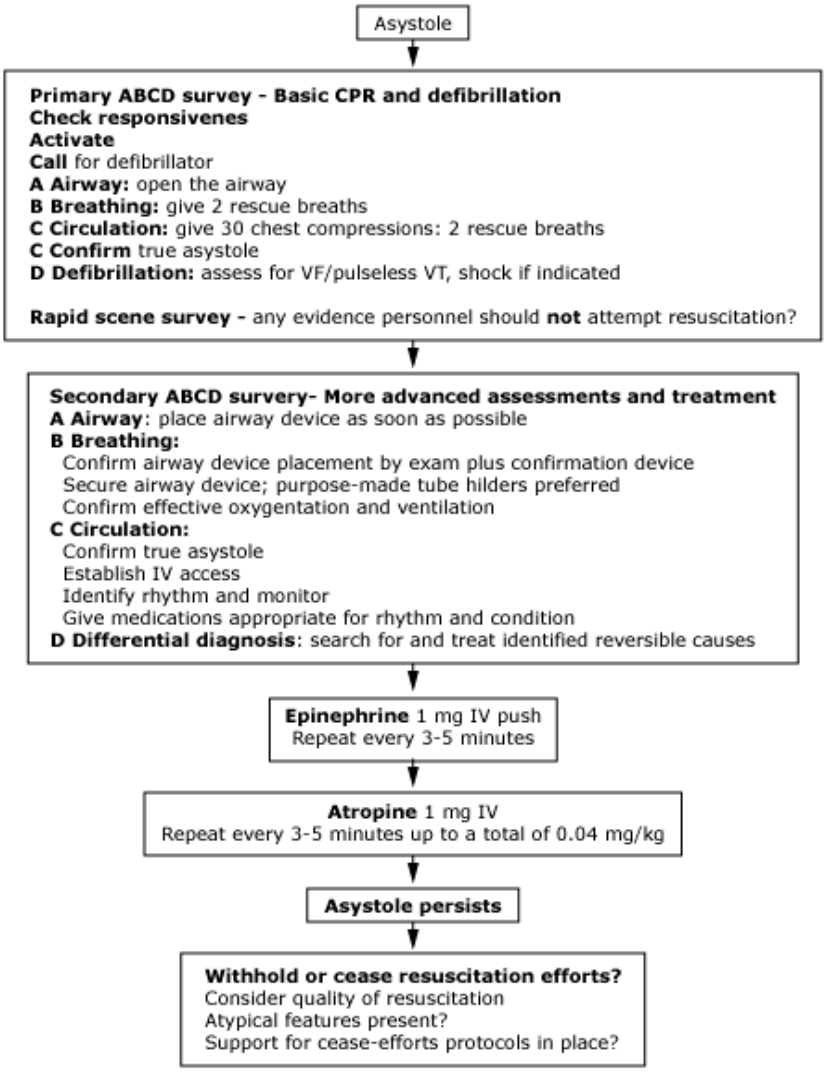
Ventricular Fibrillation/Pulseless Ventricular Tachycardia Algorithm



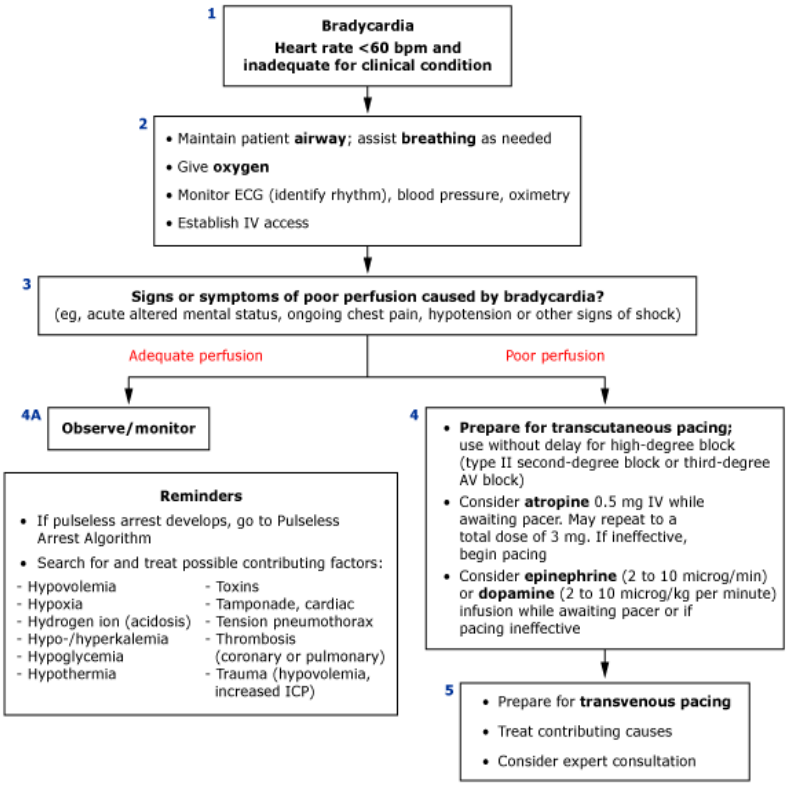
Pulseless Electrical Activity Algorithm



Asystole Treatment Algorithm



ACLS Bradycardia Algorithm



ACLS Tachycardia Algorithm