the 46th Annual

VAIL OB-GYN
CONFERENCE

Week of Presidents’ Day
February 16-21, 2020
Vail, Colorado

2020 Syllabus
Now available!
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Presented by
Obstetrics and Gynecology
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS
At the end of this activity, learners will be able to:

1. Identify benign breast disease and how that impacts screening and cancer risks.
2. Assess degrees of sexual dysfunction and appropriate therapy.
3. Discuss contraceptive measures and identify their mechanism of action.
4. Develop depression screening in OB practice.
5. Assess fetal growth restriction and identify appropriate management.

Conference Co-Directors

Ronald S. Gibbs, MD
Vail Conference Co-Director
Professor Emeritus
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

K. Joseph Hurt, MD, PhD
Vail Conference Co-Director
Assistant Professor
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Nanette F. Santoro, MD
Vail Conference Co-Director
Professor and E. Stewart Taylor Chair
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

L. Chesney Thompson, MD
Vail Conference Director
Professor and Vice Chair
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Conference Learning Objectives

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Conference Accreditation

The University of Colorado School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The University of Colorado School of Medicine designates this live activity for a maximum of 25 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
FEATURED GUEST SPEAKERS

Alison G. Cahill, MD, MSCI
Professor
Division Of Maternal-Fetal Medicine
Department Of Women’s Health
University of Texas at Austin, Dell Medical School

Christine R. Isaacs, MD
Professor and Division Head
Division of General Obstetrics and Gynecology
Department of Obstetrics and Gynecology
VCU School of Medicine

Ritu Salani, MD, MBA
Professor
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
The Ohio State University College of Medicine

WORKSHOP FACILITATOR

Helen Feltovich, MD, MS
Attending Physician
Division of Maternal-Fetal Medicine
Department of Obstetrics and Gynecology
Intermountain Healthcare
Adjunct Assistant Professor
Department of Obstetrics and Gynecology
University of Utah
Associate Scientist
Medical Physics Department
University of Wisconsin-Madison
CONFERENCE FACULTY

Leslie C. Appiah, MD
Visiting Associate Professor and Division Chief
Director, Fertility Preservation and Reproductive Late Effects Program
Division of General Obstetrics and Gynecology
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Jaime Arruda, MD
Associate Professor of Clinical Practice
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Linda Barbour, MD, MSPH
Professor
Divisions of Maternal-Fetal Medicine & Endocrinology, Metabolism and Diabetes
Departments of Obstetrics and Gynecology & Medicine
University of Colorado, School of Medicine

Kathleen Connell, MD
Associate Professor and Division Chief
Divisions of Urogynecology and Reconstructive Pelvic Surgery & Reproductive Sciences
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

John P. Curtin, MD, MBA
Visiting Professor and Director of Service for Obstetrics and Gynecology at Denver Health
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Jill K. Davies, MD
Associate Professor and Medical Director
Denver Health Diabetes in Pregnancy Clinic
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Henry Galan, MD
Professor
Division of Maternal-Fetal Medicine
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine
Co-Director, Colorado Fetal Care Center
Children's Hospital Colorado

Saketh Guntupalli, MD
Associate Professor and Division Chief
Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Terry Harper, MD
Associate Professor and Division Chief
Division of Maternal-Fetal Medicine
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Tricia Huguelet, MD
Associate Professor
Division of General Obstetrics and Gynecology
Department of Obstetrics and Gynecology
Chair, Pediatric and Adolescent Gynecology
Children’s Hospital Colorado
CONFERENCE FACULTY

K. Joseph Hurt, MD, PhD
Assistant Professor
Divisions of Maternal-Fetal Medicine & Reproductive Sciences
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Paul Montero, MD
Associate Professor
Sections of Gastrointestinal, Tumor, and Endocrine Surgery
Department of Surgery
University of Colorado, School of Medicine

Andrew M. Novick, MD, PhD
Assistant Professor
Women’s Behavioral Health Service/Epperson Research Lab
Department of Psychiatry
University of Colorado, School of Medicine

Jason Papazian, MD
Associate Professor
Department of Anesthesiology
University of Colorado, School of Medicine

Nanette F. Santoro, MD
Professor and E. Stewart Taylor Chair
Divisions of Reproductive Endocrinology and Infertility & Reproductive Sciences
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University of Colorado, School of Medicine

Joyce Sung, MD
Associate Professor
Division of Maternal-Fetal Medicine
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

Stephanie Teal, MD, MPH
Professor and Division Chief
Division of Family Planning
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine

L. Chesney Thompson, MD
Professor and Vice Chair
Division of General Obstetrics and Gynecology
Department of Obstetrics and Gynecology
University of Colorado, School of Medicine
Sunday, February 16, 2020

4:00 PM  Welcome

4:15 PM  **Fake News in Menopausal Medicine**
Nanette F. Santoro, MD
*University of Colorado, School of Medicine*

4:45 PM  Q&A

5:00 PM  **Oncofertility Best Practices: Optimizing Reproductive Outcomes in Cancer**
Leslie C. Appiah, MD
*University of Colorado, School of Medicine*

5:30 PM  Q&A

5:45 PM  **Featured Guest Speaker**
**Female Sexual Dysfunction: Facts & Fiction**
Christine R. Isaacs, MD
*VCU School of Medicine*

6:15 PM  Q&A

6:30 PM – 7:30 PM  Reception

*Please note that schedule and speakers are subject to change.*
Monday, February 17, 2020

6:45 AM  Breakfast with Professors  
Nanette Santoro, MD | Leslie Appiah, MD | Christine Isaacs, MD

7:15 AM  Featured Guest Speaker  
Female Sexual Dysfunction: Facts & Fiction, Part 2  
Christine R. Isaacs, MD  
VCU School of Medicine

7:45 AM  Q&A

7:55 AM  Travel in Pregnancy 2020:  
What to do when my pregnant patient plans to travel  
Jill K. Davies, MD  
University of Colorado, School of Medicine

8:25 AM  Q&A

8:35 AM  Depression in Pregnancy  
Andrew M. Novick, MD, PhD  
University of Colorado, School of Medicine

9:05 AM  Q&A

9:15 AM – 3:30 PM  Mid-Day Break

3:30 PM – 4:00 PM  Après-Ski

4:00 PM  LSC Complications  
Kathleen Connell, MD  
University of Colorado, School of Medicine

4:30 PM  Q&A

4:45 PM  Break

5:00 PM  Featured Guest Speaker  
Over-the-Counter & Emergency Contraception  
Christine R. Isaacs, MD  
VCU School of Medicine

5:30 PM  Q&A

5:40 PM  Featured Guest Speaker  
Management of the Second Stage: The Truth About Laboring Down  
Alison G. Cahill, MD, MSCI  
University of Texas at Austin, Dell Medical School

6:10 PM  Q&A

6:20 PM  Adjourn

*Please note that schedule and speakers are subject to change.*
Tuesday, February 18, 2020

6:45 AM  Breakfast with Professors
Alison G. Cahill, MD, MSCI | Kathleen Connell, MD

7:15 AM  Featured Guest Speaker
Breast Fundamentals for the Gynecologist
Christine R. Isaacs, MD
**VCU School of Medicine**

7:45 AM  Q&A

7:55 AM  Featured Guest Speaker
Evidence-Based Management of Category II EFM
Alison G. Cahill, MD, MSCI
**University of Texas at Austin, Dell Medical School**

8:25 AM  Q&A

8:35 AM  Modern Obstetric Anesthesiology
Jason Papazian, MD
**University of Colorado, School of Medicine**

9:05 AM  Q&A

9:15 AM – 3:30 PM  Mid-Day Break

3:30 PM – 4:00 PM  Après-Ski

4:00 PM  When to Refer: Case-Based Discussion
John P. Curtin, MD, MBA
**University of Colorado, School of Medicine**

4:30 PM  Q&A

4:45 PM  Break

5:00 PM  Pragmatic Approach to the Dx and Rx of Thyroid Disease in Pregnancy: Evading the Quagmires
Linda Barbour, MD, MSPH
**University of Colorado, School of Medicine**

5:30 PM  Q&A

5:40 PM  Featured Guest Speaker
ARRIVE Trial: Results & Implementation
Alison G. Cahill, MD, MSCI
**University of Texas at Austin, Dell Medical School**

6:10 PM  Q&A

6:20 PM  Adjourn

*Please note that schedule and speakers are subject to change.*
Wednesday, February 19, 2020

6:45 AM Breakfast with Professors
Helen Feltovich, MD | Stephanie Teal, MD, MPH | John Curtin, MD, MBA

7:15 AM Featured Guest Speaker
Reducing the First Cesarean in Real Life
Alison G. Cahill, MD, MSCI
University of Texas at Austin, Dell Medical School

7:45 AM Q&A

7:55 AM Update on STIs
L. Chesney Thompson, MD
University of Colorado, School of Medicine

8:25 AM Q&A

8:35 AM LARC and Birth Outcomes
Stephanie Teal, MD, MPH
University of Colorado, School of Medicine

9:05 AM Q&A

9:15 AM – 3:30 PM Mid-Day Break

9:30 AM – 12:00 PM Optional Workshop (Registration Required)
Transvaginal Cervical Length Screening Training Workshop
Helen Feltovich, MD
University of Wisconsin School of Medicine and Public Health

3:30 PM – 4:00 PM Après-Ski

4:00 PM Bundles for Quality Care in OBGYN
Saketh Guntupalli, MD
University of Colorado, School of Medicine

4:30 PM Q&A

4:45 PM Break

5:00 PM Updates on Prenatal Genetic Screening in the Office
K. Joseph Hurt, MD, PhD
University of Colorado, School of Medicine

5:30 PM Q&A

5:40 PM The Role of Gynecology in Transgender Care
Tricia Huguelet, MD
University of Colorado, School of Medicine

6:10 PM Q&A

6:20 PM Adjourn

*Please note that schedule and speakers are subject to change.
Thursday, February 20, 2020

6:45 AM  Breakfast with Professors
Ritu Salani, MD, MBA | Terry Harper, MD | Henry Galan, MD

7:15 AM  Featured Guest Speaker
Surgical Considerations in the Morbidly Obese Patient
Ritu Salani, MD, MBA
*The Ohio State University College of Medicine*

7:45 AM  Q&A

7:55 AM  Delivery of Obstetric Telemedicine Services
Terry Harper, MD
*University of Colorado, School of Medicine*

8:25 AM  Q&A

8:35 AM  Recurrent Pregnancy Loss
Henry Galan, MD
*University of Colorado, School of Medicine*

9:05 AM  Q&A

9:15 AM – 3:30 PM  Mid-Day Break

3:30 PM – 4:00 PM  Après-Ski

4:00 PM  Operating on the Challenging Patient: Robotic surgery and other tricks
Jaime Arruda, MD
*University of Colorado, School of Medicine*

4:30 PM  Q&A

4:45 PM  Break

5:00 PM  Featured Guest Speaker
BRCA and Genetics in Gynecologic Malignancies
Ritu Salani, MD, MBA
*The Ohio State University College of Medicine*

5:30 PM  Q&A

5:40 PM  Featured Guest Speaker
Follow-Up of Women after Treatment for Gynecologic Malignancies
Ritu Salani, MD, MBA
*The Ohio State University College of Medicine*

6:10 PM  Q&A

6:20 PM  Adjourn

*Please note that schedule and speakers are subject to change.*
**Friday, February 21, 2020**

6:45 AM  **Breakfast with Professors**  
Jaime Arruda, MD | Joyce Sung, MD | Paul Montero, MD

7:15 AM  **Management of HIV on Labor and Delivery**  
Joyce Sung, MD  
*University of Colorado, School of Medicine*

7:45 AM  **Q&A**

7:55 AM  **Featured Guest Speaker**  
*Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)*  
Ritu Salani, MD, MBA  
*The Ohio State University College of Medicine*

8:25 AM  **Q&A**

8:35 AM  **Important Hernia Concepts for the OB/GYN Patient**  
Paul Montero, MD  
*University of Colorado, School of Medicine*

9:05 AM  **Q&A**

9:15 AM  **Adjourn**

*Please note that schedule and speakers are subject to change.*
THANK YOU TO OUR EXHIBITORS!

AbbVie  Ansh Labs  Avanos  Bayer  CAE
Colorado Fetal Care Center  Ferring  GE Healthcare  Integrated Genetics  KARL STORZ
Natera  NxGen MDx  Samsung Healthcare
Disclosure of Relevant Financial Relationships

46th Annual Vail Obstetrics and Gynecology Conference
February 16-21, 2019
Vail, CO

As a sponsor accredited by the Accreditation Council for Continuing Medical Education, the University of Colorado School of Medicine must ensure balance, independence, objectivity, and scientific rigor in all its sponsored educational activities. All speakers/contributors participating in a sponsored activity are expected to disclose to the accredited provider any relevant financial interest or other relationship(s) involving themselves or their spouse/partner within the last 12 months with any proprietary entity producing health care goods or services related to the content of the activity. The intent of this disclosure is not to prevent a speaker with a relevant financial or other relationship from making the presentation, but rather to identify and resolve any conflicts of interest that may control the content of the activity. It is also intended that any potential conflict be identified openly so that the listeners have a full disclosure of the facts and may form their own judgments about the presentation. It remains for the audience to determine whether the speaker's interests or relationships may influence the presentation with regard to exposition or conclusion.

The following faculty/contributors have reported commercial affiliation associate with this conference as follows:

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Organization</th>
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</thead>
<tbody>
<tr>
<td>Jaime Arruda, MD</td>
<td>Consultant</td>
<td>Eximis Surgical</td>
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<tr>
<td>Ronald Gibbs, MD</td>
<td>Data Safety Monitoring Board</td>
<td>Novavax</td>
</tr>
<tr>
<td>Stephanie Teal, MD</td>
<td>Consultant</td>
<td>Bayer &amp; Merck</td>
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</table>

All other faculty/contributors have reported no commercial affiliation associated with this conference and no intentions to discuss unapproved uses for drug products and/or devices.
Sunday
LEARNING OBJECTIVES

- At the end of this talk, the learner is expected to:
  - Be able to direct patients to reputable sources of information
  - Maintain a professional stance when discussing non-fact-based and miracle treatments
  - Present risks of FDA-approved treatments in an accurate but non-alarming fashion
  - Engage in shared decision making with patients that incorporates their values but minimizes potential harm

Fake News was a term first coined by:

A. Donald Trump
B. Kellyanne Conway
C. Adolph Hitler
D. William Hearst
FAKE NEWS IS NOT NEW
- 13th Century BC: Ramses the Great misrepresented his stalemate battle of Kadesh as an Egyptian victory
- 1st Century BC: Octavian engineered a disinformation campaign to unseat Mark Antony
- 2nd and 3rd Centuries AD: Disinformation about Christians—cannibalism and incest
- 15th Century: Anti-Semitic blood libels begin
- 19th Century: Spanish-American War largely driven by Pulitzer/Hearst rivalry

CURRENT STATE OF AFFAIRS: INFORMATION POLLUTION
- Clickbait
- Propaganda
- Satire/Parody
- Sloppy Journalism
- Misleading Headings
- Biased or Slanted News

THE INTERNET IS KIND TO FAKE NEWS
- Parity of Esteem: There is no simple way to assess veracity of information
- Search engine optimization: You can pay to be seen
- The best visual appeal ‘wins’ the attention of the viewer
- Style triumphs over substance
CALL-OUT CULTURE AND RAGE CULTURE

• Not necessary to have all the facts
• All that's needed is your cell phone and an attitude
• Women are frequently the hardest hit targets (Gamergate)

HOW DID PIZZAGATE COME ABOUT?

• John Podesta emails hacked in 3/16, posted in WikiLeaks
• False claims that Comet Ping Pong Restaurant (among others) was involved in a Democratic Party pedophile human trafficking operation
• Claim was spread by alt-right and anti-Clinton
• Culminated in a trip by an armed citizen, Edgar Welch, from NC to Washington to 'free the children'

DEEP FAKE CLIPS...ARE REALISTIC ENOUGH TO TRICK USERS INTO MAKING FINANCIAL, POLITICAL, AND PERSONAL DECISIONS BASED ON THE FAKE TESTIMONY OF OTHERS

HOW THIS PLAYS OUT IN OB/GYN

FAKE NEWS IN MENOPAUSE WORLD

FAKE NEWS #1: MENOPAUSE IS HELL

THE MESSAGE:

• MENOPAUSE IS A CATASTROPHE—AND MUST BE MEDICALLY TREATED
WHAT IS THE REALITY

• ABOUT 6% OF MENOPAUSAL WOMEN USE HORMONE THERAPY (SWAN STUDY)
• MOST WOMEN VIEW MENOPAUSE IN A NEUTRAL TO POSITIVE MANNER:
  * FREEDOM FROM MENSTRUAL PERIODS
  * FREEDOM FROM CONTRACEPTION

WHY DOES THIS IMAGE PERSIST?

• THE MOST EFFECTIVE TREATMENT—HORMONES—IS FEARED (THANKS FOR MORE FAKE NEWS!)
• AGING WOMEN ARE VIEWED NEGATIVELY BY OUR SOCIETY—AND MENOPAUSE IS A MARKER OF AGING
• BECAUSE MENOPAUSE IS A DRAMATIC HORMONAL EVENT FOR WOMEN, DELAYING OR AVOIDING IT BY GIVING BACK ‘REPLACEMENT’ HORMONES IS EQUATED WITH AVOIDANCE OF AGING ITSELF

SO WHY IS THIS FAKE NEWS HARMFUL?

• IT FRAMES MENOPAUSE AS A MEDICAL CONDITION IN DIRE NEED OF TREATMENT
• THERE ARE (ALMOST) NO OTHER APPROVED TREATMENTS BEYOND HORMONE THERAPY
• THE FLOODGATES ARE NOW OPEN TO INNUMERABLE UNTESTED ‘ALTERNATIVES’
FAKE NEWS PART 2: RESTORING HORMONES TO NORMAL LEVELS PREVENTS AGING

DO ALL OF YOUR MENOPAUSAL PATIENTS FIT INTO THEIR SKINNY JEANS?

THE REALITY: WAIST Girth and Fat Mass Go Up in Just About Every Woman

WHY THIS FAKE NEWS IS HARMFUL

It sets up the expectation that there are magical treatments that keep women looking young, skinny, and unwrinkled forever!
**FAKE NEWS #3: THE RIGHT KIND OF ESTROGEN (OR OTHER HORMONE(S)) WILL PROTECT WOMEN FROM HEART DISEASE...IF ONLY THOSE DOCTORS WOULD DO THE CORRECT STUDY!**

**THE REALITY: THERE IS NO CONSISTENT EVIDENCE TO SUPPORT THIS NOTION**

**KEEPS: the Kronos Early Estrogen Prevention Study:**
No difference in carotid intimal medial thickness with 4 yrs of CEE, TDE or placebo

*Ann Int Med 2014; 161: 249*

**ELITE: NEW ENGLAND JOURNAL OF MEDICINE: THE TIMING HYPOTHESIS IS ‘PROVEN’**

*New Engl J Med 2016; 374: 1221*
<table>
<thead>
<tr>
<th>KEEP (2014)</th>
<th>ELITE (2016)</th>
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<tr>
<td>N=727</td>
<td>N=643</td>
</tr>
<tr>
<td>≤4 yrs FMP, &lt;54 yrs</td>
<td>≤6 or &gt;10 yrs FMP</td>
</tr>
<tr>
<td>CEE or TEE, CYCLICAL VAGINAL P GEL</td>
<td>ORAL E2, CYCLICAL VAGINAL P GEL</td>
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<td>PLACEBO CONTROLLED</td>
<td>PLACEBO CONTROLLED</td>
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<td>1st OUTCOME: CIMT</td>
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<td>2nd OUTCOME: CAC</td>
<td>2nd OUTCOME: CAC</td>
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<td>CIMT LAB: USC</td>
<td>CIMT LAB: USC</td>
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**WHY THIS FAKE NEWS IS HARMFUL**

- It bullies women into believing that they must do something to avoid later life disease
- God help you if you miss your chance

**FAKE NEWS #4: 'BIODENTICAL' HORMONES HAVE NO RISKS, PREVENT AGING**

Actual claims from actual websites:

- [HTTPS://WWW.BIOTEMEDICAL.COM](https://www.biotemedical.com)

  - We only use bioidentical hormones that have fewer of the unwanted side effects of synthetic hormones
  - Having one's hormones checked regularly will reveal whether their hormones are optimized and help avoid hormonal imbalance in a woman's endocrine system.
BLACK BOX WARNING FOR FDA APPROVED HORMONES:
WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA
IN THE ABSENCE OF COMPARABLE DATA, THESE RISKS SHOULD BE ASSUMED TO BE SIMILAR FOR OTHER DOSES OF CE AND OTHER DOSAGE FORMS OF ESTROGENS
IN THE ABSENCE OF COMPARABLE DATA, THESE RISKS SHOULD BE ASSUMED TO BE SIMILAR FOR OTHER DOSES OF CE AND MPA, AND OTHER COMBINATIONS AND DOSAGE FORMS OF ESTROGENS AND PROGESTINS.

YET, NO SUCH LABELLING IS REQUIRED FOR BIOIDENTICAL HORMONES

* THEY ARE CONSIDERED 'DIETARY SUPPLEMENTS' AND THEREFORE EXEMPTED FROM FDA REQUIREMENTS TO PROVE EFFICACY AND SAFETY

MORE ACTUAL CLAIMS
* WHEN WE HELP BALANCE FEMALE HORMONES, IT MAY PROVIDE AN INDIVIDUAL WITH A GREATLY IMPROVED QUALITY OF LIFE. IN ADDITION TO FEELING GREAT, STUDIES HAVE SHOWN THAT BALANCING HORMONES IN WOMEN MAY BE ABLE TO HELP REDUCE ONE'S CHANCE OF CONTRACTING CERTAIN DISEASES AS WELL AS THE SERIOUSNESS OF PARTICULAR CONDITIONS.
* HTTPS://WWW.MEDICALNEWSTODAY.COM/ARTICLES/319465.PHP
* HORMONE REPLACEMENT THERAPY, OR HORMONE THERAPY, CAN ALSO LOWER THE RISK OF BRITTLE BONES AND HEART DISEASE.
* HOWEVER, IN 2002, THE WOMEN'S HEALTH INITIATIVE WARNED AGAINST THE LONG-TERM USE OF TRADITIONAL HORMONE THERAPY (HT). THEIR CONCERN WAS DUE TO THE INCREASED RISK OF BREAST CANCER, BLOOD CLUTES, STROKE, AND EVEN HEART DISEASE. SINCE THIS SAFETY WARNING CAME OUT AGAINST THE USE OF TRADITIONAL HORMONE THERAPY, ALTERNATIVE METHODS, SUCH AS BIOIDENTICAL HORMONE THERAPY HAVE BEEN DEVELOPED.
WHY THIS FAKE NEWS IS DAMAGING

- IT DIRECTS PATIENTS TO NON-FDA APPROVED, NON-EVIDENCE-BASED TREATMENTS FOR THEIR MENOPAUSAL SYMPTOMS
- IT FRAMES THE ISSUE IN A WAY THAT MAKES PATIENTS NOT WANT TO TRUST THEIR DOCTORS

FAKE NEWS #5: THE GUARDIAN: “NEW PROCEDURE THAT CAN DELAY MENOPAUSE UP TO 20 YEARS!”

- DELAYING THE ONSET OF MORE COMMON SYMPTOMS OF THE MENOPAUSE, WHICH RANGE FROM LOW MOOD, ANXIETY AND DIFFICULTY SLEEPING, TO HOT Flushes, NIGHT Sweats AND A REDUCED SEX DRIVE
- COULD BENEFIT THOUSANDS OF WOMEN WHO EXPERIENCE SERIOUS HEALTH PROBLEMS, SUCH AS HEART CONDITIONS AND BONE-WEAKENING OSTEOPOROSIS, THAT ARE BROUGHT ON BY THE MENOPAUSE.

OVARIAN TISSUE CRYOPRESERVATION

- NINE WOMEN HAVE HAD ELECTIVE SURGERY TO REMOVE OVARIAN TISSUE AND CRYOPRESERVE IT FOR LATER REIMPLANTATION, THUS OUTSMARTING MENOPAUSE
- REQUIRES 2 OPERATIONS
- WILL CONTINUE ENDOGENOUS OVARIAN HORMONE PRODUCTION BEYOND THE AGE AT NATURAL MENOPAUSE
- WILL REQUIRE CONTINUED USE OF CONTRACEPTION, MENSTRUAL PRODUCTS, ETC
- REALLY?
WHY THIS FAKE NEWS IS HARMFUL

• It destroys scientific credibility
• It again implies the continuing hormone production well after menopause is good for women (if only it could be done correctly)
• It distracts people from the day to day healthy behaviors that have been proven to prevent disease

THE FAIRNESS DOCTRINE

• 1949 FCC policy that holders of broadcast licenses were held to reporting on public matters of consequences in a manner that was "honest, equitable and balanced"
• Policy eliminated in 1987, concurrent with the establishment of Fox News
• Rule removed in 2011—leading to the ironic motto of ‘fair and balanced’ for Fox News

OTHER TOXIC EFFECTS OF THE ‘FAKE NEWS’ ENVIRONMENT

• Distortion of factual data to accommodate opinions
• Eventual ‘turning away’ of reasonable people who cannot resolve the apparent debate examples:
  • Vaccination promoting hubs debating ‘anti-vaxxers’ on the same public platform appears to assign the scientific arguments similar gravitas
  • Climate change scientists debating climate change deniers, similar dynamic
• There is a loss of commonly agreed upon, objective truth
MORE SUBTLE EROSIONS OF TRUTH ACCOMPANY THE 'FAKE NEWS' ONSLAUGHT

- Assumptions are made that every possible fact or statistic has a counterpoint
- "There are lies, there are damn lies, and then there are statistics"—Mark Twain
- Call-out and outrage culture can shout down some of the sanest voices in the room
- Viral items gain credibility fast—well before they can be verified

AND IT DOESN'T EVEN HAVE TO BE TOTALLY FAKE TO WORK AGAINST TRUTH...

JAMA VIEWPOINT

October 18, 2019
Neglecting Major Health Problems and Broadcasting Minor, Uncertain Issues in Lifestyle Science
IOANNIDIS, VIEWPONT JAMA 10-19

Is impartiality possible for research performed within charged environments, where even leading scientists may lobby to silence dissenters or block publication of opposing views?

Most people believe:
- That they can sort fact from fiction
- That a thorough search through the internet will allow them to balance the information they are acquiring and arrive at ‘truth’
- That trolling and disinformation is rarer than it is

In our current climate:
- Hard to distinguish reporting from opinion
- Few ways to defend against fake news unless it is defamatory
- We can unwittingly help disperse questionable material
HOW TO INOCULATE YOURSELF AND YOUR PATIENTS AGAINST FAKE NEWS

- Promote evidence-based sources of data: Menopause.org, ACOG.org, Endocrine.org, etc.
- Have literature available for patients.
- Direct patients to high-quality research findings and summaries available online.

MEDIA LITERACY

- What type of article are you reading (opinion piece, original research, editorial)?
- Is it peer reviewed?
- Is it a clinical trial?
- Is the clinical trial reported to ClinicalTrials.gov?
- Was there a control group? Was the study randomized? To whom do the data apply?
- Are the references all internally concatenating?
- What else has been written by this author?

SOME FACT CHECKING SITES

- Snopes.com
- FactCheck.org
- Politifact.com
SUMMARY

• The world wide web has both brought us closer together and farther apart
• We are only just beginning to appreciate the impact of instant and constant information exposure
• The human mind was not designed to cope with viral news

SUMMARY

• The bad guys win when the loudest voice is the only one that gets heard
• We need to slow the flow for our patients (and ourselves)
• Learn to assess the sources of information before reacting to it
• Teach others to do the same
Oncofertility Best Practices: Optimizing Reproductive Outcomes in Cancer

Leslie Coker Appiah MD
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February 16th, 2020

Objectives

• Explain the effects of cancer treatments on fertility and limits of risk stratification.
• Discuss standard and novel fertility preservation therapies for patients with cancer.
• Identify and manage reproductive late effects in survivorship.

1.7 million new cases in 2019
• 10,270 between ages 0 and 14
  - 85% five-year survival rate
• 70,000 between ages 15 and 39
  - 70% five-year survival rate
• 500,000 childhood cancer survivors estimated by 2020

US Incidence and Survival

• Health outcomes in 1,713 survivors median age 32 yrs (18-60 yrs)
• Prevalence of primary ovarian failure 12% in at risk females
• Prevalence of male germ cell dysfunction 66%
• Prevalence of Leydig cell failure 12%

Clinical Ascertainment of Health Outcomes Among Adults Treated for Childhood Cancer
Melissa M Hudson et al., JAMA. 2013;309(22):2371-2381

• Young adult survivors ages 18 – 39 years 38% less likely to conceive compared to controls

The impact of cancer on subsequent chance of pregnancy: a population-based analysis.

How is Risk Quantified?
Chemoradiation and Follicular Development

Chemotherapy and Sperm Quality
- Genetic damage induced by DNA cross-linking and single-strand breaks.
- Mutations incurred by spermatogonial cells can be repaired or undergo apoptosis.
- Differentiated spermatogenic cells poorly repair DNA damage; ejaculated spermatozoa may harbor extensive genomic damage.
- Sustained mutations lead to lifetime production of mutation-carrying sperm.

Testicular Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Acute effects of chemotherapy on the testes</th>
<th>Recovery Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capetax</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Cytarabine</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Fludarabine</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Adriamycin</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Taxol</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Mitomycin</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Cyclophosphamide and methotrexate</td>
<td>Good</td>
<td>1 year</td>
</tr>
<tr>
<td>Vincristine, Bleomycin, doxorubicin and cyclophosphamide</td>
<td>Moderate</td>
<td>3 years</td>
</tr>
<tr>
<td>Doxorubicin, Bleomycin, etoposide and cyclophosphamide</td>
<td>Moderate</td>
<td>3 years</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Poor</td>
<td>5 years</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Poor</td>
<td>5 years</td>
</tr>
<tr>
<td>Mitomycin</td>
<td>Poor</td>
<td>5 years</td>
</tr>
<tr>
<td>Cyclophosphamide and methotrexate</td>
<td>Poor</td>
<td>5 years</td>
</tr>
</tbody>
</table>
• Testicular involution leads to azoospermia within 3 months.
• Time to recovery after chemotherapy and pelvic radiation ranges from 12-72 months.

Estimating Risk - CED

Gonadotoxic Risk: >80% loss of reproductive potential

- Alkylating-intensive chemotherapy
- any treatment regimen containing procarbazine
- busulfan cumulative dose >600 mg/m²
- cyclophosphamide equivalent dose (CED) ≥ 8000 mg/m²
- alkylating chemotherapy conditioning prior to SCT
- Whole abdomen/pelvic irradiation to ovaries
  - ≥15 Gy pre-pubertal, >10 Gy post-pubertal, >6 Gy adult
- Whole abdomen/pelvic irradiation to uterus ≥30 Gy
- Total body irradiation and cranial radiation ≥30 Gy

Subfertility/Infertility Risk

<table>
<thead>
<tr>
<th>High risk &gt; 80% Conditioning for BMT</th>
<th>Medium Risk 30 – 70 %</th>
<th>Low Risk &lt; 20 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hodgkin’s: w/ alkylators</td>
<td>AML</td>
<td>ALL</td>
</tr>
<tr>
<td>Soft-tissue sarcoma: metastatic</td>
<td>Breast</td>
<td>Wilms’ tumor</td>
</tr>
<tr>
<td>Ewing’s sarcoma:</td>
<td>Osteosarcoma</td>
<td>Soft-Tissue sarcoma: stage I</td>
</tr>
<tr>
<td>Localized pelvic or testicular radiation</td>
<td>Neuroblastoma</td>
<td>Retinoblastoma</td>
</tr>
<tr>
<td></td>
<td>Non-Hodgkin lymphoma</td>
<td>Germ-cell tumors</td>
</tr>
<tr>
<td></td>
<td>Hodgkin’s: alternating alkylator tx</td>
<td>(fertility sparing)</td>
</tr>
<tr>
<td></td>
<td>Craniospinal radiation &gt; 24Gy</td>
<td></td>
</tr>
</tbody>
</table>

Stem cell transplant: Non-oncologic conditions

<table>
<thead>
<tr>
<th>Anemia</th>
<th>Autoimmune conditions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aplastic anemia</td>
<td>Multiple sclerosis</td>
<td>Severe combined immuno-deficiency</td>
</tr>
<tr>
<td>Fanconi’s Diamond Blackfan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sickle-cell anemia</td>
<td>Systemic sclerosis</td>
<td>Wiskott–Aldrich disease</td>
</tr>
<tr>
<td>Thalassemia</td>
<td>Systemic lupus erythematosus</td>
<td>Metabolic storage defects</td>
</tr>
<tr>
<td></td>
<td>Rheumatoid arthritis</td>
<td>Mucopolysaccharidoses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amyloidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gaucher’s disease</td>
</tr>
</tbody>
</table>

### Gonadotoxicity of Newer Agents

- Oxaliplatin
- Irinotecan
- Bevacizumab – 30% rate of primary ovarian insufficiency
- Cetuximab
- Trastuzumab
- Erlotinib
- Imatinib

Loren et al. J Clin Oncol 2013;31:2500-2510

### Offspring of patients treated for cancer in childhood.

- 243 study progeny
- Incidence of fetal chromosomal or congenital abnormalities after chemotherapy remains the same as for the general population
- 202 pregnancies in 302 subjects
- No relation between number or cumulative dose of mutagens received and the frequency of congenital anomalies in offspring


Green et al. 1991 July;325:141-146

### Practice Pearl

- Risk of acute ovarian and testicular gamete failure after treatment of childhood cancer 12% and 66%, respectively.
- Pregnancy rates decreased by 38% for young adults after cancer treatment.
- Cyclophosphamide equivalent dose scoring system best tool for comparing alkylator therapies.
- Risk stratification remains an area of further research.
Which Fertility Preservation Options are Available?

- American Society of Clinical Oncology (ASCO) 2006, 2013
- American Society for Reproductive Medicine (ASRM) 2010
- Association of Pediatric Hematology/Oncology Nurses (APHON)
  - "Physicians should inform cancer patients about options for fertility preservation and future reproduction prior to treatment..."
  - "...regardless of the patient’s age, gender, culture, socioeconomic status, or healthcare team bias...
  - "...and continue throughout treatment and survivorship in a manner appropriate to the patient’s developmental stage at that time."

Statements supported by American College of Obstetricians and Gynecologists (ACOG) and American Academy of Pediatrics (AAP).

Gap

Less than 30% receive fertility preservation therapies

Fertility Preservation Methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Success rates</th>
<th>Partner Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mature oocyte cryopreservation</td>
<td>35 - 50%</td>
<td>10 – 14 days stimulation; surgical procedure; no ovarian function preserved; stimulation may occur at any phase of the cycle</td>
</tr>
<tr>
<td>Sperm cryopreservation</td>
<td>57%</td>
<td>At least two samples recommended prior to exposure</td>
</tr>
<tr>
<td>Embryo cryopreservation</td>
<td>40%</td>
<td>10 – 14 days stimulation; surgical procedure; no preservation of ovarian function; embryo ownership concerns</td>
</tr>
<tr>
<td>Ovarian transposition</td>
<td>60-90%</td>
<td>Undenutilized</td>
</tr>
<tr>
<td>Ovarian shielding</td>
<td>75-80%</td>
<td>Scatter effect; consider concomitant chemotherapy</td>
</tr>
</tbody>
</table>

Fertility preservation using controlled ovarian hyperstimulation and oocyte cryopreservation in a premenarcheal female with myelodysplastic syndrome

- Potentially higher gonadotropin doses in early puberty
- Transabdominal monitoring with sedated transvaginal retrieval
- Efficiency in adolescents needs to be confirmed [Cil and Oktay](Cil and Oktay et al. Fertil Steril 2013;100:492-9)
  - 28.1% live-birth at age 25 for 2 oocytes thawed after vitrification
  - Probability increased to 31.3% with 6 oocytes

Fertility Preservation Methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Partner</th>
<th>Considerations</th>
</tr>
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<tbody>
<tr>
<td>Immature oocyte cryopreservation</td>
<td>No</td>
<td>No stimulation; surgical procedure; costs; no ovarian function preserved</td>
</tr>
<tr>
<td>Ovarian tissue freezing – no longer investigational</td>
<td>No</td>
<td>Surgical procedure; costs; transplantation not suitable with high gonadal involvement or hormone sensitive tumor; preservation of gonadal function</td>
</tr>
<tr>
<td>Testicular tissue freezing</td>
<td>No</td>
<td>Similar to OTC</td>
</tr>
<tr>
<td>GnRHa ovarian suppression</td>
<td>No</td>
<td>Conflicting data; recent Cochrane study clearer evidence</td>
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### Indications for Ovarian Tissue Cryopreservation

- Edinburgh criteria for malignant disorders (modified):
  - High risk of gonadal failure (> 50%) after cancer treatment
  - Absence of previous high gonadotoxic chemotherapy
- Nonmalignant disorders treated with immunosuppression or SCT
- Individuals with gender and sex diversity
- Genetic predisposition to accelerated follicular loss

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### Ovarian Tissue Cryopreservation


- 130 children born worldwide
- 4700+ cryopreserved tissues with 360 transplantations
- Age range pre-pubertal to mid 30’s
- 29 - 32% delivery rate with half of singletons conceived naturally
- No longer experimental
Fertility Preservation in Females with Turner Syndrome: A Comprehensive Review and Practical Guidelines

- Early identification of TS patients with ovarian reserve
- Salvage existing viable oocytes
- Pre-pubertal girls
  - Sufficient ovarian reserve (AMH > 2 ng/ml)
  - Serial serum AMH to delay intervention to post-puberty
  - Ovarian tissue cryopreservation if AMH falls to < 2 ng/ml
  - Oocyte cryopreservation at a post-pubertal age
- Insufficient reserve (AMH ≤ 2 ng/ml) → ovarian tissue cryopreservation
- Post-pubertal girls
  - Recommend fertility preservation regardless of the initial AMH

In Vitro Maturation

- 21 yo s/p interval bilateral oophorectomy for ovarian serous carcinomas
- OTC at second surgery followed by aspiration of all visible follicles
- ICSI followed by 2 embryo transfer and delivery of healthy infant
- 20-35% live birth rate after IVM of growing follicles
- Presence of abnormal non-growing follicles with slow in vitro growth and maturation in pre-pubertal ovaries
### Fertility Preservation Methods

<table>
<thead>
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<th>Investigational Methods</th>
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<th>Considerations</th>
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<td>GnRHa ovarian suppression</td>
<td>N/A</td>
<td>Conflicting data; recent Cochrane study supports use</td>
</tr>
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### Cochrane Review 2019

**GnRHa appears to be effective in protecting the ovaries during chemotherapy, in terms of maintenance and resumption of menstruation, treatment-related premature ovarian failure and ovulation. Evidence for protection of fertility was insufficient and needs further investigation.**
Menstrual Suppression

- Leuprolide acetate 11.25 mg IM or 22.5 mg SC every 12 weeks for patients at risk of profound anemia Bates et al 2011
  - administer prior to chemotherapy
  - final dose to be administered at final chemotherapy infusion

- Norethindrone acetate add-back to minimize hot flashes and protect bone DiVasta 2013.
  - start with or before leuprolide and discontinue 12 weeks after final dose

Fertility Preservation Costs

<table>
<thead>
<tr>
<th>Methods</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm cryopreservation</td>
<td>$400 + $175 for semen analysis</td>
</tr>
<tr>
<td>Oocyte cryopreservation</td>
<td>$8000 plus meds</td>
</tr>
<tr>
<td></td>
<td>$4000 - $6000 (reduced costs through Livestrong) free meds</td>
</tr>
<tr>
<td>Embryo cryopreservation</td>
<td>$6500 - $13000 plus meds</td>
</tr>
<tr>
<td>Long term storage</td>
<td>$275 yearly</td>
</tr>
<tr>
<td></td>
<td>$75 reduced costs</td>
</tr>
<tr>
<td>Ovarian tissue</td>
<td>$10000 - $30000 oophorectomy</td>
</tr>
<tr>
<td>cryopreservation</td>
<td></td>
</tr>
</tbody>
</table>

Practice Pearl

- Fertility preservation should be offered to male and female patients prior to chemotherapy.

- Fertility preservation extends beyond oncology diagnoses.

- Ovarian stimulation may be offered in post-pubertal adolescents.

- GnRHa should be offered for ovarian protection during treatment.
Assessing the Reproductive Window?

- Limited data on Copper and Levonorgestrel IUD use in women immunosuppressed due to cancer treatment
- Category 1 and 2
  - HIV immunosuppression
  - Systemic lupus erythematosus
  - Uncomplicated solid organ transplant

Surveillance
- Recurrence rates
- Tumor characteristics
- Stage of disease
- Treatments received
- Time to monitor relapse for most cancers: 2 to 5 years
- Maternal-fetal medicine consult as indicated

Nagarajam et al., 2015; Muller et al. 2009; Reulen et al. 2009
Oncofertility Best Practices:
Optimizing Reproductive Outcomes in Cancer

Regulation of ovarian follicular development in primates: facts and hypotheses.

- Growth span from primordial to pre-ovulatory follicle: 6 months
- Risk of mutagenesis maximal during this maturation phase
- Recommendation: delay conception for 6 months after completion of treatment

Gougeon et al., Endocr Rev. 1996 Apr;17(2):121-55
Meirow et al., J Reprod Infertil. 2007;59(4):21-8
Chang et al., Fertil Steril 2013 Sep;100(3):442

Reproductive risk quantification difficult to assess due to absence of evidence-based clinical consensus.

- Sperm DNA breakage present up to 24 months post chemotherapy.
- European Society for Medical Oncology (ESMO) recommendation:
  - defer childbearing for at least 12 months after cancer therapy
  (Grade C recommendation; Level IV evidence)

How to Screen for Reproductive Late Effects?
Oncofertility Best Practices: Optimizing Reproductive Outcomes in Cancer

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Reproductive Late Effects

- Infertility
- Hypoestrogenism
- Vasomotor/GSM/bone loss
- Delayed puberty

- Diminished uterine volume
- Fetal loss
- Low birthweight
- Vaginal stenosis

- Genital Graft Versus Host Disease
- Sexual Dysfunction
- Decreased libido
- Diminished self esteem
- Dyspareunia/Lost intimacy

- Vaginal stenosis
- Hematocolpos

- Diminished uterine volume

- Fetal loss
- Low birthweight
- Vaginal stenosis

- Infertility
- Hypoestrogenism
- Vasomotor/GSM/bone loss
- Delayed puberty

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Children's Oncology Group Long-Term Follow-up Guidelines: Alkylators and Radiation

<table>
<thead>
<tr>
<th>History and Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset and tempo of puberty</td>
</tr>
<tr>
<td>Menstrual history</td>
</tr>
<tr>
<td>Sexual function (vaginal dryness, libido)</td>
</tr>
<tr>
<td>Menopausal symptoms</td>
</tr>
<tr>
<td>Tanner staging and growth yearly until mature</td>
</tr>
<tr>
<td>Hair and breast and/or endocrine/gynecology referral</td>
</tr>
<tr>
<td>No signs of puberty at age 13</td>
</tr>
<tr>
<td>Failure of pubertal progression</td>
</tr>
<tr>
<td>Abnormal menstrual pattern or menopausal symptoms</td>
</tr>
<tr>
<td>Bone density evaluation with ovarian hormone deficiency</td>
</tr>
<tr>
<td>Hormone replacement when benefits outweigh risks</td>
</tr>
</tbody>
</table>

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Hormone Replacement Therapy: Estrogen Effects on Physiology

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Oral</th>
<th>Transdermal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability</td>
<td>Lower</td>
<td><strong>Higher</strong></td>
</tr>
<tr>
<td>First pass through liver</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- Transdermal 17b-estradiol no increased VTE risk (OR 0.9)

- WHI findings cannot be extrapolated to pediatric and adult population less than age 60 years

<table>
<thead>
<tr>
<th>Effect</th>
<th>Oral</th>
<th>Transdermal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine growth</td>
<td>Decreases</td>
<td>No effect</td>
</tr>
</tbody>
</table>

---


WHI findings cannot be extrapolated to pediatric and adult population less than age 60 years

Kmietowicz et al. BMJ 2019;364:l157

Serum AMH (picomoles per liter) in 568 healthy infants, girls, adolescents, and adult women.


Ovarian Reserve Testing

<table>
<thead>
<tr>
<th>AMH ng/ml</th>
<th>Clinical Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low (≤0.5)</td>
<td>Impending onset of premature menopause</td>
</tr>
<tr>
<td>Low (0.5 - 1.0)</td>
<td>Limited egg supply, Diminished reserve</td>
</tr>
<tr>
<td>Mid-range (&gt;1-3.5)</td>
<td>Normal testing, Diminished reserve</td>
</tr>
<tr>
<td>Elevated (&gt;3.5)</td>
<td>Polycystic ovaries, Risk of OHSS</td>
</tr>
</tbody>
</table>

Participants with pretreatment AMH level > 2 ng/ml recovered their AMH level at a rate of 11.9% per month after chemotherapy

Dillon et al.

Participants with pretreatment AMH < 2 ng/ml recovered at a rate of 2.6% per month.

AMH shown to decrease before the onset of irregular cycles and before the rise of FSH levels

Grynnerup et al.

Ovarian Function Monitoring

- Currently no guidelines to recommend fertility preservation based on pre-treatment FSH, AMH or AFC.
- Currently no standard of care regarding post-treatment monitoring in the absence of clinical signs of ovarian insufficiency for patients.
- Consider: Yearly monitoring if AMH within reference range for age and FSH < 10.
- Consider: Referral to REI if AMH less than reference range for age or FSH > 10.

Radiation Injury to the Uterus

- Doses between 14 and 30 Gy
  - Myometrial fibrosis
  - Reduced uterine volume by 40%
  - Reduced or undetectable blood supply
  - Absent endometrium
- Doses > 30 Gy irreversible damage

Pregnancy Outcomes in Females after Treatment for Childhood Cancer

<table>
<thead>
<tr>
<th>TABLE 4. Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Pregnancy Outcomes by Total Dose of Radiation to Pelvis and abdomen (N = 316 pregnancies) among females Childhood Cancer Survivors.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure (N = 316)</td>
</tr>
<tr>
<td>--------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Radiation dose (Gy)</td>
</tr>
<tr>
<td>≤ 14</td>
</tr>
<tr>
<td>15-24</td>
</tr>
<tr>
<td>≥ 25</td>
</tr>
<tr>
<td>Parity</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>&lt; 30</td>
</tr>
<tr>
<td>30-39</td>
</tr>
<tr>
<td>≥ 40</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
</tr>
<tr>
<td>&lt; 25</td>
</tr>
<tr>
<td>25-29</td>
</tr>
<tr>
<td>≥ 30</td>
</tr>
<tr>
<td>Education level</td>
</tr>
<tr>
<td>≤ high school</td>
</tr>
<tr>
<td>≥ college degree</td>
</tr>
<tr>
<td>Family income</td>
</tr>
<tr>
<td>&lt; median</td>
</tr>
<tr>
<td>≥ median</td>
</tr>
<tr>
<td>Occupation</td>
</tr>
<tr>
<td>Blue collar</td>
</tr>
<tr>
<td>White collar</td>
</tr>
<tr>
<td>Number of years since diagnosis</td>
</tr>
<tr>
<td>&lt; 5</td>
</tr>
<tr>
<td>≥ 10</td>
</tr>
</tbody>
</table>

Epidemiology, March 2000, Vol. 11 No. 2
GVHD occurs in > 50% of HSCT patients
- Skin, GI tract, and liver most affected organs
- Incidence of concurrent genital GVHD 25-49%
- Vulva 68% - Vulvovaginal 28%
- Typically occurs 7-10 months s/p HSCT
- Late disease occurs 1-2 years later


**Treatment Strength**

1. Reduce mechanical or chemical irritation
   - Avoid perfumed emollients and soaps
   - AIIIb

2. Topical class IV corticosteroids to rapidly control inflammation
   - Clobetasol propionate qhs x 4 weeks
   - Bib

3. Topical calcineurin inhibitors for long-term treatment
   - Tacrolimus or pimecrolimus
   - CIIb

4. Topical estrogen as supportive therapy to increase epithelial thickness and improve resilience
   - Bib

5. Regular intercourse or use of dilators to prevent narrowing and stenosis
   - CIIa

6. Manual lysis of adhesions under anesthesia if refractory to therapy
   - CIIa

**Sexual Dysfunction**

- Adolescent survivors engage in risky health behaviors at rates generally equivalent to their siblings

- 77% of adult survivors of childhood cancer reported sexual dysfunction irrespective of gender or age

Existing paradigm

Emerging paradigm

Coady 2016; Masters et al., 1996; Basson 2000
Sexual Dysfunction: Management Approach

- Multi-disciplinary approach that incorporates a biopsychological model of the sexual response
- Psychologist or sex therapist
- Physical therapist trained in pelvic floor disorders
- Promote relaxation of tight, tender pelvic floor muscles
- Direct dilator therapy
- Decrease fear of penetration

Breast Cancer Screening After Radiation

<table>
<thead>
<tr>
<th>Clinical Breast Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yearly beginning at puberty until age 25 then every 6 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Screening Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yearly mammogram beginning 8 years after radiation or at age 25 whichever occurs last</td>
</tr>
<tr>
<td>Yearly MRI (adjunct) beginning 8 years after radiation or at age 25 whichever occurs last</td>
</tr>
</tbody>
</table>

Cervical Cancer Screening: Immunocompromised

- If 3 consecutive normal cytology, cytology every 3 years
- If 3 consecutive normal cytology, cytology every 3 years
- Perform annual cytology
- < age 30
- Screen within 1 year of sexual debut with cytology only
- < age 21
- Perform annual cytology
- Perform annual cytology
- < age 30
- Screen within 1 year of sexual debut with cytology only
- < age 21
### Practice Pearl

- Evaluation of reproductive late effects - more than just fertility
- Preventive screening guidelines for immunocompromised patients
- Early evaluation for GVHD and vaginal stenosis recommended
- Estrogen therapy should not be delayed when indicated
- Contraception and sexual function management is vitally important

### Future Directions

- Identify targeted agents that minimize gonadal injury
- Improve risk stratification to better identify candidates for fertility preservation pre-treatment
- Standardize assessment and management of reproductive late effects in survivorship
- Optimize ovarian tissue transplantation procedures
Patient Experiences

“75% of cancer survivors without children stated they wanted to have children in the future.”

“Women counseled about their risk of infertility by an oncologist and a fertility specialist had significantly less regret about their decision to preserve fertility that those counseled only by an oncology team.”

“Patients experience less regret and have improved quality of life when counseled about fertility preservation options even if no option is pursued.”


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Save the Date!
Fertility Preservation and Reproductive Late Effects Conference

University of Colorado Cancer Center | Children's Hospital Colorado
Friday May 21st and Saturday May 22nd, 2021
Denver, Colorado, USA
Chair: Leslie Coker Appiah, MD and Co-chair Anna Franklin, MD
FEMALE SEXUAL DYSFUNCTION... 
FACTS & FICTION

Christine Isaacs, MD
Professor
Department of Obstetrics & Gynecology

CONFLICTS: NONE

Objectives:
1. Review the prevalence of sexual dysfunction disorders in women
2. Identify barriers that exist in identifying disorders
3. Understand the current model of the sexual response cycle

The Sex Talk...
Part 1

1,769 miles
44-57% OF MIDDLE-AGED AND POSTMENOPAUSAL WOMEN EXPERIENCE SOME INVOLUNTARY URINE LOSS

ACOG Practice Bulletin No. 155

15% OF COUPLES ARE AFFECTED BY INFERTILITY

ACOG Committee Opinion, No. 781
43% OF AMERICAN WOMEN REPORT EXPERIENCING A SEXUAL PROBLEM

ACOG Practice Bulletin No. 213

WHAT IS NORMAL?

(A misleading concept... Sexually speaking)

MODELS OF “NORMAL”...

Masters & Johnson, 1966
“Linear Model”

Kaplan & Leif, 1979
Modified to Include Desire

(Kingsberg and Woodard, Obstet Gynecol 2015)
COMPONENTS OF DESIRE:

- Biologic drive
  - Spontaneous sexual interest
  - Not fully understood
  - Declines with aging in men and women
- Cognition
  - Expectations, beliefs and values
- Motivation
  - Willingness

Linear based model...relies on spontaneous sexual desire
COULD ANOTHER MODEL EXIST?

- One that incorporates the importance of...
  - Intimacy
  - Sexual stimuli
  - Relationship satisfaction

Acknowledging the complexity of women’s sexual functioning

BASSON’S NONLINEAR MODEL

- Women can begin from a point of sexual neutrality
- Desire can result from arousal in the context of a loving relationship

(Basson, Obstet Gynecol 2001)

(Basson, Obstet & Gyn 2001)

(Basgby and Woodard, Obstet Gynecol 2013)
DYSFUNCTION...WHEN SOMETHING GOES WRONG

- Desire disorder
- Arousal disorder
- Orgasmic disorder
- Pain disorder

SEXUAL DYSFUNCTION

HOW COMMON IS THIS?
• 43% of American women report a sexual problem.
• 12% report that it leads to personal distress.
• Problems increase with advancing age.

(Predominance of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking (PRESIDE), 2008)

Distressing problems PEAK in women in midlife.
Cross-sectional population-based survey of female adults in the US.

n=31,581

(Prevalence of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking (PRESIDE), 2008)

WE HAVE A SMALL PROBLEM....

• International Survey of 27,800 men and women age 40-80
  • 80% had experienced at least 1 sexual problem
  • Only 5% had been asked about their sexual health during a routine visit during the past year.
2004 SURVEY ANNUAL MEETINGS OF FOUR MAJOR SPECIALTY SOCIETIES...

- ACOG
- ACM
- Endocrine Society
- NAMS
- American Society for Reproductive Medicine

Biggest obstacles to discussing sexual health with patients?
(Bachmann G. J Sex Med 2006;3:639)

22

ANSWER?

- #1...Limited time!
- Embarrassment
- Lack of effective treatment options
- Limited training on female sexual function
- Reliance on patients to initiate the discussion
- 60% of respondents rated their knowledge and comfort level with FSD as only fair to poor

23

3,807 WOMEN ASKED WHY THEY DID NOT SEEK HELP FOR SEXUAL PROBLEMS...

- Embarrassed
- Fear of provider embarrassment
- Fear they could not get help/no treatment
- It didn’t occur to seek help from a doctor

(Parish, Sex Med Rev 2016; 4:103-120)

24
Reflects the constant evolution and thinking of the time...

1st edition (1952) listed diagnosis of "impotence" and "frigidity"
SEXUAL DISORDERS...DSM-5

- Must be associated with PERSONAL DISTRESS
- Requires a minimum duration of 6 months
- Must experience the disorder 75-100% of the time

DSM IV
LINEAR model (5 dysfunctions)
1. Desire
2. Arousal
3. Orgasm
4. Dyspareunia
5. Vaginismus

DSM V
Complex model (3 dysfunctions)
1. Female Sexual Interest/Arousal Disorder
2. Orgasm
3. Genitopelvic Pain/Penetration Disorder
SUMMARY OF WHAT WE NOW KNOW...

1. Female Sexual Dysfunction is very common in your patients
2. Newer “circular” models illustrate the complexity of the female sexual response cycle…perhaps a good thing!
3. There are LOTS of barriers to discussing/helping patients

WHAT IS THE CLINICIAN TO DO?

How can you fix things?
Part 2...stay tuned...
Monday
CONFLICTS: NONE

Objectives:
1. Review the evaluation of female sexual dysfunction (FSD)
2. Understand common medication(s) affecting FSD
3. Discuss interventions to aid the patient with distressing female sexual dysfunction(s)
BARRIERS!

>40% of women

WHAT WE DO?

1st...

Ask!
SCREENING TOOLS....

LOGIC OF ONE KEY QUESTION®

“Do you have any problems/concerns with your sex life?”

6 month duration?
Causing distress?
Experienced 75% or more of the time?

2ND IDENTIFY THE TYPE OF FSD

- Sexual interest/arousal disorder
- Orgasmic disorder
- Genitopelvic pain/penetration disorder
- Substance/medication-induced dysfunction
Female Sexual Dysfunction: Facts & Fiction,
Part 2

1. Desire
2. Arousal
3. Orgasm
4. Dyspareunia
5. Vaginismus

Complex model (3 dysfunctions)
1. Female Sexual Interest/Arousal Disorder
2. Orgasm
3. Genitopelvic Pain/Penetration Disorder

3rd...
- Reassure patient
- Normalize the problem
- No quick fix

4th... REVIEW MEDICATIONS
Incidence of SSRI sexual dysfunction 30-50%

Typically manifesting as:
- delayed/absent orgasm
- decreased libido

[Table of Medications Associated With Sexual Problems]

- Adderall 15-30mg BID
- Mirtazapine 15-45mg BID
- Venlafaxine 75-225mg BID
- Bupropion 150mg BID

[REVIEW MEDICATIONS]

- Cochrane Database of Systematic Reviews, 2013
  - 25 trials
  - 1,866 participants (men & women)
  - Addition of Bupropion 150mg BID “most promising approach” studied
  - Absence of trials assessing:
    - Switching agents
    - Psychological interventions
    - Drug holidays

[Note: My sources for managing sexual dysfunction associated with antidepressant medications. Cochrane Database of Systematic Reviews 2013, issue 6.]
**5TH... MEDICATIONS TREATMENT?**

1. Sexual interest/arousal disorder  
2. Orgasmic disorder  
3. Genitopelvic pain/penetration disorder

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**SEXUAL INTEREST/AROUSAL DISORDER MEDICATIONS...**

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* Stay tuned for practical advice
GENITOPELVIC PAIN/PENETRATION DISORDER

- Life long or acquired
  - Medical
  - Structural
  - Psychosocial etiologies
- Often resolves in response to treatment of the etiology
- "Genitourinary syndrome of menopause"
  - Symptoms associated with declining levels of estrogen
  - Affects up to 50% of menopausal women

6TH ... GIVE SPECIFIC SUGGESTIONS

"In the author's clinical experience, sometimes, in the most uncomplicated cases, a new and attractive partner is all that is needed."

**INTRODUCE NOVELTY**

- Lubricants
- Enlarge as appropriate
- Sexual devices
- Fantasy
- Various treatments can be used independently or in conjunction with each other
- *Be specific!*

(Basson, Clinical Update Women's Health Care 2014;XIII(2))

**LUBRICANTS**

- Encourage trial-and-error
  - Water-based
  - Silicone-based
  - Oil-based

(Lubricants available on Amazon, search🔍: “personal lubricants”)

(Images sourced from Google Image Search)

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**Female Sexual Dysfunction: Facts & Fiction, Part 2**

1/24/20

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22

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23

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24
Propose a schedule!

IT TAKES 21 DAYS TO MAKE OR BREAK A HABIT.
Let's get started.

ACOG WEB SITE...PATIENT RESOURCES

www.acog.org

Your Sexual Health

The purpose of this brochure is to:
1. Define sexual and reproductive health
2. Provide information on issues related to sexual and reproductive health
3. Help you make informed decisions about your health

www.acog.org
REVIEW….

1. Ask!
2. Determine the dysfunction
3. Reassure/normalize
   - 40%
4. Review medications
   - SSRI use?
5. Discuss the utility of medications
6. Give specific suggestions
   - Novelty/fantasy/devices/schedules/ACOG.org
7. Make a follow up plan!
   - Appointments/patient portals

EFFECTIVE LECTURES….

- Your attention span to listen is between 10-15 minutes
- Students capture ~20-40% of main ideas
- After 3 weeks, you remember less than 10% of what was said

20-40%....

1. Ask!
2. Determine the FSD
3. Reassure
4. Review medication
5. Advise medication?
6. Novelty!
7. Follow up

10%....

"SEX APPEAL IS 50% WHAT YOU’VE GOT...
AND 50% WHAT PEOPLE THINK YOU’VE GOT."

-Sophia Loren
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Jill K Davies MD
Associate Professor, Department of Obstetrics & Gynecology
Denver Health Medical Center
University of Colorado School of Medicine

National Center on Birth Defects and Developmental Disabilities

Travel During Pregnancy: Beyond Zika

IDSOG Annual Meeting
August 9, 2019

Dana Meaney-Delman, MD MPH FACOG
Chief, Prevention Research and Translation Branch
Centers for Disease Control and Prevention

THANKS TO DR. MEANEY-DELMAN AT CDC FOR USE OF HER SLIDES

Disclosure

- No conflicts of interest to report.

- The opinions presented are those of the presenter and do not necessarily represent the official position of CDC.
Disclosures

1. Before Zika, I rarely asked my patients about travel.
2. During Zika, I only asked my patients about travel to Zika-affected areas.
3. Now, I try to remember to ask all my patients about travel during pregnancy to assess their risk of infectious diseases associated with travel.
Travel During Pregnancy

5-59% of women travel internationally during pregnancy
- Trips to see family and friends
- “Babymoon” or other pre-baby vacation
- Work trips
- Majority of pregnant women do not seek pre-travel advice
- If pre-travel advice is sought, it’s close to time of travel

CDC Recommendations for Pregnant Travelers

Pretravel Care and Travel Health Insurance

The first thing you should do when planning an international trip is to make an appointment with a healthcare provider who specializes in travel medicine. You should ideally visit the travel clinic at least 6 weeks before you leave. A travel medicine specialist can review your itinerary, make recommendations based on the health risks at your destination, and give you any vaccines you may need. You should also talk to your obstetrician or ODM about your trip and advice on whether it’s safe for you to travel. Your travel medicine doctor and your obstetrician should talk to each other about your care.


What about travel health insurance? Medical evacuation?


Pregnant Travelers

Frequent questions about travel safety with a baby

Pregnant women can generally travel safely with a baby, but they should avoid some destinations, including those with Zika and malaria risk. Learn about steps you can take if you’re pregnant and planning an international trip, especially to a high-risk country, as in the Netherlands country. For more information, contact your doctor and your baby’s safety and health.
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Zika Travel Recommendations

- **CDC Zika travel guidance: January 2020**
  - Pregnant women **should not travel to areas with Zika outbreaks**, and should talk to their HCP about risks and possible consequences before traveling to an area with current or past transmission of Zika.

- **WHO travel guidance: January 2020**
  - Pregnant women avoid **travel to areas with Zika virus transmission**, particularly during outbreaks, based on the increased risk of microcephaly and severe congenital malformations in infants born to women infected with Zika virus during pregnancy.
  - If pregnant women or women who may become pregnant must travel, talk with HCP and consider risks and possible consequences of infection before traveling to areas where there may be Zika virus transmission.


CDC Zika Clinical Guidance: A History

<table>
<thead>
<tr>
<th>Year</th>
<th>Pregnant women guidance</th>
<th>Pregnancy guidance</th>
<th>Pregnancy guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>openhagen and pregnant women should be advised to avoid travel to areas with Zika virus transmission.</td>
<td>Updated guidance for women of reproductive age</td>
<td>WHO travel guidance: January 2020</td>
</tr>
<tr>
<td>2017</td>
<td>Updated guidance for women of reproductive age</td>
<td>WHO travel guidance: January 2020</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>WHO travel guidance: January 2020</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>WHO travel guidance: January 2020</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

World Map of Areas at Risk of Zika

Map Legend
- Countries or territories with current Zika outbreaks
- Countries or territories with past Zika outbreaks
- Countries or territories with no reported Zika virus transmission
- Countries or territories with no reported Zika virus transmission in humans
- Countries or territories with no reported Zika virus transmission in humans and no reported Zika virus transmission in non-human primates

Aedes aegypti mosquitoes also transmit dengue virus
Honduras experiencing outbreak of dengue, 34k cases, ~60 deaths
Currently (Jan 2020) dengue infections outnumber Zika 200:1

CDC Updated Testing Recommendations: June 2019
Symptomatic pregnant women should receive Zika and dengue virus testing concurrently. Testing recommendations for asymptomatic pregnant women have not changed

Dengue During Pregnancy
- Perinatal transmission can occur
- Increased risk of adverse outcomes
  - Premature birth (OR=2.4; 95% CI 1.3 to 4.4)
  - Late stillbirth (OR=4.2; 95% CI 1.1 to 4.3)
  - Fetal death (≥50 increases risk)
- Dengue infection in neonates can cause:
  - Thrombocytopenia
  - Ascites or pleural effusions
  - Fever
  - Hemorrhage
  - Hypotension
- Treatment: supportive
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Pre-Travel Preparations

Pre-Travel Considerations

- Location specific risks for endemic diseases + outbreaks based on epidemiology*
- Existing immunity and immunization status
- Prophylactic medications
- Preventative behavior for insect, food, and water risks
- Emergency care options at destination

*Infectious disease surveillance varies widely by country

Pre-Travel Counseling: Patient A

26-year-old healthy woman at 20 weeks gestation comes for a OB visit & "surprise" pre-travel consultation. She will be going to Israel to visit family for 3 weeks.

- What are you concerned about?
- What guidance would you give her?
- Where would you get more information?
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

### Tools for Travel Recommendations

1. **Pre-travel PREP**
   - CDC’s Travelers’ Health Website

2. **Heading Home Safely** — info on post return to stay healthy (Mass Gen + CDC + TravEpiNet)

### Recommendations for Patient A

- **Routine vaccines**
  - Tdap
  - Influenza

- **Location-specific vaccines**
  - Hepatitis A
  - Inactivated typhoid

- **Preventative behavior**
  - Avoid insect bites that may carry vector-borne diseases
  - Safe eating and drinking to avoid infectious diseases (e.g., Hep A, Listeria)
  - Wearing helmet/seatbelt

### Additional Behavioral Precautions

- Good hand hygiene
- Contaminated food and water:
  - Traveler’s diarrhea
  - Hep A and Hep E
  - Parasitic infections
- Avoid tap water; ice made from tap water; raw foods mixed with tap water
- Osborne’s rule: meat bacterial and viral pathogens
- Rotavirus cysts of Giardia, Enterobiasis & cysts of Cryptosporidium survive
- Boiled, treated or bottled water can be used
- Carbonated beverages, beer, wine and drinks made with bottled water are safe
- Produce peeled by the traveler may be eaten (e.g., orange, banana)
- Food should be well cooked and eaten while hot
- Avoid unpasteurized dairy products and undercooked meat and fish
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

**Behavioral Precautions-2**
- Travel to areas with VECTOR BORNE DISEASES (malaria, dengue, chikungunya, Zika)
- Prevent bites
  - Avoid outdoor exposure during feeding time—between dusk & dawn for malaria, West Nile virus and Japanese encephalitis
  - During the day for dengue, chikungunya and Zika
- Wear clothing that reduces the amount of exposed skin
- Use insect repellent
- Insecticide treated fabrics
- Swimming & beaches
  - Avoid swimming in fresh water where schistosomiasis is prevalent
  - Even short exposures to infected water during rafting or swimming enough for transmission
  - Swimming in chlorinated or salt water is safe
  - Rafting or exposure to flood waters can expose to leptospirosis
  - Walking barefoot or with open shoes on beaches, soil or water that may be contaminated with human or canine feces may lead to contact with hookworm or Strongoloides larvae
- Sunglasses and sunblock — UVA & UVB protection
- Avoid approaching animals

**Hepatitis A**
- Pregnant women are not at an increased risk of hepatitis A infection nor do they experience more severe infection
- Maternal infection during pregnancy rarely results in adverse outcomes; some reports of preterm labor, placental abruption, premature rupture of membranes
- Pregnant women with travel-related risk should receive at least one dose of Hep A vaccine prior to travel: pregnant women appear less likely to get vaccine (28% vs 51%)
  - Inactivated vaccine so safe for pregnant women
- IgG is effective for post-exposure prophylaxis and can be administered during pregnancy if indicated

**Typhoid Fever**
- Fever may last longer among pregnant women
- Reports of intrauterine transmission, preterm birth and pregnancy loss
- Pregnant women with travel-related specific risk should consider the inactivated vaccine; oral vaccine is live attenuated so not preferred
  - Pregnant women less likely to get typhoid vaccination (35 vs 74%)
- Treatment
  - Antimicrobial therapy shortens the duration of fever and reduces the risk for death; however, antimicrobial resistance is widespread
  - Azithromycin is the drug of choice to treat multidrug-resistant strains causing uncomplicated disease; severe infections should be treated with a carbapenem

![Travel Advice. Aug 2019](https://www.cdc.gov/hepatitis/hav/havfaq.htm)

**Typhoid Fever during pregnancy**
Pre-Travel Counseling: Patient B

31-year-old healthy woman at 30 weeks gestation comes for a pre-travel consultation. She is planning to travel to Ghana for 1 week to attend a funeral of a family member.

- What are you concerned about?
- What guidance would you give her?

Recommendations for Patient B

- Consider postponing travel
- If traveling:
  - Routine vaccines
  - Location specific vaccines
    - Hepatitis A and B
    - Typhoid
  - Antimalarials
  - Preventative behavior
    - Avoid insect bites
    - Safe eating and drinking

Safe Eating & Drinking

- Good hand hygiene—also carry hand sanitizer
- Contaminated food and water:
  - Traveler’s diarrhea
  - Hepatitis A and E, Listeria
  - Parasitic infections such as toxo & schistosomiasis
  - Avoid tap water, ice made from tap water, raw foods
  - Chlorination kills most bacterial and viral pathogens
  - Boiled or treated water (can be used)
  - Sealed carbonated beverages, beer, wine and drinks made with boiled water are safe
  - Produce peeled by the traveler may be eaten (eg orange, banana)
  - Food should be well cooked and eaten while hot
- Avoid unpasteurized dairy products and undercooked meat and fish

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2860824/
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Behavioral Precautions-2

- Travel to areas with vector borne diseases (malaria, dengue, chikungunya, Zika)
  - Wear long-sleeved shirts and pants
  - Use insect repellent
  - Insecticide treated fabrics

- Prevent bites
  - Avoid outdoor exposure during feeding time — between dusk & dawn for malaria, West Nile virus and Japanese encephalitis
  - During the day for dengue, chikungunya and Zika
  - Wear clothing that reduces the amount of exposed skin
  - Use insect repellent
  - Insecticide treated fabrics

- Swimming & beaches
  - Avoid swimming in fresh water where schistosomiasis is prevalent
  - Even short exposures to infected water during rafting or swimming enough for transmission
  - Swimming in chlorinated or salt water is safe
  - Rafting or exposure to flood waters can expose to leptospirosis
  - Cutting or trauma of skin with open wounds on beaches, sand or water that may be contaminated with human or canine feces

- Sunglasses and sunblock—UVA & UVB protection
  - Avoid approaching animals

Prevention of Mosquito-borne Diseases

- Use Environmental Protection Agency (EPA)-registered insect repellent*
  - DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol, or 2-undecanone
- Wear long-sleeved shirts and pants and permethrin-treated clothing
- Stay in places with air conditioning or with door and window screens
- Sleep under an insecticide-treated bed net

*Malaria

- Pregnant women are at higher risk of severe disease and adverse pregnancy outcomes
- No prophylactic regimen provides complete protection
- Pregnant women should ideally avoid travel to malaria endemic areas. If travel is unavoidable, pregnant women should take precautions to avoid mosquito bites and use an effective prophylactic regimen

- For pregnant women traveling to malaria endemic areas
  - Recommended drugs
    - Chloroquine
    - Mefloquine (for areas with chloroquine resistance)
  - Contraindicated drugs
    - Doxycycline
    - Primaquine (infant can’t be tested for G6PD deficiency)

https://www.cdc.gov/malaria/travelers/drugs.html
**Most Common Illness: Travelers’ Diarrhea**

- Attack rates of 30-70%
  - “boil it, cook it, peel it, or forget it” prevents most
- Enterotoxigenic E. coli is the most common cause, but other bacteria, viruses, and protozoa can cause illness
- Prevention measures include safe eating and drinking and proper handwashing, but prophylactic antibiotics may be considered for short-term travelers
  - Risks of prophylactic antibiotics weighed against benefit of prompt self-treatment when moderate/severe TD occurs, shortening duration of illness to 6-24 hours
  - Bismuth subsalicylate not recommended for pregnant women—otherwise ppx can decrease TD by 50%


---

**Treatment of Travelers’ Diarrhea**

- For mild illness, oral rehydration therapy (ORT) is recommended
- For moderate illness, antibiotics may be used in addition to ORT
  - Azithromycin is the preferred treatment
- For severe illness, antibiotics should be used in addition to ORT
  - Azithromycin is the preferred treatment
- Pregnant women should seek medical care for any moderate to severe diarrhea because of risks of dehydration


---

**Summary of Pre-Travel Considerations**

- Review
  - Location specific risks for endemic diseases + outbreaks based on epidemiology
  - Existing immunity and immunizations status
  - Prophylactic medications
  - Preventative behavior for insect, food, and water risks
  - Emergency care options at destination

Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Post-Travel Considerations

Illnesses associated with fever within first 2 weeks post-travel

<table>
<thead>
<tr>
<th>Systemic febrile illness with initial nonspecific symptoms</th>
<th>Fever with central nervous system involvement</th>
<th>Fever with respiratory symptoms</th>
<th>Fever and skin rash</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>Dengue</td>
<td>Typhoid fever</td>
<td>Ricinoidal diseases (such as scrub typhus, spotted fever)</td>
</tr>
<tr>
<td>African trypanosomiasis</td>
<td>Acute HIV infection</td>
<td>Leptospirosis</td>
<td>Yellow fever</td>
</tr>
<tr>
<td>Viral hemorrhagic fever</td>
<td>- Meningococcal meningitis</td>
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<tr>
<td>- Malaria</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- Acute viral encephalitis (such as Japanese encephalitis or West Nile virus)</td>
<td></td>
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<tr>
<td>- African trypanosomiasis</td>
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</tr>
<tr>
<td>- Typhus</td>
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</tbody>
</table>


Post-travel: Clinical Case #1

21-year-old healthy woman presents to your office at 22 weeks gestation with history of fever, malaise, cough, and conjunctivitis for 5 days and then developed a maculopapular rash. She has recently traveled to Ukraine to see her family.

What are you concerned about?

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Post-travel: Clinical Case #1

On further questioning, she reports that several others in her family have had the same symptoms.

She then discloses that she has not been vaccinated for any infectious diseases because it is against her beliefs.

Clinical Presentation

Reported Measles Cases
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Recent Measles Cases in the US States

February 2019
40 cases
December 2019
1382 cases as of December 31

Measles and Pregnancy

- Pregnant women at higher risk for adverse outcomes
  - More likely to be hospitalized (60-96%)
  - More likely to develop pneumonia (10-40%)
  - More likely to die (3-18%)
- Increased risk of adverse pregnancy outcomes
  - Low birthweight (11-17%), preterm birth, admission to NICU
  - Possible association with spontaneous abortion, intrauterine fetal death, neonatal mortality
  - No conclusive evidence for birth defects
- Congenital measles (0-12.5%)
  - Mortality and panencephalitis

Rasmussen and Jamieson, 2015

Treatment of Measles

- Measles incubation period ranges from 7 to 21 days from exposure to onset of fever; rash usually appears about 14 days after exposure
- Airborne isolation for 4 days after appearance of rash
- Supportive care
- Intravenous immunoglobulin within 6 days of exposure as post-exposure prophylaxis

Rasmussen and Jamieson, 2015
Post-travel: Clinical Case #2

24-year-old healthy woman presents to your office at 23 weeks gestation with high fever and flu-like symptoms 10 days after a 2-week trip to Nigeria. She reports staying in “rustic” accommodations, and sleeping with windows open.

– What are you concerned about?
– How does travel history affect your differential diagnosis?
– What could help you narrow the diagnosis?
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Malaria During Pregnancy

- Uncomplicated malaria: symptoms present without signs of vital organ dysfunction
  - High fever, chills, sweats and headache
- Severe malaria: infection complicated by serious organ failures, abnormalities in the patient’s blood or metabolism, for example:
  - Neurologic, renal, respiratory or cardiovascular failure
  - Anemia, hypoglycemia, metabolic acidosis
  - Hyperparasitemia
- Congenital malaria is rare and resembles neonatal sepsis

Malaria Treatment

- Treatment depends on the Plasmodium species, drug resistance, and severity of disease
- CDC website lists drug resistance by country to inform treatment decisions
- Uncomplicated malaria
  - Chloroquine (if sensitive)
  - Quinine and clindamycin
  - Mefloquine
  - Artemether/Lumefantrine in 2nd and 3rd trimester (1st trimester too if no other options)
- Severe malaria
  - IV artesunate for 48 hours
  - After the course of IV artesunate is completed, a follow-up drug must be administered

Summary of Post-Travel Considerations

- Assess for symptoms; onset of illness relative to travel
- Determine
  - travel history (itinerary and duration)
  - exposure by country
  - behavior risks (insect precautions, food and water consumption, sexual activity)
  - Immunizations prophylaxis
- Prompt treatment
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Take Home

- Pregnant women are traveling more frequently; assess risk during prenatal care and monitor epidemiology
- Pre-travel planning and counseling can help pregnant women make informed travel decisions and prevent infectious diseases
  - Vaccines
  - Prophylaxis
  - Behaviors
- Post-travel awareness of exposure, symptoms and treatment options can mitigate adverse outcomes

Resources

- CDC Yellow Book
- CDC Travelers’ Health Website
  - https://wwwnc.cdc.gov/travel
- Global TravEpiNet Pre-travel Prep Tool
  - https://gten.travel/prep/prep
- Malaria Information and Prophylaxis, by Country
  - https://www.cdc.gov/malaria/travelers/country_table
- Yellow Fever Vaccination Clinics

Acknowledgements

Kristina Angelo
Cheryl Broussard
Carly Goodroe
Susanne Gilboa
Peggy Homan

Meredith Moore
Ruth Perou
Kara Polen
Cathy Young
Ali Walker

For more information, contact CDC

(800) CDC-INFO (232-4636)
TTY: (888) 232-6466

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

![Laboratory-Confirmed Symptomatic Zika Virus Disease Cases* with Illness Onset in 2016–2018](image)

**Laboratory-Confirmed Symptomatic Zika Virus Disease Cases* with Illness Onset in 2016–2018**

*Includes reported confirmed and probable Zika virus disease cases per the CSTE case definitions

![Rubella Reported Cases per Million (12M period)](image)

**Rubella Reported Cases per Million (12M period)**

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>Rate</th>
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</thead>
<tbody>
<tr>
<td>China</td>
<td>31717</td>
<td>22.600</td>
</tr>
<tr>
<td>India</td>
<td>2930</td>
<td>2.210</td>
</tr>
<tr>
<td>Japan</td>
<td>2369</td>
<td>18.540</td>
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<tr>
<td>Nigeria</td>
<td>1681</td>
<td>9.040</td>
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<tr>
<td>South Africa</td>
<td>1150</td>
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<td>Pakistan</td>
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<tr>
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<td>DR Congo</td>
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<td>Uganda</td>
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<td>8.050</td>
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<tr>
<td>Poland</td>
<td>310</td>
<td>8.110</td>
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<td>Other countries with high incidence rates***</td>
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<tr>
<td>Central African Republic</td>
<td>178</td>
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<tr>
<td>Timor-Leste</td>
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<tr>
<td>United Arab Emirates</td>
<td>107</td>
<td>11.540</td>
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<td>Tunisia</td>
<td>120</td>
<td>10.520</td>
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<tr>
<td>Liberia</td>
<td>39</td>
<td>8.450</td>
</tr>
</tbody>
</table>

**Notes:** Based on data received 2020-01 and covering the period between 2018-12 and 2019-11. Incidence: Number of cases / population size.

![Current Ebola Outbreak in DRC](image)

**Current Ebola Outbreak in DRC**
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

**Human to Human Transmission**

Ebola virus can be found in all body fluids:

- Blood
- Feces/Vomit
- Urine
- Tears
- Saliva
- Breast milk
- Amniotic fluid
- Vaginal Secretions
- Sweat
- Semen

Contact (through a break in skin, mouth, eyes) with the body fluids of a person that is sick or has died of EVD.

**Ebola Outbreak**

- August 1, 2018: DRC declaration of outbreak
- June 12: Spread to Uganda (3 cases)
- July 17: WHO declared Public Health Emergency of International Concern

**Outbreak Progression**

As of August 6, 2019:

- 2,781 total cases (2687 confirmed, 94 probable)
- 1886 total deaths (67% case fatality proportion)
- ~ 120 total healthcare worker infections
Ebola and Pregnancy

- Limited information
- No evidence of increased susceptibility
- Increased risk for severe disease and death
  - Maternal mortality about 90% in prior outbreaks, lower in 2014-2016 outbreak
- Increased risk for spontaneous abortion, stillbirth, and pregnancy-related hemorrhage
- High perinatal mortality rates among infants of Ebola-infected women
- Ebola virus can cross the placenta and maternal-fetal transmission is likely

https://www.cdc.gov/vhf/ebola/clinicians/evd/pregnant-women.html

Recombinant Vesicular Stomatitis Virus-Based Ebola Virus Vaccine

- Live vaccine containing a piece of Ebola virus
- Experimental
- Given as a single dose
- Protects only against Ebola virus (species Zaire ebolavirus)

Offered to:
- Contacts and contacts of contacts of EVD cases (deceased or alive) through a ring vaccination strategy
- Frontline healthcare workers

Eligibility criteria:
- Children >6 months of age
- Adults, including pregnant and lactating women

Treatment

- No FDA approved treatments for EVD
- Early supportive care alone can significantly improve chances of survival
- 4 experimental treatments approved for use in DRC through a randomized clinical control trial

<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>Type of Drug</th>
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<tbody>
<tr>
<td>ZMapp</td>
<td>Triple monoclonal antibody cocktail</td>
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<tr>
<td>Regeneron</td>
<td>Triple monoclonal antibody cocktail</td>
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<tr>
<td>mAb 114</td>
<td>Monoclonal antibody</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>Antivirus</td>
</tr>
</tbody>
</table>
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

### Treatment
- Pregnant women with EVD should be treated the same as any other adult
  - Provide fluids and electrolytes
  - Use oxygen therapy to maintain oxygen saturation
  - Support blood pressure
  - Reduce vomiting and diarrhea
  - Manage fever and pain
  - Treat other infections

- Obstetric management should consider risks to woman and potential benefits to neonate

### Management of Ebola and Pregnancy
- History of travel within 21 days from DRC, or recent contact (within 21 days) with a person with Ebola virus disease (EVD), screen for fever and symptoms of EVD
  - If signs or symptoms of EVD, immediate isolation and appropriate infection control
  - Asymptomatic pregnant women who have no other epidemiologic risk factors should receive routine obstetric care.
    - Risk factors include contact with: body fluids from a person with EVD, objects contaminated with body fluids, infected bats or primates, semen from a man with EVD

### Current Ebola Response Challenges
- Complex humanitarian emergency
  - >1 million internally displaced persons in DRC
  - Continuous movement of refugees to neighboring countries, including Uganda, Rwanda, and South Sudan
  - Incidents of violence against response teams & pockets of community resistance
  - High number of EVD deaths occurring outside of an Ebola treatment unit in the community
  - Low number of confirmed cases under surveillance as contacts at the time of notification
  - Transmission chains linked to nosocomial exposures
  - Delays in detection and isolation of cases
Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel

Response Efforts

- DRC Ministry of Health leading response efforts, with assistance from local and international partners, including the World Health Organization (WHO)
- Response activities divided into pillars to include:
  - Surveillance
  - Infection Prevention & Control
  - Points of Entry
  - Laboratory
  - Psychosocial
  - Community engagement
  - Safe and dignified burials
  - Case management
  - Logistics
  - Security
  - Vaccination
  - Laboratory
  - Psychosocial
  - Community engagement

CDC’s role

- United States government, including CDC, working with DRC MOH and other partners to provide technical assistance and expertise in several critical areas, including:
  - Surveillance
  - Data analysis/management
  - Emergency management
  - Health communications
  - Infection prevention and control
  - Vaccination
- As of June 11, 187 CDC staff have completed 278 deployments to the DRC, Uganda, South Sudan, Geneva

Laboratory-Confirmed Symptomatic Zika Virus Disease Cases* with Illness Onset in 2016-2018
Depression in Pregnancy

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Disclosures
I declare that I have no conflicts of interest, financial or otherwise.

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Depression in Pregnancy

Why Perinatal Psychiatry?

Roadmap
- Depression in Pregnancy: The Basics
- Risks of Depression in Pregnancy
- Prevention
- Screening
- Treatment: Focus on Antidepressants

The Myth of Pregnancy as Antidepressant
- Marcus et al., 2003. Journal of Women’s Health

Depression in Reproductive aged Females
Depression in Pregnant Females
Nosology and Nomenclature

DSM-V Criteria for Major Depressive Disorder (MDD) with Peripartum Onset

5 or more of the following during same 2 week period:

- Depressed Mood
- Diminished Interest or Pleasure
- Appetite/Weight
- Sleep
- Psychomotor
- Energy
- Concentration
- Guilt/Worthlessness
- Suicidal Ideation

But can we narrow that down?

1st Trimester Perinatal onset of MDD = anxious/melancholic subtype of depression:

- High anxiety
- Decreased Sleep
- Decreased Appetite
- Psychomotor agitation

Postpartum Onset of MDD more likely to be atypical subtype of depression:

- Anhedonia
- Increased Sleep
- Increased Appetite
- Psychomotor retardation

Who is at risk?

- History of depression
- Discontinuing antidepressants in pregnancy (5 fold increased risk)
- Family history
- Childhood maltreatment
- Single motherhood
- More than three children
- Cigarette smoking
- Low income
- Age <20
- Domestic violence
- Insufficient social support
- Pre-existing hypertension

References:

- Putnam et al 2017. The Lancet Psychiatry
**Depression in Pregnancy**

**Obstetrical Associations with Perinatal Depression**

- Planned C-Sections
- Increased Nausea and Vomiting
- Epidural Analgesia

*Anderson et al. (2004) Obstetrics and Gynecology*

**Associated Risks of Perinatal Depression**

- Pre-term birth (<37 weeks) (RR 1.39; Grote et al. 2010)
- Nerve Growth Factor (NGF) in placental tissue of untreated depression AND controls
- Serotonin
- Triphasic Factors (e.g., NGF)

*Grote et al. (2010) JAMA Psychiatry
Kahoka et al. (2015) PLOS ONE
Dhaval et al. (2013) J Ob Gynecol Neonat Care*

**Associated Risks of Perinatal Depression: Infants**

- 6 fold increased risk of postpartum depression (Beck et al. 2006)
- Low Birth Weight
- Intrauterine Growth Restriction
- Higher plasma cort and norepinephrine in infants, decreased dopamine and serotonin
- Right frontal EEG asymmetry early marker of negative affect
- Increased crying and fussing compared to infants of postpartum onset
- Anxiety levels and increased cortisol age 7 to 8.
- Increased central adiposity at age 3 compared to children of postpartum onset

*Genute et al. (2017) Neuroscience*
Prevention, Screening, and Treatment

- Prevent – Identify at risk individuals
- Screen – Identify MDD in pregnancy
- Treat – Select appropriate strategy

Prevention

- US Preventive Task Force Recs:
  - Refer to counseling services for pregnant women with certain risk factors
  - History of depression
  - Current Subclinical depressive symptoms
  - Low income
  - Adolescents
  - Single parenthood
  - Intimate partner violence
  - History of Adverse Childhood Experiences

  Cognitive Behavioral Therapy and Interpersonal Therapy: NNT 13.5

Screening

- ACDG Screening Recommendations
  - At least once during perinatal period
  - Patient Health Questionnaire-9
    - 5-9 (Mild); 10-14 (Moderate); 15-19 (Moderately Severe); 20-27 (Severe)
  - Edinburgh Postnatal Depression Screen (validated for pregnancy)
    - 7-10 (mild); 11-19 (moderate); 20-36 (severe)
### Basic Treatment Algorithm

**Is depression in severe range?**
- **Yes**: Antidepressant + Psychotherapy Referral
- **No**: Negative/Inadequate response to medication?
  - **Yes**: Psychiatric referral
  - **No**: Inadequate response/worsening?
    - If >19 EPDS or >15 PHQ-9*
      - Caveats: Bipolar Disorder/Psychotic features/Psychiatric emergencies
    - Otherwise: Antidepressant

*Caveats: Bipolar Disorder/Psychotic features/Psychiatric emergencies*

### Choosing an antidepressant: General Principles

- Monotherapy better than polypharmacy
- Use what’s worked
- Use what we have data on
- Use the Lowest **EFFECTIVE** dose
  - But be prepared to increase over course of pregnancy
- Avoid lowering dose/stopping prior to delivery
- Undertreated when entering postpartum
- No evidence of dose relationship to Neonatal Adaptation Syndrome

### Risks of antidepressants

- The limits of observational research
  - Data is confusing and conflicting
  - Confounds
    - Confounding by indication
      - Comparing Antidepressant Exposed vs unexposed VS. Antidepressant exposed vs unmeditated depression
    - More frequent monitoring -> more likely to find minor malformations

Risks of antidepressants

- No impact of on fertility
- Does not increase rate of spontaneous abortion
- Pre-term birth – mean difference of 3 days (Ross et al 2013, JAMA Psychiatry; Lindqvist et al 2014, J Thomb Haemost)
  - Possible dose effect (Roca et al 2011, J Affect Disorders)
- Low birth weight – mean difference 74g (Ross et al 2013)

Risks of Antidepressants: Congenital Malformations

- Sertraline
  - Traditionally the “safe” go to.
  - Recent metanalysis 36% increased risk of cardiovascular related malformations and atrial/ventricular septal defects (Shen et al 2017, Br J Clin Pharmacology)
  - But 3 large meta-analyses negative
- Paroxetine
  - Traditionally the “no no”. Three large meta-analyses. Effect sizes noted to be small.
  - Recent data on paroxetine of >8000 exposed in first trimester compared to depressed unexposed found no increase. (Huybrechts et al 2014, NEJM)

Huybrechts et al 2014 NEJM

- 1,000,000 million enrolled in Medicaid
  - 64,000 on antidepressants in first trimester
  - Outcomes any cardiac malformation, right ventricular outflow tract obstruction, and ventricular septal defect, other cardiac malformation
  - Controlled for risk factors for malformation: maternal illness, other medications
  - Controlled for depression and severity of depression using proxies (number of diagnoses, pain diagnoses, sleep disorders)
Huybrects et al 2014 NEJM

- After adjustment for confounders:
  - No significant association for any antidepressant
    - SSRIs (Paroxetine, Sertraline, Fluoxetine)
    - SNRI (Venlafaxine, Duloxetine)
    - Tricyclic Antidepressant
    - Bupropion

Other risks

- Persistent Pulmonary Hypertension of the Newborn:
  - Either no association or small
    (additional 3 per 1000 infants)

- Postpartum Hemorrhage:
  - No increased risk or small risk
    (Number needed to harm 80-100)

- Poor Neonatal Abstinence Syndrome:
  - 5-85% of cases exposed
  - Resolves within days to two weeks.

Take home: antidepressants

- Data is difficult, conflicting and evolving
- Antidepressants are not major teratogens
- Additional risks (e.g. pre-term birth) may not be clinically significant
- Use a risk – risk model
  for informed consent

Antidepressants vs risks of untreated depression
Summing it all up

- Pregnancy doesn’t protect against Depression
- Depression has risks for mother and infant
- Prevention
  - Identify at risk individuals and refer to counseling
- Treatment
  - Psychotherapy is first line in mild-moderate depression
  - Antidepressants + Psychotherapy in severe depression
  - Not without risk, but consider in context of untreated depression

Where to get help

- MGH Center for Women’s Mental Health
  - [www.womensmentalhealth.org](http://www.womensmentalhealth.org)
  - Up to date information on medications in pregnancy and additional resources
- Colorado Center for Women’s Behavioral Health and Wellness
  - Referrals contact [WBHW@ucdenver.edu](mailto:WBHW@ucdenver.edu)
  - Questions? Want to talk over a case?
    - [Andrew.M.Novick@cuanszhutz.edu](mailto:Andrew.M.Novick@cuanszhutz.edu)
Disclosures: None

- Objectives:
  1. Review educational gaps regarding barrier contraception knowledge
  2. Discuss Emergency Contraception & barriers to access
Clinicians who are not knowledgeable about a contraceptive method may be less inclined to offer that method and thereby limit a patient’s choice.

**Goal:** Assess ob-gyn resident knowledge and training with barrier and over-the-counter contraceptives

**Hypothesis:**

- Survey
  - 50 of 253 Obstetrics-Gynecology residency programs in the US selected via random number table
  - Program coordinators contacted and asked to circulate the survey amongst their residents
  - Surveys were completely anonymous
  - All 9 regions of the country as recognized by the ACGME were represented
  - Both university (56%) and community based (41%) participation

**Results:**

- With regard to condom use, what percentage of residents thought they had adequate knowledge to counsel patients?

  - PGY 1 (27%)
  - PGY 2 (27%)
  - PGY 3 (24%)
  - PGY 4 (22%)
    - 17%
    - 27%
    - 57%
    - 97%
Gender differences?

Percentage of respondents that felt they had adequate knowledge to counsel with respect to ALL condom options?

52% 75%

*Statistically significant. (Miklavcic, Isaacs, 2012)

Was their knowledge actually correct?

Fun facts...

- 96% of residents (n=193) knew that spermicides did not protect against STDs
- 17% had fit or prescribed a diaphragm
- 83% had NO formal education on condoms
- 87% wanted to learn more about the topics on the survey
Condoms...

- **TYPES OF MATERIAL:**
  1. Latex rubber
  2. Synthetic rubber
  - polyurethane
  - polyisoprene
  - nitrile rubber
  3. Natural membrane

- **EFFECTIVENESS:**
  - 13 pregnancies per 100 women as **COMMONLY used**
  - 2 pregnancies per 100 women with **CORRECT use with every act of sex**

(From: *Family Planning: A Global Handbook for Providers*; 2017)
Over-the-Counter & Emergency Contraception

1/24/20

*Latex rubber...

- 80% of condom use in the US
- Avoid oil-based lubricants (baby, coconut, mineral, lotions, butters... this can damage latex
- Safe lubricants:
  - Water
  - Saliva
  - Silicone-based lubricants
- Avoid if allergic to latex

(Family Planning: A Global Handbook for Providers, 2018)

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Latex allergy...

- Severe allergic reactions to condoms are extremely rare
- Mild reactions may involve:
  - Redness
  - Itching
  - Rash
  - Swelling
- Can occur in both men and women
- Estimated 1-4% of US population is allergic to latex
- Prevalence is higher in certain groups:
  - Health care workers

(Natl Inst for Occup Safety and Health, 1997)

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*Synthetic materials...

- Accounts for 15% of condom use
- Expected to provide the same protection as latex
- Less studied
- Compatible with oil and water based lubricants
- Longer shelf life
- More expensive

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Over-the-Counter & Emergency Contraception

*Natural Membrane...

- 5% of condom use
- What is it?
  - Intestinal cecum of lambs
- Not as effective for preventing STIs including HIV...contains small pores which permit the passage of viruses

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*Should spermicide-coated condoms be advised?*

- Prelubricated with nonoxynol-9 spermicide
- Higher cost
- Shorter shelf life
- No more effective than lubricated condoms
- Increased risk of UTI

*NO*

17

* Kling-Tite™ band at base to hold condom in place

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What percentage of condoms break, tear or slip off completely leading to under protection?

- 2%
- Primarily because they are used incorrectly

Emergency Contraception

In 2011, 45% of pregnancies in the US were unintended
- Down from 51% in 2008

www.guttmacher.org accessed Sept 2019

Questions....

- How old do you have to be to get Emergency Contraception (Ex: Plan B One Step®)?
- Do I need a prescription?
- Can my male partner get it?
69% of randomly selected dispensaries in Colorado recommended cannabis products to a woman posing as pregnant with nausea. Few recommended consultation with a health care provider. Women were unlikely to obtain information about marijuana use from their health care provider, relying on anecdotal experience, advice from friends, family and internet.

69% of randomly selected dispensaries in Colorado recommended cannabis products to a woman posing as pregnant with nausea. Few recommended consultation with a health care provider. (Dickson, Mansfield et al. Obstet Gynecology 2018)
Facts...
• Methods of EC have been available in the US since the 1960s
• Age restrictions limited levonorgestrel-EC access to women over the age of 17 until June 2013
• Levonorgestrel 1.5mg (Plan B Once Step®) is over-the-counter emergency contraception
  • No gender restriction
  • No age restriction

Results...
• >50% of inquiries received some form of incorrect information
  • Most common error: age requirements
  • Second most common error: inability of men to purchase
  • Male caller was 1.7 times more likely to be transferred and escalated to a "more knowledgeable" source
  • Females and males were equally likely to get some misinformation

Questions....
• How old do you have to be to get Emergency Contraception (Ex: Plan B One Step®)?
• Do I need a prescription?
• Can my male partner go get it?

What's the lesson learned?
Be vigilant...

• If you are poor, foreign born, or not a high school graduate… you are less likely to have knowledge about emergency contraception

• In a 2008 U.S. survey, 1 in 5 practitioners were reluctant to provide education on the subject of emergency contraception to sexually active adolescents

[ACOG Practice Bulletin, Nov. 102, 2018]

The amount of misinformation on provided regarding EC at point of sale

---

Committee Opinion #768

“ACOG supports over-the-counter access to hormonal contraception without age restrictions.”

“Barriers to access are one reason for inconsistent or nonuse of contraception.”

September, 2019
Management of the Second Stage: The Truth About Laboring Down

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Disclosures
• No financial
• Vice-Chair of Committee for OB Practice for ACOG,
  Editor for Gabbe, Oral board examiner for ABOG

Objectives
• Definitions
• The context
• Data
  – Trials
  – Observations
• OMSS trial
Management of the Second Stage: The Truth About Laboring Down

Second Stage
Definition
• Begins at complete cervical dilation
• Ends with the delivery of the infant

Second Stage Management
• Delayed pushing (laboring down)

Context
• Epidural anesthesia
• Nullipara

Are epidurals bad?

The Risk of Cesarean Delivery with Neuraxial Analgesia Given Early versus Late in Labor
• Randomized trial of term nullips at < 4cm
• Early epidural vs. systemic anesthesia early in labor
• Findings:
  – No difference in rate of cesarean
  – Shorter time-to-delivery in epidural group
  – Better pain control in epidural group

ACOG

“Labor causes pain for many women. There is no other circumstance where it is considered acceptable for an individual to experience untreated severe pain, amendable to safe intervention, while under a physician’s care. In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labor.”

Committee Opinion 339, June 2006

Epidurals

• Here to stay
• Effective for pain reduction
• Associated with longer second stage

Should women delay pushing when complete?

Laboring Down Trials
Management of the Second Stage: The Truth About Laboring Down

Hansen et al
- Nullips + multips, term, regional anesthesia
- Induced or spontaneous
- 312 randomized (252 analyzed)
- Delay: 120 min (nullips), 60 min (multips)
  - Or, head at introitus (evaluated q 30 min)
- Compared to immediate

Hansen SL et al. Obstet & Gynecol, 2002;99:29-34

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Hansen et al
- Delay:
  - Longer second stage
  - Reduce time pushing
  - Reduce fatigue (nullips only)
- No Difference:
  - pH or Apgars
  - Injury, operative delivery, endomyometritis

Hansen SL et al. Obstet & Gynecol, 2002;99:29-34

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Plunkett et al
- Nulliparous, regional anesthesia
- Induced or spontaneous
- 202 randomized
- Delay: 90 min
  - Or, strong urge to push (evaluated q 30 min)
- Compared to immediate


12
Management of the Second Stage: The Truth About Laboring Down

Plunkett et al

- **Delay:**
  - Longer second stage
- **No Difference:**
  - Time pushing
  - Cesarean
  - SVD
  - pH, Apgars
  - Fever, hemorrhage


Gillesby et al

- Nulliparous, regional anesthesia, ≥ 36 weeks
- Induced or spontaneous
- Excluded: women ≥ 275 pounds
- 77 randomized
- **Delay:** 120 min
  - Evaluated q 30 min
- Compared to immediate (within 15 minutes)

Gillesby et al. JOGNN, 2010;29:635-644

<table>
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<tr>
<th></th>
<th>Delay (n=37)</th>
<th>Immediate (n=36)</th>
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<tr>
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<td>68.2</td>
<td>95.8</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Length of 2nd Stage (min)</strong></td>
<td>166.3</td>
<td>107.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Spontaneous VD</strong></td>
<td>81 %</td>
<td>75 %</td>
<td>0.82</td>
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<tr>
<td><strong>5-minute Apgar</strong></td>
<td>9.0</td>
<td>8.9</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Energy</strong></td>
<td>57.9</td>
<td>53.5</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Tiredness</strong></td>
<td>90.1</td>
<td>90.5</td>
<td>0.95</td>
</tr>
<tr>
<td><strong>Overall Satisfaction</strong></td>
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</tbody>
</table>

Gillesby et al. JOGNN, 2010;29:635-644
Fitzpatrick et al

• Nulliparous, term, regional anesthesia
• Induced or spontaneous
• 178 randomized
• Delay: 60 min
• Compared to immediate
• Pushing for all groups: limited to 60 min (local standard)

Fitzpatrick M et al. BJOG, 2002;109:1359-1365

Fitzpatrick et al

• Delay:
  – Longer second stage
• No Difference:
  – Time pushing
  – SVD
  – Augmentation need
  – Neonatal or maternal morbidities
  – Patient satisfaction

Fitzpatrick M et al. BJOG, 2002;109:1359-1365

Frasier et al: PEOPLE Trial

• Multicenter
• Nulliparous, term, regional anesthesia
• Induced or spontaneous
• 1,862 randomized, stratified by oxytocin aug.
• Delay: 120 min
  – or irresistible urge
  – or head at introitus (examined q 15 minutes)
• Compared to immediate

Frasier WD et al. AOGD, 2000;182:1165-72
Frasier et al

• Delay:
  – Decreased ‘difficult delivery’
  – Increased maternal fever
  – Increased low neonatal pH
• No difference:
  – SVD
  – Cesarean
  – Patient Satisfaction

Frasier WD et al. AJOG, 2000;182:1165-72

<table>
<thead>
<tr>
<th></th>
<th>Delay (n=936)</th>
<th>Immediate (n=926)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficult Delivery</td>
<td>17.8%</td>
<td>22.5%</td>
<td>0.79 (0.66 – 0.95)</td>
</tr>
<tr>
<td>Mid-pelvic procedures</td>
<td>9.3%</td>
<td>13.0%</td>
<td>0.72 (0.55 – 0.93)</td>
</tr>
<tr>
<td>Low-pelvic procedures</td>
<td>3.5%</td>
<td>3.8%</td>
<td>0.93 (0.58 – 1.49)</td>
</tr>
<tr>
<td>Cesarean</td>
<td>5.0%</td>
<td>5.7%</td>
<td>0.88 (0.60 – 1.29)</td>
</tr>
<tr>
<td>Spontaneous VD</td>
<td>57.5%</td>
<td>52.7%</td>
<td>1.09 (0.98 – 1.18)</td>
</tr>
</tbody>
</table>

Frasier WD et al. AJOG, 2000;182:1165-72

Meta-Analysis
Management of the Second Stage: The Truth About Laboring Down

RCOG et al

- Delayed vs. Early Pushing
  - With epidural anesthesia
- Delay
  - Longer second stage
  - Reduced pushing time
- No difference: all others, except 2
  - Decreased mid-pelvic procedures
  - Increase fevers

RCOG BJOG, 2004;111:1333-340

Instrumental deliveries

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beattie et al</td>
<td>16</td>
<td>1.69 (1.04 to 3.99)</td>
</tr>
<tr>
<td>Frapart et al</td>
<td>25</td>
<td>1.43 (1.03 to 1.98)</td>
</tr>
<tr>
<td>Fossey et al</td>
<td>24</td>
<td>1.43 (0.90 to 2.28)</td>
</tr>
<tr>
<td>Goodfellow et al</td>
<td>92</td>
<td>0.57 (0.32 to 1.01)</td>
</tr>
<tr>
<td>Hamers et al</td>
<td>1448</td>
<td>0.70 (0.42 to 1.19)</td>
</tr>
<tr>
<td>Hasun et al</td>
<td>265</td>
<td>1.24 (0.55 to 1.55)</td>
</tr>
<tr>
<td>MacQueen et al</td>
<td>37</td>
<td>0.35 (0.25 to 0.88)</td>
</tr>
<tr>
<td>Puhak et al</td>
<td>20</td>
<td>1.27 (0.74 to 2.19)</td>
</tr>
<tr>
<td>Vanc et al</td>
<td>25</td>
<td>1.28 (0.95 to 1.70)</td>
</tr>
</tbody>
</table>

Q = 16.6, df = 8, P = 0.03, F = 1.89

RCOG BJOG, 2004;111:1333-340

Second stage caesarean section

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beattie et al</td>
<td>22</td>
<td>0.29 (0.01 to 0.72)</td>
</tr>
<tr>
<td>Fossey et al</td>
<td>388</td>
<td>0.15 (0.05 to 0.49)</td>
</tr>
<tr>
<td>Hamers et al</td>
<td>479</td>
<td>0.61 (0.30 to 1.28)</td>
</tr>
<tr>
<td>Maloney et al</td>
<td>564</td>
<td>0.16 (0.01 to 1.03)</td>
</tr>
<tr>
<td>Puhak et al</td>
<td>712</td>
<td>0.57 (0.32 to 1.01)</td>
</tr>
<tr>
<td>Vanc et al</td>
<td>20</td>
<td>0.49 (0.10 to 2.36)</td>
</tr>
</tbody>
</table>

Q = 21.6, df = 6, P = 0.001, F = 3.39

RCOG BJOG, 2004;111:1333-340
Tuuli et al

- Delayed vs. Early Pushing
  - Quality

Tuuli O&G, 2012;120:660-8

Spontaneous Vaginal Delivery

Tuuli O&G, 2012;120:660-8

Length of the Second Stage

Tuuli O&G, 2012;120:660-8
Do we care about a longer 2\textsuperscript{nd} stage?

Rouse et al
- Retrospective cohort (FOX trial)
- 4,126 women, \( \geq \) 36 weeks
- Each hour increase duration of second stage
- Maternal and neonatal outcomes
  - Maternal: chorio, 3\textsuperscript{rd} and 4\textsuperscript{th} degree lacs, atony
  - Neonatal: NICU admission

Le Ray et al
- Retrospective cohort (PEOPLE trial)
- 1,862 nullips with epidurals
- Each hour increase duration of second stage
- Maternal and neonatal outcomes
  - Maternal: chorio, hemorrhage, cesarean
  - Neonatal: lower pH

Rouse DJ AJOG, 2009;201:357
Le Ray C AJOG, 2009;201:361
Le Ray et al: Probability of SVD without sign of asphyxia (pH > 7.10 and 5-minute Apgar score > 7)

Allen et al
- Population-based cohort
- 121,517 women, low-risk, term
- Duration of second stage
  - Nullips ≥ 3 hrs
  - Multips ≥ 2 hrs
- Maternal and neonatal outcomes
  - Maternal: chorio, trauma, hemorrhage
  - Neonatal: NICU, low Apgar, low pH

Laughon et al
- Retrospective cohort, MFM-U
- 43,810 nullips and 59,605 multips
- 'Prolonged' vs. 'Within guideline' duration
- Adverse maternal and neonatal outcomes
  - Maternal: chorio, severe laceration, hospital stay
  - Neonatal: NICU admission, sepsis, low Apgars
Grobman et al

- Retrospective cohort study
- 53,285 women at term
- Primary outcomes: cesarean, nn composite
- Longer pushing in nullips and multips:
  - Increased cesarean
  - Increased nn morbidity

Grobman W et al. Obstet & Gynecol 2016; vol 127; 4

All together ...

- Delayed pushing
  - May or may not shorten pushing (in nullips)
  - Prolongs second stage
  - Not improved or worse outcomes
- Prolonged second stage
  - Worse maternal outcomes
  - Worse neonatal outcomes
Management of the Second Stage: The Truth About Laboring Down

Cahill AG et al. JAMA 2018;320:14; 1444-1454

OMSS

- More than 12,000 nulliparous women were screened
- Neuraxial anesthesia
- 2,400+ randomized at complete dilation to
  - Immediate pushing vs. Delay pushing for 60 min
- Primary outcome: SVD

Cahill AG et al. JAMA 2018;320:14; 1444-1454

STOPPED EARLY

Cahill AG et al. JAMA 2018;320:14; 1444-1454
Management of the Second Stage: The Truth About Laboring Down

| Table 1: Management of the Second Stage
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

**Table 2: Characteristics of Natalia Y.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>32 years</td>
</tr>
<tr>
<td>Gestation</td>
<td>39 weeks</td>
</tr>
<tr>
<td>Birth Weight</td>
<td>3.5 kg</td>
</tr>
<tr>
<td>Duration of Second Stage</td>
<td>2.5 hours</td>
</tr>
</tbody>
</table>

**Table 3: Management of the Second Stage in Different Groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Technique</th>
<th>Mean Time (min)</th>
<th>Standard Error</th>
<th>Mean Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Abdominal Traction</td>
<td>90.6</td>
<td>3.4</td>
<td>-4.2 (0.0 to 8.6)</td>
<td>0.26 (0.04 to 0.48)</td>
</tr>
<tr>
<td>Intervention</td>
<td>Forceps Delivery</td>
<td>37.5</td>
<td>2.5</td>
<td>-19.5 (-24.4 to -4.7)</td>
<td>0.36 (0.05 to 0.66)</td>
</tr>
<tr>
<td></td>
<td>Vacuum Extraction</td>
<td>31.2</td>
<td>2.1</td>
<td>-21.5 (-26.8 to -6.3)</td>
<td>0.45 (0.14 to 0.76)</td>
</tr>
<tr>
<td></td>
<td>Augmentation Pessary</td>
<td>36.8</td>
<td>2.3</td>
<td>-17.9 (-23.7 to -2.2)</td>
<td>0.39 (0.07 to 0.71)</td>
</tr>
</tbody>
</table>

Cahill AG et al. JAMA 2018;320:14; 1444-1454

---

Further details and analyses are presented in the full manuscript, available at [Cahill AG et al. JAMA 2018;320:14; 1444-1454](#).
OMSS - Summary

- Delayed pushing in nullips
  - Does not increase the SVD rate
- Delayed pushing
  - Increase in:
    - Post-partum hemorrhage
    - Chorioamnionitis
    - Neonatal acidemia
    - Neonatal sepsis/suspected sepsis

Cahill AG et al. JAMA 2018;320:14; 1444-1454

Cesarean Prevention

- A specific maximum length of the second stage for all has not been identified
- Allow for the historical amount of time for pushing with epidural
- Longer durations may be appropriate on an individual basis

OCC #1 Obstet & Gynecol 2014
Management of the Second Stage: The Truth
About Laboring Down

1/24/20


Second Stage – Questions Remain

• Many...
  ❖ How pushing happens
  ❖ Coached vs. not
  ❖ Oxytocin use and dosing
  ❖ Position

❖ How long is too long?
Thank you
Tuesday
Breast Fundamentals for the Gynecologist

Christine Isaacs, MD

Conflicts of Interest: None

- Objectives
  - Understand what is currently known about breast cancer and why/where variations exist
  - Understand how the American Cancer Society plans breast cancer screening
  - Be conversant in starting the conversation on genetic counseling

What are the current recommendations for breast cancer screening?

- It depends who you ask
Screening Breast exams....

- Proposed in the hopes to detect breast cancer at earlier stages
- Proposed in the hope to decrease mortality & improve survival outcomes

- **Clinical breast exam**: done by a health care provider
- **Self breast exam**: done by women themselves

**SCREENING test**...can have associated harms

- Anxiety
- Fear
- Cost
- Inconvenience
- Additional imaging and biopsies
- Over-diagnosis of benign & malignant findings

The breast exam...

Self breast exam (SBE)...

- General (consensus among groups): NOT in recommended breast self-examination (ACOG, USPSTF, ACS)

- Shanghai Trial
  - 766,665 women, randomized trial in a BRCA1/2 mutation carrier
  - No significant difference in BC incidence in the group of women who did breast self-exams
  - Women in the SBE group: more breast biopsies

- AANR Trial
  - 3,097 women randomized to standard of care vs. follow-up
  - No benefit seen due to breast self-exams: No difference
  - Twice as many biopsies performed in the SBE group
Breast Fundamentals for the Gynecologist

Clinical breast exam...
- American Cancer Society 2012, showed AGAINST.
- U.S. Preventive Services Task Force 2016, showed AGAINST.
- Canadian Task Force on Preventive Health Care 2011, showed AGAINST.
- The World Health Organization 2009, showed may be appropriate in low-resource settings.

Breast exams...
- Well-intended advice
- Not based on science
- Implies that breast should be smooth & perfect
- Not Barbie!

American Cancer Society 2019, no longer recommending clinical breast exams or breast self-exams as part of clinical breast cancer screening. This does not mean that these exams should cease to exist. In some situations, particularly at higher than average risk, breast self-exams may still be useful. Clinical breast exams may also help to promote breast self-exams along with providing an opportunity to review risk and family history. Women might still want to engage in screening activities that they find helpful.
HRSA is supporting the Women's Preventive Services Initiative (WPSI) to develop clinical recommendations. Under the Affordable Care Act, women's preventive health care—such as mammography, screenings for cervical cancer, prenatal care, and other services—generally must be covered with no cost-sharing.

Breast Cancer Screening for Average-Risk Women

- Initiate mammography no earlier than age 40 and no later than age 50.
- Screen biennially vs annually.
- Continue through at least age 74.

“Doctor...I have dense breasts”
Breast Fundamentals for the Gynecologist

How should a mammogram result of dense breast tissue be managed?

- Mostly fatty
- Scattered fibroglandular density
- Heterogeneously dense (can obscure small masses)
- Extremely dense

Established BI-RADS categories
Assessment is subjective

State specific verbiage/patient notification

Women with dense breasts have a modestly increased risk of breast cancer and experience reduced sensitivity of mammography
How should a mammogram result of dense breast tissue be managed?

ACOG does NOT recommend supplemental screening in addition to mammography in women with dense breast tissue or additional risk factors.

No meaningful outcome benefits (reduction in breast cancer mortality) in currently published evidence.

Conclusion: Supplemental US for extremely dense breasts substantially increases costs with little benefit.

No major guidelines recommend supplemental screening.

Sprague et al. 2015; Funded by NCI

- Supplemental US screening after a negative mammogram... for extremely dense breasts
- Averted 0.36 additional breast cancer deaths
- Resulted in 354 biopsies after false positive US results per 1,000 women
- Cost $256,000 per QALY gained
Call backs...

- In the absence of consensus regarding the definition of abnormal exams for screening and diagnosis, the National Comprehensive Cancer Network recommends that women with an abnormal exam be called back to undergo additional exams.

- Most women with an abnormal exam are not at increased risk for breast cancer.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Number of Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with 100% sensitivity</td>
<td>390</td>
</tr>
<tr>
<td>Additional local recurrences</td>
<td>390</td>
</tr>
<tr>
<td>PA examination</td>
<td>390</td>
</tr>
<tr>
<td>BI-RADS 4 mammograms</td>
<td>390</td>
</tr>
<tr>
<td>BI-RADS 5 mammograms</td>
<td>390</td>
</tr>
<tr>
<td>200 (60% mammograms)</td>
<td>390</td>
</tr>
<tr>
<td>60 (60% mammograms)</td>
<td>390</td>
</tr>
</tbody>
</table>

The positive predictive value...

- The percentage of initial screening exams with an abnormal initial interpretation that result in a true diagnosis of cancer within 1 year:
  - 4.4%

[Caption: Image of a graph or table related to screening benchmarks, accessed 11/24/19]
Breast Fundamentals for the Gynecologist

Follow-up Testing Risks of Mammography Screening

Out of every 10 women who get a screening mammogram:

- 90% will not get the mammogram recalled.
- 10% may get recalled for further mammography evaluation.

3-D Mammography: breast tomosynthesis

- 3.5 - 4.5 images of the breast, no overlap
- 3-dimensional picture
- Not universally covered by insurance
- Incremental cancer detection rate of 1-2/1000
- Can decrease recalls up to 30% (take into account patient callback rates)
- Gold standard with data driven mortality reduction: 20% is still the modeled 3D mammogram
Heart disease is the #1 cause of death in US women.
Evidence-Based Management of Category II EFM

Alison G. Cahill, M.D., M.S.C.I
Professor
Department of Women's Health
Maternal Fetal Medicine
The University of Texas at Austin Dell Medical School

Disclosures

• No financial

• Vice-Chair of Committee for OB Practice for ACOG,
  Editor for Gabbe, Oral board examiner for ABOG

Primary Cesarean Indications

Barber et al. Obstet & Gynecol. 2012
EFM, 2020

- Most commonly used instrument in obstetrics
  - 3.7 million births, 2018
- U.S. Preventative Services Task Force = D
  - Lack of evidence for benefit; potential harm
- Cesarean rates
  - 1970: 7%
  - 2018: 32%
- Cerebral palsy
- Stillbirth
- Perceived standard of care
Speaking a Common Language

The 2008 National Institute of Child Health and Human Development Workshop Report on Electronic Fetal Monitoring
Update on Delirations, Interpretation, and Research Guidelines

- 3 tier system
  - Category I: normal
  - Category II: indeterminate
  - Category III: abnormal

Macones et al, 2008, AJOG

Frey et al. BJOG 2018

What we see

- Category I
  - Incidence: 4.1 – 6.0%
  - 2 features: strongly associated with pH ≥ 7.20

- Category III
  - Incidence: 0.4 – 2.1%
  - 2 features: presence of both, pH ≤ 7.00

- Category II
  - The rest
  - No data

EFM Test Characteristics

<table>
<thead>
<tr>
<th>Category</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>0.0%</td>
<td>97.7%</td>
<td>0.0%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Category II</td>
<td>100.0%</td>
<td>2.4%</td>
<td>1.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Category III</td>
<td>0.0%</td>
<td>99.9%</td>
<td>0.0%</td>
<td>98.9%</td>
</tr>
</tbody>
</table>


Learning More about Category II
All models are adjusted for nulliparity, fever, prolonged first stage, and obesity.

AUC, area under the curve; EFM, electronic fetal monitoring.

Cahill AG, et al. Obstet & Gynecol 2012

Other Ways to Look at Cat II

Cat II – Myth Busting

Association of Atypical Decelerations With Acidemia

Allan G. Cahill, MD, et al. Kimberly A. Soeld, MD, Annette D. Wald, MD, and George A. Baram, MD, 2012

- No association with acidemia
  - Shoulders
  - Over-shoots
  - Slow returns

Cahill AG, et al. Obstet & Gynecol 2012

DOBETRICS

Interpreting category II fetal heart rate tracings: does meconium matter?

Heather A. Frey, MD; R. M. Cahill, MD, MPH; Anthony L. Sherman, MD; George A. Mason, MD, MSC; Allan G. Cahill, MD; MSC

- Prospective cohort, 5000 women
- Presence of meconium with Category II
  ➢ Greater likelihood of acidemia and morbidity
  ➢ Worse with thick meconium

Evidence-Based Management of Category II

EFM

Electronic fetal monitoring patterns associated with respiratory morbidity in term neonates

- Prospective cohort, 5000 women, 37 weeks of after
- EFM pattern associated with respiratory morbidity
  - Tachycardia
  - Marked variability
  - Prolonged decelerations


Other Clinical Factors and Cat II

- Magnesium exposure
- Intrauterine growth restriction

Epplin KA et al. Am J Perinatol. 2015

PANORAMA

- Prospective cohort study, 8580 women, 37 weeks or beyond
- 2 hours of EFM prior to delivery
- Patterns predictive of acidemia and neonatal morbidity

Cahill AG, et al. AJOG 2018
Figure 1. Participants

- Non-delivered singleton, non-anomalous deliveries
- Eligible participants
- Excluded: Preterm births, major anomalies, multiple gestations
- Excluded: Cesarean delivery prior to labor
- Excluded: Insufficient EFM, no umbilical cord gas
- Excluded: Incarcerated patients

- Acute acidemia
- No acute acidemia

Cahill AG, et al. AJOG 2018

Predicting Acidemia

<table>
<thead>
<tr>
<th></th>
<th>AUC (95% CI)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever Category III</td>
<td>0.62 (0.57, 0.66)</td>
<td>69.1%</td>
<td>50.0%</td>
<td>2.4%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Total deceleration area</td>
<td>0.76 (0.72, 0.80)</td>
<td>73.5%</td>
<td>67.2%</td>
<td>4.0%</td>
<td>99.3%</td>
</tr>
<tr>
<td>Total deceleration area &amp; ever tachycardic</td>
<td>0.77 (0.73, 0.80)</td>
<td>76.0%</td>
<td>76.2%</td>
<td>5.0%</td>
<td>99.2%</td>
</tr>
<tr>
<td>Total deceleration area, ever tachycardic &amp; always moderate variability</td>
<td>0.77 (0.75, 0.81)</td>
<td>71.4%</td>
<td>68.5%</td>
<td>4.0%</td>
<td>99.2%</td>
</tr>
<tr>
<td>Ever Category III</td>
<td>0.53 (0.49, 0.57)</td>
<td>68.2%</td>
<td>58.7%</td>
<td>11.8%</td>
<td>95.0%</td>
</tr>
<tr>
<td>Total deceleration area</td>
<td>0.66 (0.64, 0.68)</td>
<td>74.8%</td>
<td>54.0%</td>
<td>13.4%</td>
<td>95.7%</td>
</tr>
<tr>
<td>Total deceleration area &amp; ever tachycardic</td>
<td>0.77 (0.75, 0.79)</td>
<td>75.5%</td>
<td>84.6%</td>
<td>26.2%</td>
<td>94.4%</td>
</tr>
<tr>
<td>Total deceleration area, ever tachycardic &amp; always moderate variability</td>
<td>0.77 (0.75, 0.79)</td>
<td>75.5%</td>
<td>85.7%</td>
<td>26.9%</td>
<td>95.2%</td>
</tr>
</tbody>
</table>

Figure 2. Comparisons for acidemia (A) and composite neonatal morbidity (B)

P = .97

P = .01
Clinical Translation

- Deceleration area threshold = 42,000 – 50,000
  - NNT = 5 (acidemia)
  - NNT = 6 (neonatal morbidity)
- Example:
  - Contracting q3 (~40 contractions in the last 120 min), 24-28 decelerations 60 beats below baseline


Problem: How we use the tool

Cahill AG, et al. AJOG 2018
Gain knowledge about the tool

- What do we do when we see this?

ACOG and AWONN

- Maternal lateral repositioning
- Intravenous fluid bolus
- Decrease oxytocin and/or administer tocolytic
- Amnioinfusion
- Maternal oxygen administration

Maternal Positioning

- In theory...
  - Change maternal position → improve placental perfusion → improve fetal oxygenation
  - 20% resolution of decelerations with maternal repositioning
  - Data from 15 laboring women:

<table>
<thead>
<tr>
<th>Maternal position</th>
<th>Left lateral</th>
<th>Supine</th>
<th>Right lateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean blood pressure</td>
<td>98.6 ± 4.1</td>
<td>98.1 ± 6.2</td>
<td>98 ± 4.1</td>
</tr>
<tr>
<td>Mean SBP</td>
<td>91.0 ± 8.7</td>
<td>96.7 ± 9.0</td>
<td>95.3 ± 9.9</td>
</tr>
<tr>
<td>Mean DBP</td>
<td>62.5 ± 4.4</td>
<td>68.0 ± 5.0</td>
<td>64.3 ± 4.1</td>
</tr>
</tbody>
</table>
ACOG and AWONN

- Maternal lateral repositioning
- Intravenous fluid bolus
- Decrease oxytocin and/or administer tocolytic
- Amnioinfusion
- Maternal oxygen administration

Intravenous fluid bolus

At time of epidural?

- 10-14% incidence of hypotension after neuraxial analgesia
- RCT of 1.5L IV fluid preload vs no fluid preload at time of epidural
  - No difference in incidence of hypotension
- May be beneficial in volume depleted patients
Unanswered Questions

- Amount of fluid
- Type of fluid
- Impact on fetal heart tracings
- Impact on uterine contractility

ACOG and AWONN

- Maternal lateral repositioning
- Intravenous fluid bolus
- Decrease oxytocin and/or administer tocolytic
- Amnioinfusion
- Maternal oxygen administration

Tachysystole

- Average of >5 contractions in 10 min over 30 min period
- 11% of all deliveries, 32% with associated FHR changes
- Inadequate relaxation
- Associated with neonatal acidemia and cesarean for non-reassuring fetal status
**Benefit to Uterine Relaxation?**

- Decrease or discontinue oxytocin
- Betamimetics associated with improvement in fetal heart rate abnormalities (RR 0.26, 95% CI 0.13-0.53)
- Cardiovascular adverse effects

**Unanswered questions**

- Useful for Category II without tachysystole?
- Nitroglycerine?
- Neonatal outcomes?
- Oxidative stress?

**ACOG and AWONN**

- Maternal lateral repositioning
- Intravenous fluid bolus
- Decrease oxytocin and/or administer tocolytic
- Amniocentesis
- Maternal oxygen administration
Amnioinfusion

- Alleviating cord compression by infusion of fluid

<table>
<thead>
<tr>
<th>Benefit</th>
<th>No benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Occurrence of variable decelerations</td>
<td>Prophylactic amnioinfusion</td>
</tr>
<tr>
<td>↓ Cesarean for NRFS</td>
<td>Chorioamnionitis</td>
</tr>
<tr>
<td></td>
<td>Meconium</td>
</tr>
</tbody>
</table>

37

- 60% reduction in FHR abnormalities compared with controls
- Reduction in cesarean for nonreassuring fetal status (RR 0.46, 95% CI 0.31-0.68)

38

Unanswered Questions

- Type of fluid (LR vs NS)
- Temperature of fluid
- Rate (Intermittent vs Continuous)
- Effect on labor/contractility
- Effect on neonatal outcomes

39
ACOG and AWONN

- Maternal lateral repositioning
- Intravenous fluid bolus
- Decrease oxytocin and/or administer tocolytic
- Amnioinfusion
- Maternal oxygen administration

Maternal Oxygen (O₂) Supplementation

- Fetal hypoxia
- Anaerobic metabolism
- Metabolic acidosis (↓pH ↑Lactate)
- Oxygen
Hyperoxygenation is harmful

- Neonate
  - Bronchopulmonary dysplasia, retinopathy, abnormal neurodevelopment
- Adult
  - AVOID trial: Increased size of myocardial infarct
  - Oxygen-ICU trial: Increased ICU mortality with liberal O₂ supplementation

Hamel et al. AJOG 2013  Raghuraman et al. Obstet Gynecol 2017

- Randomized controlled noninferiority trial
- Inclusion: Term, singleton pregnancies admitted for spontaneous labor or induction of labor
- Exclusion: Fetal anomaly, maternal hypoxia
- Primary outcome: Umbilical artery lactate
### Results

#### Mean difference

- **Room air**
  - pH: 7.26 (7.24, 7.28)
  - Base excess: -3.62 (-4.3, -2.9)
  - pO\(_2\): 19.7 (17.5, 22.0)
  - pCO\(_2\): 55.9 (53.5, 58.2)
- **Oxygen**
  - pH: 7.25 (7.23, 7.27)
  - Base excess: -3.6 (-4.3, -2.9)
  - pO\(_2\): 24.4 (20.8, 28.8)
  - pCO\(_2\): 57.4 (54.2, 60.6)

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>Room air (N=51)</th>
<th>Oxygen (N=48)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesarean delivery</td>
<td>2 (3.9)</td>
<td>6 (12.5)</td>
<td>0.14 (0.07, 1.48)</td>
</tr>
<tr>
<td>Cesarean delivery for NRFS</td>
<td>0 (0.0)</td>
<td>2 (4.2)</td>
<td>--</td>
</tr>
<tr>
<td>Operative vaginal delivery</td>
<td>6 (11.8)</td>
<td>1 (2.1)</td>
<td>0.10 (0.03, 45.20)</td>
</tr>
</tbody>
</table>

#### What happens to electronic fetal monitoring?

- **Resolution of recurrent decelerations**
  - Room air: 49 (98.0)
  - Oxygen: 48 (97.6)
  - Relative Risk: 0.15
Unanswered Questions

1. Does this work?
2. At what dose? For how long?
3. On whom?
4. Are there harms/risks?

Cat II Management

• Cesarean = no more things to do

Summary

• Learning more about Cat II tracings
• Clinical factors to consider in interpretation
• Almost no evidence for the elements of ‘conservative management’
• Open to new evidence
Thank you

O₂C₂ Trial

**Admission to L&D**
- Active labor and Category II FHT necessitating resuscitation

**Enrollment**

**Randomization**
- O₂: 10L/min facemask
- RA: No facemask

Summary of RCTs

<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th>Findings in O₂ Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thorp et al., 1995</td>
<td>85</td>
<td>↓ Umbilical artery pH ↑ Neonatal acidemia</td>
</tr>
<tr>
<td>Nesterenko et al., 2012</td>
<td>56</td>
<td>↑ Oxidative stress ↑ Delivery room resuscitation</td>
</tr>
<tr>
<td>Khaw et al., 2002</td>
<td>44</td>
<td>↑ Maternal and fetal free radical activity</td>
</tr>
<tr>
<td>Qian et al., 2017</td>
<td>443</td>
<td>↓ Umbilical artery pH</td>
</tr>
</tbody>
</table>
Cochrane: Oxygen

Cochrane

- “There is not enough evidence to support the use of prophylactic oxygen therapy for women in labor, nor to evaluate its effectiveness for fetal distress”
- “In view of the widespread use of oxygen administration during labor and the possibility that it may be ineffective or harmful, there is an urgent need for randomized trials to assess its effects”

Modern Obstetric Anesthesiology

Jason Papazian, MD
Obstetric Anesthesiologist
University of Colorado SOM
January 6, 2020

Disclosures
• None

Learning Objectives
• At the conclusion of this presentation, the participant should be able to:
  1. Summarize the OB anesthesiologist’s role on and off the labor and delivery unit.
  2. Apply modern obstetric practice to up-to-date evidence-based OB anesthesiology.
  3. Analyze the different types of coagulation screening and recognize their implications as they pertain to OB anesthesiology.
  4. Identify maternal co-morbidities that may affect OB anesthetic options.
Case 1

• 31yF G1P0 at 39w gestation, o/w healthy,
• Seen at clinic found to be breech
• Strongly desires vaginal delivery
  • Wants external cephalic version
  • Wants to discuss spinal because RN suggested it might be a good option
  • Desires neuraxial for labor (even better)

Neuraxial Anesthesia for ECV

• ↑ Success
• M+M similar
• Any dose!
Case 2

- 23yo G1P0 at 35w2d gestation
- PMHx:
  - Factor V Leiden, no clot history.
  - Runner, o/w healthy.
- Meds: Lovenox 40mg QD, last dose 22 hours ago
- Arrive to triage with headache
- BP: 147/80 (repeat), HR 87, RR 18, Temp 37.3
- HELLP labs: Plt. count 90 (5 days ago was 121), LFTs/LDH wnl
- Headache resolves with conservative measures.
- Strongly desires vaginal delivery. Magnesium, IOL planned.

Wants to know analgesic options:

Nitrous Oxide? Other Options?

Has read a lot online about "Epidurals"

Nitrous oxide in Labor

- Safe?
  - Worldwide use
  - Few, if any, maternal adverse events; easily reversible
  - No increased NICU admission or changed APGARS
- Effective?
  - High satisfaction scores regardless of pain scores
  - Alternative if epidural not possible, contraindicated
  - High conversion rate to neuraxial

• Gets anesthesiologist in the room!
Other alternatives to an epidural

- Remifentanil
  - Significant respiratory depression events and even arrest
  - Requires complex monitoring. Anesthesia provider in room.
  - Impractical, probably unsafe
- Dexmedetomidine
  - Minimal placental transfer
  - Likely much safer, but limited experience and data
  - Still impractical except in rare specific circumstances
- Bottom line: Nitrous probably the best alternative

Cochrane Database of Systematic Reviews 2017:CD011989
Anesth Analg 2017;124:1208, 1211, and 60
J Obstet Gynaecol Obstet Gynecol 2017;130:1097

Myth: Epidurals make labor longer and increase surgical delivery rates.

- When modern low-dose epidural infusions are used there is NO increase in:
  - First stage
  - Second Stage
  - Instrumentation
  - Cesarean Section
Myth: Early Epidurals cause problems

**Cesarean Birth: Consensus Statement**

National Partnership for Maternal Safety
Consensus Bundle on Safe Reduction of Primary Cesarean Births—Supporting Intended Vaginal Births

David C. Langer, MD, Luu K. Lee, MD, CMB, Rita Brennan, MD, DSC, E. M. Swigart, MD, PM, Janet P. Davey, MD, J. E. W. A. Adams, MD, P. C. Wicks, MD, WC, Mary A. Naughton, MD, and Jane Jeffe, MD

- Low infusion concentration!
- "Too early" for an epidural is NOT evidence based
- Maintain motor function
- Continue in 2nd stage
- Allow patient control (PCEA)

Myth: Epidurals impact breastfeeding success

- Unlikely
- Poor pain control might NEGATIVELY impact

Myth: Epidurals increase Depression risk

- No increase in short term
- DECREASE in long term
- PAIN associated with increased PPD risk
Myth: Epidurals Paralyze people

Overall Risk ~ 1:200,000-300,000 if appropriate epidural placement

Myth: Anticoagulated patients can’t ever get epidurals

Drug Dose Time Interval for Neuraxial Procedure after Last Dose Restart medication after procedure (spinal or epidural PLACEMENT)
Indwelling cath on anticoagulation.
Time to stop & wait prior to removal
Time Interval to restart Med after Catheter is removed

UFH 10,000–15,000 IU SQ daily dose (i.e. 5,000 SQ BID or TID) 4–6 hours Immediate ok 4–6 hours Immediate ok
UFH >15,000–20,000 IU SQ daily dose (i.e. 7,500 SQ BID or 10,000 SQ BID) 12 hours & aPTT 1 hour 4–6 hours 1 hour
UFH IV heparin 4–6 hours & aPTT 1 hour 4–6 hours & coags 1 hour
Enoxaparin PPx dosing (i.e. 40mg SQ, or BID) 12 hours 12 hours Not recommended 4 hours (if >12 total hours since placement)
Enoxaparin Therapeutic dosing 24 hours 24 hours Not recommended 4 hours (if >24 total hours since placement)

ASA Any dose (UCH specific guideline, not national)

Notes:
1. Concurrent use of ASA (within 1 week) with LMWH/heparin = 24h interval (hold LMWH/heparin for 24h) for neuraxial procedure
2. If on heparin therapy for >4 days or any concern for coagulation status, check platelet count.
3. AntiXa is used to monitor LMWH. Prophylactic dosing levels: 0.2–0.4 IU/mL. Therapeutic dosing levels: 0.5–1.0 IU/mL. Not validated for use in neuraxial blockade.
4. These are intended to be minimal guidelines and may be altered at the discretion of the anesthesiologist. Individual cases may vary and risk/benefit of neuraxial vs. general anesthesia should always be considered.

Myth: Thrombocytopenia Contraindicates Epidurals

Risk of Epidural Hematoma after Neuraxial Techniques

- No guidelines – yet
- Platelets >70-100k probably ok*
- Trend more important than absolute number
- HELLP more worrisome than ITP/Gestational
- Patient individualization!!!

*depending on patient specific, must individualize
Myth: Preeclampsia contraindicates epidurals

**Practice Guidelines for Obstetric Anesthesia**

An Updated Report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology

- Consider early insertion of a neuraxial catheter for obstetric (e.g., twin gestation, preeclampsia) or aesthetic indications (e.g., anticipated difficult airway or obesity) to reduce the need for GA if an emergent procedure becomes necessary.

---

Myth: All Epidurals are the same

CSE vs. DPE vs. Epidural

- Spinal access/dose: Analgesia onset rapid
- Confirms neuraxial location: Decreased need to replace epidural
- Confirms midline position: Increased ideal bilateral blockade
- Improved rate of need for top-ups: Less need to call anesthesiologist
- Overall: Increased epidural success and satisfaction

- Intrathecal dose that is given is multifactorial, depends on:
  - Patient factors
  - Stage and progress of labor
  - Specific anesthesiologist

---

Myth: All epidural infusions are the same

- Programmed Intermittent Bolus (PIB):
  - ↓ breakthrough pain
  - ↓ hourly consumption of local anesthetic
  - ↑ maternal satisfaction
  - NO Difference in:
    - Duration of labor
    - Forceps or C/S
    - Neonatal M+M
    - ↓ motor block
A picture is worth 1000 words...

- 10 ml/hr continuous infusion
- 10ml/hr intermittent boluses

Patient satisfaction is individual...

"I was beginning to think I just couldn’t do it [labor]. But after talking to you I wasn’t scared of the epidural anymore and it didn’t take the experience of my birth away. It made me feel empowered."

A real patient who came in with a detailed birth plan and desire for natural childbirth who ended up with an epidural
Case 3

- 32yo G1P0 38w patient arrives in Triage painfully contracting
- Vertex, 3cm, 50%, +2
- MHx, SHx: None. Meds: PNs.
- Anesthesia discusses options
  - Patient says she “want to wait”
- Soon after arrival FHR
  \(\rightarrow\) Sustained fetal bradycardia
  - Emergent move to operating room
  - Splash prep \(\rightarrow\) Drapes \(\rightarrow\) Induction of GA \(\rightarrow\) Airway
  \(\rightarrow\) “cut” \(\rightarrow\) Incision \(\rightarrow\) Baby out in <1 min

Continued: Intraoperative PPH

- Cesarean Delivery without difficulty
- APGARs 6 and 9
- 15 minutes in EBL is 1500
- General anesthesia increases risk of hemorrhage
  - ATONY EFFECT!!
    - Volatile anesthetics (“sevo” “des” “iso”)
    - Convert to partial nitrous +/- “TIVA”
- RN asked to get Tranexamic Acid.
We ask for TXA but it isn’t in the OR. Nurse needs to get it. Why?

Intrathecal TXA → Seizure, Myoclonus, and likely DEATH

BUT: Why General? Why not a Spinal?

Neuraxial the gold standard, right??

- **AVOIDABLE GETA**
  - Increased Surgical Infection
  - Increased Thromboembolism
  - Increased anesthesia complications
  - No increase in death or cardiac arrest
High Spinal almost 6x more common than failed intubation

ASA CLOSED CLAIMS DATA

Major causes of maternal death by type of anesthesia:

<table>
<thead>
<tr>
<th>NEURAXIAL ANESTHESIA</th>
<th>GENERAL ANESTHESIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive blood loss - 25%</td>
<td>Excessive blood loss – 53%</td>
</tr>
<tr>
<td>High block / total spinal – 20%</td>
<td>Embolic events – 16%</td>
</tr>
<tr>
<td>Embolic events – 20%</td>
<td>Difficult intubation – 6%</td>
</tr>
<tr>
<td>Neuraxial cardiac arrest – 5%</td>
<td>Other respiratory events – 6% (aspiration, bronchospasm, etc.)</td>
</tr>
</tbody>
</table>
So... mom will probably be ok.
But what about the baby?

FDA Drug Safety Communication 2017:
“The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains.”

• Key contributing factor: DELAY IN CARE
  • Not in hospital
  • Inappropriate choice of regional over general

Time
Matters
Emergent "CRASH" Delivery

Position for spinal, monitors
1 min
Chlorprep back, spinal kit, spinal meds
3 min
Spinal dose
1 min suck
5-15m (or more)

But if we start before the spinal is FULLY set the time difference is less...

- 42% surgery allowed to start with inadequate block
- Despite inadequate block reluctance to convert to GETA
Case 4

- 27y G3P2 at 27 weeks gestation presents for right ORIF humerus
- Surgeon requests no nerve block/regional until postop for assessment radial nerve function
- GETA planned
- Patient is otherwise healthy
- Betamethasone timing appropriate
  - Patient seen in PPS days prior
  - OB consulted by surgical team days prior for planning
- Assigned anesthesia team is not OB specialized
  - Phone Call to me from my partner: “So what do I need to do different for this patient?”

**Not much!**

“Shouldn’t we wait till after she gives birth?”

* ACOG COMMITTEE OPINION

- Key: A pregnant woman should never be denied medically necessary treatment or have it delayed.
- **No conclusive evidence for in utero anesthesia/sedation drugs effects on the developing brain**
- Steroids benefit / fetal monitoring where appropriate.

**Summary of Modern Obstetric Anesthesia**

- **The OB anesthesiologist should:**
  - Contribute positively to a “normal” birth experience
  - And when that’s not possible, contribute to maximum safety for mom (and by extension, baby)
  - Aid in minimization of unnecessary/unwanted cesarean section
  - Be an advocate for maternal care optimization
  - Be available for formal/informal consult and discussion
  - Be a resource of information for OB providers and non-OB anesthesiologist colleagues
Thank You!

- Dr. Joy Hawkins
- Dr. Vesna Jevtovic-Todorovic
- Dr. Brenda Bucklin
- Dr. Rachel Kacmar
- Dr. Cristina Wood
- All of YOU!!

Questions?

Exposure to GETA for Cesarean and Odds of Severe PPD?!!

- No control for emergent delivery
- No control for comorbidities
- No CAUSAL relationship found, only association
- Does appropriately indicate that GETA should be avoided, when avoidable, but doesn’t give an evidenced based reason for this...
- Overall a VERY poorly done study, fully observational so no causal relationship able to be determine but still IMPLIED.
When to Refer: Case-Based Discussion

John P. Curtin MD
Director
Division of Obstetrics and Gynecology
Denver Health

When to Refer

Objectives
- Review indications for referral of premenopausal women with adnexal mass.
- Discuss management of early cervical cancer including when referral is not needed.
- Importance of referrals for imaging and pathology review.

When to Refer

Disclosures
- Nothing to Disclose
When to Refer: Adnexal Mass in Women > 50 years

- Ovarian cancer is disease of postmenopausal women (70% of patient > 55 years)
- For patients with small simple cysts no surgery-follow up US often not needed
- Most other patients should be referred

ACOG: PB #174 (2016). Evaluation and Management of Adnexal Masses

When to Refer: Adnexal Mass in Reproductive Age

- Size of mass >10 cm
- Elevated serum tumor markers – Ca125
- Presence of ascites
- Mention the use of scoring systems – IOTA “simple rules”

ACOG: PB #174 (2016). Evaluation and Management of Adnexal Masses

Simple US based Rules

<table>
<thead>
<tr>
<th>Rule for predicting a malignant tumor (M-rules)</th>
<th>Rule for predicting a benign tumor (B-rules)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1 Irregular solid tumor ● □</td>
<td>B1 Unilocular □ ●</td>
</tr>
<tr>
<td>M2 Presence of ascites ● ●</td>
<td>B2 Presence of solid component where the largest □ ●</td>
</tr>
<tr>
<td>M3 Irregular multilocular solid tumor with largest □ □</td>
<td>B3 Presence of acoustic shadows □ ●</td>
</tr>
<tr>
<td>M4 Irregular multilocular solid tumor with largest □ □</td>
<td>B4 Smooth multilocular tumor with largest diameter &lt; 100 mm □ ●</td>
</tr>
<tr>
<td>M5 Diameter ≥ 100 mm ● ●</td>
<td>B5 Smooth multilocular tumor with largest diameter &lt; 100 mm □ ●</td>
</tr>
<tr>
<td>M6 Very strong blood flow (color score 4) □</td>
<td>B6 No blood flow (color score 0) □ ●</td>
</tr>
</tbody>
</table>
IOTA Simple US based Rules

- If one or more M-rules apply in the absence of a B-rule then consider mass to be malignant
- If one or more B-rules apply in the absence of a M-rule then consider mass to be Benign
- If both M and B rules apply then mass cannot be classified.

Case Review

- 31 yo G0 patient presents with occasional pelvic pain
- Possible mass noted on exam
- TV US ordered

When To Refer: Case Review

- 31 yo G0 patient presents with occasional pelvic pain
- Possible mass noted on exam
- TV US ordered
When to Refer: Case-Based Discussion

When to Refer: Case Review

- 29 yo G2P2 patient presents with occasional pelvic pain
- Possible mass noted on exam
- TV US ordered

When to Refer: Case Review

- 31 yo G0 patient presents with occasional pelvic pain
- TV US ordered - diagnosis concerning for LMP
- Laparoscopy done with RSO
- Pathology - Dermoid

When to Refer: Case Review

- 29 yo G2P2 patient presents with occasional pelvic pain
- Possible mass noted on exam
- TV US ordered
When to Refer: Case-Based Discussion

When to Refer: Case Review
- 29 yo G2P2 patient presents with occasional pelvic pain
- Due to size (>10 cm) and elevated Ca125 and CEA referred to Gyn Onc
- Laparotomy and RSO omental biopsies
- Stage IIIB mucinous LMP

When To Refer: Adnexal Mass
- In patient with ovarian mass consider referral for expert ultrasound review
- If post-menopausal and needs surgery—refer
- For fertility preservation perform conservative procedure
- Don’t depend on intra-operative frozen
- May need expert pathology review

When to Refer: Adnexal Mass
- In very young patients (<18 years) with adnexal mass incidence of malignancy is higher
- Germ cell tumors more common
- Presentation is with acute symptoms in 33%
- US and tumor markers for Germ cell tumors
- Ovarian preservation
Post Surgery Surveillance: LMP Borderline

- If both ovaries removed recurrence rates are low and no routine imaging needed.
  - Recommend annual exam and evaluation of new signs/symptoms
- If ovarian cystectomy highest risk of recurrence
- For patients who have fertility preserving procedures serial US +/- tumor markers

When To Refer: Cervix Cancer

- With introduction of cervical cytology incidence of invasive cancer has dropped
- >600,000 cases of dysplasia per year in US
- 12,000 cases of invasive cervical cancer/year

When To Refer: Early Cervical Cancer

- 37 yo G4 P3 with abnormal HSIL pap smear
- Colposcopic biopsies demonstrate CIN III
- Loop excision done
- Pathology “squamous cell cancer-microinvasion”
When To Refer
Early Cervical Cancer

- 31 yo G1P1 with ASC-H and HPV 16 positive
- Pathology of excisional procedure “CIN III with microinvasion”

Early cervical cancer:
Stage IA

- T1a/FIGO IA: The carcinoma is found only in the cervix.
- T1a/FIGO IA1: Invasive carcinoma was diagnosed only by microscopy. Note: Any tumor found macroscopically (large enough to be recognized by imaging tests or to be seen/felt by the doctor) is referred to as stage T1b or FIGO IB.
- T1a1/FIGO IA1: There is a cancerous area of 3.0 millimeters (mm) or smaller in depth
- T1a2/FIGO IA2: There is a cancerous area larger than 3.0 mm but not larger than 5.0 mm

When To Refer
Early Cervical Cancer

- Diagnosis of Stage IA cervical cancer need depth of invasion and negative margins on excisional procedure (LEEP or Cold knife cone)
- Stage IA1 can be treated by simple hysterectomy
- Stage IA2- significant risk of lymph node metastases
- Fertility sparing options are available
When to Refer: Case-Based Discussion

When To Refer Early Cervical Cancer

• 37 yo G4 P3 with pathology “squamous cell cancer-microinvasion” post LEEP
• Further clarified as invasion of < 1mm and negative margins
• TVH done

When To Refer Early Cervical Cancer

• 31 yo G1P1 with ASC-H and HPV 16 positive
• Pathology of excisional procedure “CIN III with microinvasion”
• Referral to Gyn pathologist = invasive squamous cell cancer 3.5mm of invasion, LVSI and positive endocervix margin

When To Refer Early Cervical Cancer

• 31 yo G1P1 with ASC-H and HPV 16 positive
• invasive squamous cell cancer 3.5mm of invasion, LVSI and positive endocervix margin
• Stage IA2
• Desires fertility
• Referred to Gynecologic Oncologist
Early cervical cancer: Stage IA2-Stage IB1

- Patient offered radical trachelectomy
- Advanced by laparoscopic LN and renewed interest in Schuata procedure

MIS surgery and Early Cervical Cancer

- In randomized trial of MIS vs laparotomy for early cervix cancer

Death from Cervix CA:
OPEN: 2/312
MIS: 14/319

When to Refer: Conclusions

- Communication is key
- Call a “friend”
- Consultation with Gynecologic oncologist
- Remember to consider consultations with imaging specialist and/or pathology specialist
Pragmatic Approach to the Dx and Rx of Thyroid Disease in Pregnancy: Evading the Quagmires

Linda Barbour, MD, MSPH
Professor of Medicine and Obstetrics and Gynecology
Divisions of Endocrinology and Maternal-Fetal Medicine
Feb 18, 2020

Objectives:

1) Recognize why TSH norms in pregnancy have changed again and the results (and unanswered questions) from the 2017 MFMU RCT

2) Appreciate problems with free T4 and T3 assays and how TT4 and TT3 can come to your rescue

3) Identify why there is no consensus about treating Subclinical Hypothyroidism (SCHypo) and why you would ever consider TPO abs

4) Apply a pragmatic approach to prescribing LT4 for your practice and be armed with persuasive data not to prescribe T3 in pregnancy

5) Become familiar with the major maternal and fetal considerations in managing hyperthyroidism in pregnancy

2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum

March 2017;27(3):315 -89

97 Recommendations; 621 references; 162 pages

7 Recommendations; 57 references; 10 pages
Case: SCHypo in Pregnancy

• 28 y.o. G1P0 ~8 wks found to have TSH=3.7
  • No symptoms but fatigue
  • Exam unremarkable
• What Do You Recommend?
  • A. Treat with 50 ug LT4
  • B. Check TPO abs and if positive, treat as above
  • C. Do not treat
  • D. Treat if your patient has been on internet

Guidelines on Thyroid Disease in Pregnancy

Table 1: Characteristics of hypothyroidism in pregnancy guidelines included in the study

| Guideline | Publication year | Country | Language | Quality of evidence | Rigor | GRADE | 1/
<table>
<thead>
<tr>
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<td>T&amp;MA (37)</td>
<td>2013</td>
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<td>T&amp;A (15)</td>
<td>2015</td>
<td>UK</td>
<td>English</td>
<td>Not mentioned</td>
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</tr>
</tbody>
</table>

Using Appraisal of Guidelines for Research and Evaluation (AGREEII), ATA ranked highest; clear differences in rigor and TSH Rx recs

70% of recommendations based on low-quality evidence

TSH is Usually All You Need to Diagnose and Treat Hypothyroidism

• TSH has a log-linear relationship with fT4: 2 fold decrease in fT4→100 fold increase in TSH
  • TSH rise in relation to fT4 genetically determined
  • Mild: ↑ TSH alone
  • Moderate: ↑ TSH and ↓ fT4
  • Low T4 alone? Likely iodine deficiency
  • Severe: ↑ TSH, ↓ fT4, ↓ T3
  • >90% Hashimoto’s—T3 last to decrease
TSH Rises with Age

- NHANES III
  - 20-29 up to 3.56 (97.5%)
  - 60-69 up to 4.33
  - 70-79 up to 5.9
  - 80+ 7.49
  - Overall 0.45-4.1; Median 1.4 mIU/l
- Consider TSH 4.6-6 nl age 70 and 7.5 for age 80

Surks MI JCEM 2007;92:4525

Thyroid Functions During Pregnancy

Due to ↑ TBG, TT4 and TT3↑ 50% by ~ 8 wks

FTA slightly ↓ by late 2nd trimester
Equilibrium Dialysis or LC/MS/MS
↓ TSH in 20% 1st and 2nd, possibly 3rd

Prior Data Supported a 1st Trim TSH 0.1-2.5

<table>
<thead>
<tr>
<th>TSH mIU/L</th>
<th>Ref 1st Trim</th>
<th>Ref 2nd Trim</th>
<th>Ref 3rd Trim</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.3</td>
<td>0.03</td>
<td>0.02</td>
<td>0.01</td>
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<tr>
<td>2.7</td>
<td>0.02</td>
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<tr>
<td>2.6</td>
<td>0.03</td>
<td>0.02</td>
<td>0.01</td>
</tr>
</tbody>
</table>

A (n = 343, Hong Kong) Panesar Ann Clin Biochem 38:329, 2001
B (n = 17,298, USA) Casey Obstet Gynecol 105:238, 2005
C (n = 111, USA) Lee ACOG 200:260, 2009
D (n = 2272, Switzerland) Stricker EJE 157:509, 2007

TSH Normal Range
1st Trim  0.1-2.5
2nd Trim  0.2-3.0
3rd Trim 0.3-3.0

TPO+ women should be treated with LT4. Insuff evidence if -TPO

SCHypo should be treated irrespectively of TPO status

BUT—Newer Data....

Ranges of TSH Norms By Country ATA 2017

- ~97,796 women in U.S.
- At origin of trial, TSH ≤ 3 used as upper limit (97.5%)
- After 10 m0s, >6% of women had SCHypo
- Based on TSH screening in the first 15,000 using 97.5%, new range <4.0
- TSH 0.08-3.99  (Advia Centaur chemiluminescent immunoassay--2000)
- FT4 0.86-1.96   (same)
Normal TSH Upper Range (4.0 or ~0.5 Less than Non-Pregnant Range) Trimester Independent-ATA

- **Recommendation 26**
  - The pregnancy-specific TSH reference range should be defined as follows:
    - When available, population and trimester-specific reference ranges for certain TSH during pregnancy should be defined or provided to ensure reliability and meaningfully represent the typical population for whom care is provided. Reference ranges should be defined in healthy, TPOAb-negative pregnant women with optimal iodine intake and without thyroid disease. (Strong recommendation, High quality evidence)
    - When this is not feasible, pregnancy-specific TSH reference ranges obtained from similar patient populations, and performed using similar TSH assays should be submitted. (Table A1: Change recommendation, High quality evidence)

Low fT4 by 3rd Trim by Different Analog Assays (14-62%)

![Graph showing FT4 levels during pregnancy](image)

\[ FT4 \uparrow \text{TBG}, \text{Only} 0.03\% \text{of T4 is free} \]

Low fT4 by 3rd Trim by Different Analog Assays (14-62%)

- **Recommendation 43**
  - FT4 Does ↓ 1st → 3rd Trim; Immunoassays Unreliable; Use TT4 (add ~50%)
Bottom Line: TFTs in Pregnancy

- TSH is lower; in ~20% will be suppressed 1st Trim
- Subtract 0.4 from non-pregnancy lower range and 0.5 upper range; (0.1-4.0); >4.0 is definitely abnormal
  - If TSH is >4.0 -- more believable for S-Hypo if + TPO abs
  - ~20%; slightly lower in afternoon
  - Assay can also be off by ~1.0
  - Repeating test may result in late identification
- FT4 may run slightly low late 2nd or 3rd trim
  - TT4 and TT3 ↑ by ~50% above non-preg norms 4-12→6-18
  - If FT4 lowish in 2nd, 3rd trim, check TSH and TT4.
  - If TSH ≤4.0 and TT4 at upper half nl range, ignore FT4 (unlikely central). If stuck, get equilibrium dialysis assay

Are TPO abs Relevant?

- Present in 5-18% pregnant women
- Risk factor for developing SCH in pregnancy ~15%
- Present in only ~2/3 of pregnant women with ↑TSH
- Differences in Assay and Cutoffs; Some TPO neg SCHypo
- Marker of reduced thyroid reserve, autoimmunity
  - Overt Hypo-2X ↑ if +TPO; Postpartum Thyroiditis 5-7X
- Risk factor for early miscarriage (1.8-3.9) and PTD (2.0)
  - TPO abs in mice bind to pre-implantation embryos → fetal resorption/loss. Th1/Th2 and NK higher in women who miscarry

Insufficient Evidence to Test or Treat TPO+ Euthyroid Women

- Impact of Levothyroxine in Miscarriage and Preterm Delivery Rates in First Trimester Thyroid Antibody-Positive Women with TSH-2.5mIU/L. JCEM and JAMA
  - Negative Study
- ATA 2017
- ACOG

However, the results of such testing rarely lead to changes in management of women who are euthyroid or women with thyroid disease, and there currently is no evidence to support routine testing of these antibodies.

TABLET RCT in UK (completed 2019, hx of pregnancy loss and infertility)
T4Life Trial: Netherlands RCT: TPO+, with hx of ≥2 losses BEFORE conception, started in 2015, expected to be completed any time
Levitronine in Women with Thyroid Peroxidase Antibodies before Conception.

- 952 TPO+ with hx of miscarriage (45% 1-2; 20% ≥3; 35% none) OR infertility Rx 45% from 49 UK hospitals
- RCT 50 ug LT4 or placebo; plans to conceive within 12 mos
- TSH 0.44-3.63; Median TSH ~2
- 176/470 became pregnant in LT4; 178/470 in placebo
- No difference in live birth rates, miscarriage, preterm birth, or neonatal outcomes

RCT in Peking in 600 undergoing IVF/Embryo Transfer TPO+
No diff in miscarriage or live births in LT4 group Wang H, JAMA 2017

Should We Treat SCHypo??

Subclinical hypothyroidism; Retrospective studies suggested slightly decreased IQ in offspring
Overt Hypo → ↓ cardiac function, anemia, ↑TG, depression, LBW, preeclampsia, abruption
SCH: Early miscarriage and preterm delivery in some but not all studies
- T4 needed for trophoblast function
- Most of retrospective data in women with TSH 8-10
  Miraka S Thyroid 2017; 26:580

Fetal Thyroid Function

Moog NR Neuroscience 2013, Miranda A Brain and Behavior 2018
- T4 observed in embryonic circ at 4 wk postimplantation
- Critical: Motor func, cognition, attention, learning, memory consolidation, affect, anxiety
- TH ↑ GABA-ergic neurons; ↓ NorE, Epi, DA and Serotonin Act
- T4 prohormone; T3 active
- Fetal thyroid concentrates iodine and make T4 at 10-12 wk; Fetal production independent by 16-18 wk; ↑ to term
- TH transporters in fetal brain mainly T4; T3 remains low
  Neurodevelopmental deficits worse if inadequate mat T4 <13 wk
Placental Transport

- Throughout gestation, T4 in fetal circ steadily ↑ but T3 remains low during fetal life with surge at term
- Placenta D3 (T3→T3) highest early pregnancy, provides fetus with Iodine (protects fetus from early maternal Hyper)
- Transthyretin (TTN i.e. pre-Alb) expressed in placent al trophoblasts at 6 wks; binds T4 on maternal apical side and internalizes it for transport (as it does retinol)
- Primary hormone transported across placenta is T4

Moog NK Neuroscience 2005

21,846 women screened in UK and Italy
- TSH/fT4 before 16 wks: 1/2 run immediately; 1/2 after del
- Rx if fT4 lowest or TSH highest 2.5 percentile
  - TSH 0.15-3.65; Only 5% of women had both
- IQ at 3 yrs
- Intention to treat analysis NEG (24% lost to follow-up)
  - IQ < 85; 12.1% vs 14.1%
  - No difference in GA delivery, PTB, or BW
  - Huge disappointment but very mild hypothyroidism
  - Median TSH treated in CATS trial = 3.8

MFMU 15 Center Randomized, Controlled Double Blind RCT
TREATMENT OF SUBCLINICAL HYPOTHYROIDISM OR HYPOTHYROIDINEMIA IN PREGNANCY

2006-2009
Eligible if took >50% of 7-days placebo
Randomized 8-21 wks
Mean Rx started 16 4/7 in ↑TSH arm; 18 wks in ↓fT4 arm

MEDIAN TSH IN TREATMENT GROUP ONLY 4.5

No Difference in Obstetric or Neonatal Outcomes

97% in LT4 had TSH 0.1-2.5 by 21 wks
Nothing specific reported about TPO status

 Mean  Rx started 16 4/7 in ↑TSH arm; 18 wks in ↓fT4 arm
No Difference in Neurologic Outcomes at 5 yrs

Essentially the same for low FT4

Follow-up 92%

Presenter’s MFMU Conclusions and Caveats

- No difference in Obstetric, Neonatal, or Neurologic Outcomes
- Randomization ~17 wks—too late given fetal function at 16 wks?
- Very mild SCHypo: Mean TSH in Rx arm = 4.5 (0.08-3.99)
  - How many were positive TPO status?
  - What if TSH were 8????
  - Mean FT4 = 0.83 (0.86-1.9) with 85% CI 0.82-0.83
  - Analog Method
    - Low FT4 without ↑ TSH is virtually impossible unless in iodine deficient area — Highly Likely Assay Problem
  - Cognitive Function at 5 yrs more likely to be related paternal IQ, infant developmental exposures, SES, parenting skills, nutrition, medical illness, stress
- No answer for Rx of TSH 6-10

2017 ATA Guidelines Recommendations for Rx Subclinical Hypothyroidism

Treat all pregnant women with TSH 4-10 independent of TPO given assay issues Italian Guidelines (Rotondi M Thyroid 28(5) 2018:551)
ACOG: “No Evidence to Identify and Treat SCH” NO Guidance if TSH 4 vs 10

Pregnant women with overt hypothyroidism should be treated with adequate thyroid hormone replacement to minimize the risk of adverse outcomes. and these adverse obstetric outcomes (26, 31). Currently, there is no evidence that identification and treatment of subclinical hypothyroidism during pregnancy improves these outcomes (30).

What to do with Low fT4 Alone?

Unlikely to be real unless:
- Central (unlikely in pregnancy)
- Iodine deficiency since T3 will be preferentially made and will feedback on TSH resulting in normal TSH (unlikely in U.S.)

Case: SCHypo in Pregnancy

28 y.o. G1Po ~8 wks found to have TSH=3.7
- No symptoms but fatigue
- Exam unremarkable

What Do You Recommend?
- A. Treat with 50 ug LT4 (Old ES guidelines)
- B. Check TPO abs and if pos, treat as above (Consider ATA)
- C. Do not treat (My vote—no data that Rx is beneficial)
- D. Treat if your patient has been on internet (Nope—gently remind patient those are outdated now)
Reasonable Options for Rx SCH

- >10 Treat
- TSH 4-10 and +TPO—Most would treat
- TSH 4-10 and –TPO—Most would still treat
  - TSH >4.0 clearly abnormal for pregnancy, and risks unlikely to outweigh benefits
  - Treat with low doses (50 ug)
- Goal ~2.5 Monitor every 4 weeks until 20 weeks and then 6-8 weeks

Universal Screening? No ATA and ACOG (but who does this actually not include?)

Targeted screening of High Risk pops
(No screening in ATA or ACOG)
- Hx any thyroid ds, PPT, radiation neck
- Known +TPO Abs
- +FH
- +Sxs (but very non-specific or sensitive)
- Goiter
- Autoimmune Ds (Type 1 DM, Addison’s, RA)
- Assisted Reproduction (T3, TBG)
- Suspected iodine deficiency
- Meds alter function (Lithium, Interferon)

ATA 2017:
- Hx Pregnancy Loss or PTD
- ≥2 pregnancies
- Age >30
- BMI ≥40

Increased LT4 Requirement in Pregnancy

- NI preg: ↑T4 by 25-50 ug early in gestation
- ↑TBG, ↓TBG clearance from hepatic glycosylation; ↑Vol of distribution and GFR, placental transport, Type 3 placentai deiodinase (T4→T3)
- Half life of thyroid hormone is 5-7 days (~1 wk)
- Patients on T4 require 25-50% increase, especially if athyretic
- ~25% increase in 1st trim—Empirically increase by 2 tab per wk
WHAT ABOUT T3????????????

Human Thyroid Makes T4:T3 in 12:1 ratio

Are the D1 and D2 deiodinases able to increase their activity to restore normal levels of tissue T3 in athyretic individuals given T4 alone?

T3 and Armour Thyroid Should Not Be Used in Pregnancy

Pigs (Armour Thyroid) Make T4:T3 in 4:1 Ratio
- 15 mg (1/4) gr 38 ug T4; 9 ug T3
- 30 mg (1/2) gr 57 ug T4; 14 ug T3
- 60 mg (1 gr) 76 ug T4; 18 ug T3
- 90 mg (1 1/2 gr) 114 ug T4; 27 ug T3
- 120 mg (2 gr) 152 ug T4; 36 ug T3
- 180 mg (3 gr) 190 ug T4; 45 ug T3
- 240 mg (4 gr) 228 ug T4; 54 ug T3
- 300 mg (5 gr) 266 ug T4; 63 ug T3

Pragmatic Recs Rx of Hypo and SCHypo

Overt Hypo (or TSH ≥10)
- Full replacement dose (~2.0 ug/kg), measure TSH q 4-6 wks until 20 wks; 6-8 wks until term

SCH
- Treat with smaller dose (~50 ug T4)
- On Rx and ↑TSH: Give 2 ug/kg; inc by 12.5-25 ug
- Do not use T3 in pregnancy
- Crosses poorly; T4 transporters in fetal CNS
- Empty stomach; separate PNV, Fe, Ca, Soy by 4 hrs
- Reduce PP (slightly more than pre-preg dose; check 6 wks postpartum)
Hyperthyroidism
Just the Facts...

- 20% have suppressed TSH; common in twins
- Do NOT treat subclinical hyperthyroidism
  - No ↑ risk; Attempts to normalize TSH→fetal hypo
- Etiology: Grave’s 85%, hCG-induced, toxic nodules, multinod goiter, thyroiditis
  - Do not treat Gestational Thyrotoxicosis in women with hyperemesis; T4 will usually normalize by 20 wks

Grave’s Disease

Mediated by TSI (Thyroid Stim IgG)/TRAB (TSH-Rec Ab)
Usually presents 1st trim; usually improves 3rd trim due to ↑T REG cells; 70% rebound PP (Follows TSI)
Look for Pre-preg sxs, goiter, eye findings
Mat risks: CHF, wt loss, PE, a fib, storm
Fetal risks: Fetal tach, IUGR, premature
Fetal Graves overall ~5% but 20-40% if TSI or TRAB are 3X ↑ at 18-20 wks Thyroid 2018, 28(2):257
  - Monitor every 4 wks with US for Fetal Graves (thyroid goiter, tachycardia, growth restriction, advanced bone age, hydrops)

Overt Hyperthyroidism: ACOG

Either propylthiouracil or methimazole, both thioamides, can be used to treat pregnant women with overt hyperthyroidism.

However, does state that MMI likely carries high risk of mild congenital anomalies (choanal atresia, slight facial abns)

The goal is treatment with the lowest possible thioamide dose to maintain free T<sub>1</sub> levels slightly above or in the high-normal range, regardless of TSH levels (37). The T<sub>1</sub> concentrations (not TSH levels) are measured every 2-4 weeks after initiation of therapy, and the thioamide

Breastfeeding: PTU crosses less well but MMI up to 20 mg /day appears safe; preferred over PTU due to PTU-induced hepatotoxicity
Recent Practice Guidelines, Expert Reviews, High Impact Papers

- Van Dijk MM. Maternal Thyrotropin Receptor Antibody Concentration and Risk of Fetal and Neonatal Thyrotoxicosis. Thyroid 2018; 28(2):257.
- Dhillon-Smith R. Levothyroxine in women with Thyroid Peroxidase Antibodies before Conception. NEJM 2015;380:1016.
- Pearce EN et al. Consequences of iodine deficiency and excess in pregnant women: An overview of current knowns and unknowns. AMIA 2016.
- Negro, R et al. Impact of Levothyroxine in Miscarriage and Preterm Delivery Rates in First Trimester Thyroid Antibody-Positive Women with TSH<2.5 mIU/L. JCEM 2016
ARRIVE Trial: Results & Implementation

Alison G. Cahill, M.D., M.S.C.I
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Department of Women's Health
Maternal Fetal Medicine
The University of Texas at Austin Dell Medical School

Disclosures
• No financial
• Vice-Chair of Committee for OB Practice for ACOG, Editor for Gabbe, Oral board examiner for ABOG
Induction and Cesarean

Induction and cesarean delivery

- Retrospective cohort studies
  - Induction of labor prior to 41 weeks of gestation is associated with an approximately 2-fold higher risk of cesarean delivery in nulliparous women

Increasing maternal and perinatal risks after 39 weeks

Maternal
- Cesarean delivery
- Operative vaginal delivery
- 3rd and 4th degree lacerations
- Febrile morbidity
- Hemorrhage
Perinatal Complications

- Pregnancies that continue beyond 39 weeks are associated with increased risks of:
  - Stillbirth
  - Meconium aspiration syndrome
  - Mechanical ventilation
  - Birth trauma
  - Neonatal seizures/ICH/encephalopathy
  - Neonatal sepsis
  - UA pH ≤ 7/BE < -12
Severe Neonatal Complications

- 40 vs. 39 weeks: adjusted OR 1.47 (1.1, 2.0)
- 41 vs. 39 weeks: adjusted OR 2.04 (1.5, 2.78)

Induction vs. Expectant Management

<table>
<thead>
<tr>
<th>Week of Induction</th>
<th>IOL</th>
<th>Spontaneous</th>
<th>Expectant</th>
<th>aOR (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>38 weeks</td>
<td>11.9%</td>
<td>7.0%</td>
<td>13.3%</td>
<td>1.80 (1.29-2.53)</td>
</tr>
<tr>
<td>39 weeks</td>
<td>14.3%</td>
<td>9.1%</td>
<td>15.0%</td>
<td>1.39 (1.08-1.80)</td>
</tr>
<tr>
<td>40 weeks</td>
<td>20.4%</td>
<td>10.0%</td>
<td>19.0%</td>
<td>1.24 (1.07-1.42)</td>
</tr>
<tr>
<td>41 weeks</td>
<td>24.3%</td>
<td>14.0%</td>
<td>26.0%</td>
<td>1.26 (0.99-1.61)</td>
</tr>
</tbody>
</table>

Caughey et al, AJOG 2006;195:700-5

Cesarean delivery with EIOL

Osmundson et al, Obstet Gynecol 2010 & 2011
Walker et al, NEJM 2016

- 619 nulliparous women
- Age 35 years or older
- Randomized between 36 weeks and 39 6/7 weeks

Perinatal mortality and morbidity

- Only women aged 35 or older
- No idea about cervical status
- UK system very different (e.g., OVD)
- Underpowered for perinatal outcomes

70% decreased odds of meconium aspiration and mortality, respectively, in EIOL group.
Arrive

- More than 50,000 women were screened
- Low-risk nullips
- Median BMI at delivery 30kg/m²
- Median Bishop score in both groups was 4 (IQR 2-5)
Criticisms

1. ‘Strange results’
2. Number of women declined
3. Population differences
4. The way labor was managed
5. Inability to handle capacity
‘Strange results’

• Differ from older work with the wrong control group (induction v. spontaneous)
• Agree with modern work with correct control group (induction v. exp mgmt)
• Biologically plausible

Number of women who declined

Population differences
Labor management

• Protocolized
  – Participants with Bishop <5, cervical ripening
  – Induction ‘failed’ if 12 hours after ROM and oxytocin, still in latent labor

• Individual provider
  – Behave 1 way at 39 weeks and another at 41

Inability to handle capacity

• Not evidence-based
• On us to problem-solve

ARRIVE - Summary

• Labor inductions do not increase the risk of cesarean
  – Lower cesarean rate in the induction arm
• Induction at 39 weeks decreases the risk of hypertensive disease
• Practice-changing
• Logistical considerations to accommodate change

WHAT IS NEXT?

#1
Change how we counsel our patients

#2
Create initial capacity
Reduced healthcare utilization

- Secondary analysis of ARRIVE
  - 6906 women with available data
  - IOL group
    - Less likely to have an additional PNC visit
    - Less likely to have urgent or emergent visits
    - Fewer hospitalizations and tests

Grobman WA et al. AJOG, 2020 in press

Reduced healthcare utilization

- Also, in the IOL group at delivery
  - Longer median time L&D (0.83 v. 0.57 days)
  - Both IOL moms and babies had fewer stays greater than 2 days
    - Mom (17.8% v. 20.9%, p=0.002)
    - Baby (23.1% v. 26.9%, p<0.001)

Grobman WA et al. AJOG, 2020 in press

#3

Ways to improve capacity

- Outpatient cervical ripening
- Cervical ripening off of L&D?
#4
Change how we think about inductions
– Are any elective?

All together
• Practice changing & myth busting
• Labor inductions do not cause cesareans
• 39 week elective inductions
  – Decrease cesarean
  – Decrease hypertensive disorders
• Should this apply to multips too?

Thank you
Wednesday
Reducing the First Cesarean in Real Life

Alison G. Cahill, M.D., M.S.C.I
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Department of Women’s Health
Maternal Fetal Medicine
The University of Texas at Austin Dell Medical School

Disclosures
- No financial
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Cesarean Prevention

*OBSTETRIC CARE CONSENSUS*

Safe Prevention of the Primary Cesarean Delivery

OCC #1 Obstet & Gynecol 2014
Reducing the First Cesarean in Real Life

Why do we do them?
• Improved outcomes
  – Mom
  – Baby

Risks
• Infection
• Bleeding
• Wound complications
• Thromboembolism
• Abnormal placentation
Burden of Cesarean-Related Postoperative Infectious Morbidity

• Most common surgical procedure in US – 1.3 million/year
• Postcesarean infectious morbidity:
  – Endometritis, sepsis, intraabdominal abscess, maternal fever, wound complications
• Most common & costly complication – affecting 130,000


Burden of Cesarean-Related Postoperative Infectious Morbidity

• Patient Burden
  – Lead to prolonged hospitalization
  – Impair bonding and breast feeding
• Health Care Costs
  – $2800-$3500 per case
  – $390 million annually

Olsen et al., Infect Control Hosp Epidemiol; 2008; 29: 477-484
Scifres et al., Am J Obstet Gynecol. 2011 Sep;205(3):267
Olsen et al., Infect Control Hosp Epidemiol 2010; 31:276-282

Why prevent them?

• Some
  – Unnecessary ones

Who’s cesarean is necessary?
Cesarean Prevention

- Malpresentation, 13%
- Macrosomia, 4%
- Preeclampsia, 3%
- Multiple gestation, 7%
- Arrest of labor, 16%
- Nonreassuring fetal heart tracing, 23%
- Nonreassuring fetal heart tracing, 23%
- Arrest of labor, 16%

Paradigm Shift

- Changing our behavior

Labor Management
Labor Management

- Do you counsel all nulliparous 39 week IOL?
- ARRIVE
  - Reduced likelihood of cesarean
  - Reduced risk of hypertensive disease


---

Labor Management

- How do you perform inductions?
  - Agent
  - Dosing
  - Combined methods

Needs more work…

Schoen CN et al Obste Gynecol2017
Connolly KA et al, AJP 2017
Pettker CM et al, Obstet Gynecol 2008
Gallagher LT et al, AJP 2019
Carbone JF et al, Obstet Gynecol2013
Levine LD et al, Obstet Gynecol2016

---

Labor Management

- When do you admit women in spontaneous labor?
  - Admission in latent labor (5cm or less) in multips – associate with increase risk of cesarean

Wood AM et al., Am J Peri 2016
**Labor Management**

- Do you actively manage labor?
  - Early evidence that it shortens labor and reduces fever, but not cesarean
- Meta-analysis: ‘Early’ oxytocin use associated with increase in SVD
  - NNT is 20

*Frigoletto FD et al, NEJM, 1995
Wei SQ et al, Obstet Gynecol 2009*

**Labor Management**

- How do you use AROM?
  - Early amniotomy
    - Shortens labor
    - Reduces cesarean
  - Nullips and multips

*Wei S et al, Cochrane 2012
Gagnon-Gervais K, JMFNM, 2012
Macones GA et al, AJOG, 2012*

**Labor Management**

- What labor curve standard do you use?
Old school

- Friedman, 1955
- Prospective cohort study
- 622 nulliparous women
  - 500 complete data


'Ideal labor': 200 women

<table>
<thead>
<tr>
<th></th>
<th>Latent</th>
<th>Active</th>
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</thead>
<tbody>
<tr>
<td>Mean</td>
<td>8.6 hrs</td>
<td>3.0 cm/hr</td>
</tr>
<tr>
<td>95%ile</td>
<td>20.6 hrs</td>
<td>1.2 cm/hr</td>
</tr>
</tbody>
</table>
Was Friedman Wrong?

Sort of...

Analytic Problem

- G1P0, 39 5/7 weeks
- Presents in labor
  - SROM
  - Contractions q 2min
- Cervical exam: 3/100/0

Nullip: Labor Progress
Zhang: Labor Curves
- Consortium for Safe Labor, MFMU
- 19-center retrospective cohort study
- 64,415 singleton, vertex, spontaneous labor, vaginal delivery; 'normal outcome'
- Used interval-censored time-dependent analyses to estimate the labor curves; define normal

Shape of the Spontaneous Curve
- Transition to the active phase
- Progression to complete
Active Phase (4cm – 10cm)

<table>
<thead>
<tr>
<th></th>
<th>Friedman</th>
<th>Zhang</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nullips</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>3.0 cm/hour</td>
<td>1.9 cm/hour</td>
</tr>
<tr>
<td>Slowest 5%</td>
<td>1.2 cm/hour</td>
<td>0.4 cm/hour</td>
</tr>
</tbody>
</table>

Zhang: Conclusions

At ≤ 6cm
- Too many 1st stage cesareans
- Wider width around estimates of ‘normal’
Faster progress at end
- No deceleration phase

Even worse with induced labors
- High 1st stage cesarean rate

Contemporary Cesarean Patterns

- Consortium for Safe Labor
  - 19 hospitals
  - 2002-2008
  - 228,668 women

Chance of no cesarean

Hours

Zhang et al. Am J Obstet Gynecol 2010
When we do 1st stage arrest cesareans?

<table>
<thead>
<tr>
<th>cm</th>
<th>Nullips Spontaneous</th>
<th>Nullips Induced</th>
<th>Multips Spontaneous</th>
<th>Multips Induced</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>13.0 (0.3)</td>
<td>14.5 (4)</td>
<td>-0.1 (0)</td>
<td>16.0 (2)</td>
</tr>
<tr>
<td>1</td>
<td>10.0 (2)</td>
<td>9.4 (10)</td>
<td>-1.0 (0)</td>
<td>15.7 (0)</td>
</tr>
<tr>
<td>2</td>
<td>6.0 (9)</td>
<td>5.6 (15)</td>
<td>-1.0 (0)</td>
<td>6.6 (9)</td>
</tr>
<tr>
<td>3</td>
<td>4.0 (7)</td>
<td>4.3 (23)</td>
<td>0.9 (0)</td>
<td>5.5 (18)</td>
</tr>
<tr>
<td>4</td>
<td>4.0 (17)</td>
<td>4.0 (40)</td>
<td>2.7 (14)</td>
<td>3.0 (28)</td>
</tr>
<tr>
<td>5</td>
<td>3.5 (28)</td>
<td>3.2 (53)</td>
<td>4.0 (10)</td>
<td>2.6 (44)</td>
</tr>
<tr>
<td>6</td>
<td>2.0 (38)</td>
<td>2.0 (65)</td>
<td>3.6 (32)</td>
<td>2.5 (54)</td>
</tr>
<tr>
<td>7</td>
<td>2.0 (46)</td>
<td>2.2 (69)</td>
<td>2.8 (10)</td>
<td>2.6 (63)</td>
</tr>
<tr>
<td>8</td>
<td>1.5 (54)</td>
<td>2.6 (75)</td>
<td>2.6 (10)</td>
<td>2.7 (71)</td>
</tr>
<tr>
<td>9</td>
<td>2.2 (65)</td>
<td>2.3 (81)</td>
<td>2.8 (100)</td>
<td>1.7 (83)</td>
</tr>
<tr>
<td>2nd stage</td>
<td>3.8 (100)</td>
<td>3.5 (100)</td>
<td>2.9 (100)</td>
<td>2.8 (100)</td>
</tr>
</tbody>
</table>

Zhang et al. Am J Obstet Gynecol 2010

Labor Management

• Has management been improved using new curves?
  – Knowledge of the new curves demonstrated
  – Evidence of tolerating slower progress
  – No reduction in cesarean rate

Needs more work…

Labor Management

• What clinical features do you consider when assessing labor progress?
  – Parity
  – BMI
  – Fetal size
  – Induction

Rosenblum et al, AJOG, 2017

Norman SM et al, Obstet Gynecol, 2012


Blankenship S et al, AJOG, 2019
Labor Management

• How do you manage the second stage?
  – Assessment of pushing efforts
  – Assessment of descent
  – Fetal position
  – Monitoring length of the second stage

WHAT ABOUT EFM?

EFM Management

• The $ is in Category II
  – Deceleration area
  – Use of scalp stim
  – Clinical factors influence a priori risk
EFM Management

- Be aware of the lack of data (and need…)
  - Maternal lateral repositioning
  - Intravenous fluid bolus
  - Decrease oxytocin and/or administer tocolytic
  - Amnioinfusion
  - Maternal oxygen administration

Cesareans Not to Prevent

- Second Stage Arrest
- Failed TOLAC
  - OCC #1 refers to the ‘first’ cesarean
  - Labor management recommendations
- Labor arrest after 7cm

Taken together…

- Apply the best evidence we have
- Challenge our own behavior
Cesarean Prevention

- Obstetric, others, 4%
- Malpresentation, 14%
- Maternal fetal, 5%
- Elective, 3%
- Macrosomia, 6%
- Preeclampsia, 8%
- Multiple gestation, 7%
- Arrest of labor, 18%

OCC #1 Obstet & Gynecol 2014

Thank you

Should VBAC be dead?

- Is it too unsafe for mom and baby?
- Can we make VBAC safer by:
  - Choosing better candidates
  - Altering our labor management
- Is there a downside to eliminating VBAC's?
Reducing the First Cesarean in Real Life

Macones GA, et al. AJOG 2004

Landon MB, et al. NEJM 2004


Predicting Uterine Rupture

Macones GA, et al. AJOG 2006

Grobman WA, et al. AJOG 2008

Maternal and Perinatal Outcomes Associated with a Trial of Labor after Prior Cesarean Delivery

Macones GA, et al. AJOG 2006

Grobman WA, et al. AJOG 2008

Maternal complications with vaginal birth after cesarean delivery: A multicenter study

Macones GA, et al. AJOG 2006

Grobman WA, et al. AJOG 2008

Figure 1: ROC curve for testable predictive model. Adapted from Jourgen.org.

Grobman WA, et al. AJOG 2008
Reducing the First Cesarean in Real Life

TOLAC…Choose wisely...

Relative Morbidity by Mode
- Successful VBAC
- Planned repeat cesarean
- Cesarean after failed TOLAC

Predicting Failure

46

47

48
Reducing the First Cesarean in Real Life

VBAC Calculator

- Maternal age, BMI, race, prior vaginal delivery, non-recurring indication for prior c/s, prior VBAC
- https://mfmunetwork.bsc.gwu.edu/PublicBSC/MFMU/VGBirthCalc/vagbirth.html
- Recently validated in a Dutch cohort
- Editorial in BJOG about the perception of risk
- Also validated for women with 2 prior cesareans

Schoorel ENC, et al. BJOG 2014

Success Rate and Morbidity

Can a prediction model for vaginal birth after cesarean also predict the probability of morbidity related to a trial of labor?

- Predicted success rates and associated morbidity
- Morbidity for TOLAC no greater than ERCS if predicted success rate ≥ 70%

Grobman WA, et al. AJOG 2009

What about 2 scars?

- Landon et al
  - Success: 66% (compared to 73%)
  - Risk of rupture: 0.9% (compared to 0.7%)
- Macones et al
  - Success: 74.6% (compared to 75.5%)
  - Risk of rupture: 1.8% (compared to 0.9%)
- ACOG: 1 or 2 prior LTCS

Macones GA, et al. AJOG 2005
Twins?

- Cahill et al
  - Less likely to attempt
  - No increase in morbidity
  - No decrease in success
- Ford et al
  - 0.9% rupture rate
  - No increase in morbidity
- ACOG: twins are ok

Unknown Scar?

- Secondary analysis of MFMU prospective cohort of 15,519 with a prior c/s
- Compared known (n=13,059) to unknown uterine scar (n=2,460)

- Uterine rupture risk 0.71 (0.37 – 1.37)
- Also, no difference in morbidities
- ACOG: this is ok

Other Factors

- Version
- Prior cesarean for preterm delivery
What do good candidates do?

- 14 Hospital system, 5445 women with 1 prior LTCS
- Examined planned MOD among those with estimated 70% success or more
- Subgroup of 2 hospitals to examine effect of providers

- Less than 1/3 of good candidates underwent TOLAC
- One physician group in the sub-analysis had a 63% TOLAC rate

Metz TD, et al. AJOG 2013

TOLAC Management

- Not contra-indicated in the setting of TOLAC
- Limited tools
- Higher risk TOLACs

Labor Induction
Effect of Prostaglandins on Odds of Utx Rupture

  - Prostaglandins alone: 15.6 (8.1 – 30.0)
- Macones GA, et al.
  - Prostaglandins alone: 0.76 (0.22 – 2.58)
  - Oxytocin alone: 1.25 (0.81 – 1.92)
  - Prostaglandins followed by oxytocin: 7.47 (4.61 – 12.03)

Expected labor progress

<table>
<thead>
<tr>
<th>Cervical Dilatation (cm)</th>
<th>Time to Reach 10 cm Dilatation, Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>120 (90-150)</td>
</tr>
<tr>
<td>4</td>
<td>80 (60-120)</td>
</tr>
<tr>
<td>5</td>
<td>60 (40-90)</td>
</tr>
<tr>
<td>6</td>
<td>40 (30-70)</td>
</tr>
<tr>
<td>7</td>
<td>30 (20-50)</td>
</tr>
</tbody>
</table>

Expected labor progress

<table>
<thead>
<tr>
<th>Variables of labor in TOLAC vs nulliparous women in spontaneous onset of labor</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nulliparous women, onset of labor</td>
<td>10.5 (7.5-13)</td>
</tr>
<tr>
<td>TOLAC women, onset of labor</td>
<td>12.5 (9.5-15)</td>
</tr>
<tr>
<td>Nulliparous women, induction of labor</td>
<td>11.5 (8.5-14)</td>
</tr>
<tr>
<td>TOLAC women, induction of labor</td>
<td>13.5 (10.5-16)</td>
</tr>
<tr>
<td>Nulliparous women, successful spontaneous labor</td>
<td>10.5 (7.5-13)</td>
</tr>
<tr>
<td>TOLAC women, successful spontaneous labor</td>
<td>11.5 (8.5-14)</td>
</tr>
</tbody>
</table>
Induction methods

- Retrospective cohort study
- 214 TOLAC inductions, simplified Bishop ≤ 3
- Oxytocin compared to the Cook balloon (followed by oxytocin)

  - Odds of cesarean higher in the Cook balloon group
    OR 2.09 (1.05-4.18)
  - Longer labor in Cook balloon group (21.9 v. 16.3 hrs, p<0.01)

Shah U, et al. JMFNM 2017
Elective induction v. expectant management

- Secondary analysis of MFMU cesarean registry
- \( \geq 39 \) weeks, 1 prior LTCS
- Induction at \( 39 \, 0/7 - 39 \, 6/7 \) weeks associated with:
  - Increase in VBAC success, aOR 1.31 (1.03 – 1.67)
  - Increase in risk of uterine rupture, aOR 2.73 (1.22 – 6.12)

Palatnik A, et al. AJOG 2015

Induction and risk of uterine rupture

- Retrospective cohort study of TOLACs after 1 LTCS
- 4 years of deliveries in the California Kaiser system
- Compared induced to spontaneous labor
- No difference in the rate of uterine rupture (1.0% v 1.4%, \( p=0.51 \))

Ouzounian JG, et al. AJP 2011

Induction and risk of rupture

- Nested case-control study, 25,000 with a prior LTCS
- Compared rupture to no rupture
- Used time-dependent analysis to account for length of labor
- No increase in risk of rupture once length of labor was accounted for
  - HR 1.24 (0.78 – 1.99)

Oxytocin use

- Nested case-control study, 25,000 with prior LTCS
- Exposure to oxytocin (max dose) and risk of uterine rupture

<table>
<thead>
<tr>
<th>Maximum oxytocin dose (units)</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 (n = 85)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>6.20 (n = 18)</td>
<td>3.24</td>
<td>1.01 to 10.08</td>
</tr>
<tr>
<td>21.30 (n = 45)</td>
<td>1.02</td>
<td>1.30 to 14.32</td>
</tr>
<tr>
<td>31.40 (n = 15)</td>
<td>4.57</td>
<td>1.06 to 20.82</td>
</tr>
</tbody>
</table>

Cate RL et al. AJOG 2008

IUPC use

- Systematic review
- Very low quality evidence; only hyperstimulation could be analyzed
- No MVU features or those of uterine tone indicated rupture
- Not recommended by ACOG, RCOG, or in Canada

Vlemminck MWC et al. Arch Obstet Gynecol 2017

Signs and symptoms of uterine rupture

- Category II or III tracing
  - Recurrent decelerations or bradycardia
- Abdominal pain
- Vaginal bleeding
- Loss of fetal station
- Vital sign abnormalities
  - Tachycardia
  - Hypotension
Epidural dosing

- Nested case-control study within 25,000 cohort with prior LTCS

Summary of patient selection

- Antepartum counseling
  - Complete review of benefits, risks, and alternatives
  - Individual factors that influence candidacy

- Idea that things could change, i.e.
  - Presents in labor
  - Needs induction for pre-eclampsia at 27 weeks
  - Is post dates and closed/L/high
Summary of labor management

- Have a good understanding of expected, normal labor progress
- Induction is reasonable, but consider the context
- Long labors are the enemy
- IUPCs for normal obstetric indications
- Vigilance for evidence of uterine rupture; in the setting of epidural, additional dosing can be a surrogate

Trends in TOLAC location

OBSTETRICS
Vaginal birth after cesarean: neonatal outcomes and United States birth setting
Ellen L. Tilden, PhD, CNM; Melissa Cheyney, PhD, CPNM, LDRH; Joanne-Marie Guise, MD, MPH; Cathy Edwards, MD, CNM; Joel Lapinski, PhD, Frances M. Bler, MPH, M.S., Jack Wierzb, MS, Jonathan M. Brown, PhD

VBAC in 2018

- Not dead
- Continue to resuscitate TOLAC
- Choosing great candidates
- Careful intrapartum care and decision-making
Other ways to reduce cesarean?
UPDATE ON STIs

46TH VAIL OB/GYN CONFERENCE
FEB 19, 2020
VAIL, CO

L. C. Thompson

1

• I have no conflicts to declare

2

Learning Objectives

• Apply recommended screening guidelines
• Implement EPT as appropriate
• Describe Pre-Exposure mitigation of STIs
• Recognize threat of antimicrobial resistance

3
The Bad News

- WHO: 357 M new infections w Ng, Ct, Tv, or Syphilis/yr or IM/IV

- US: 35,000 new cases syphilis 2018, steady increase from historic low 2000: 36% 2017-18

- Congenital syphilis on the rise, 1300 cases in 2018 40% increase

- US: 800,000 Ng/yr 75% since 2009 low.

- US: 1.8 M new cases of Ct infections in 2018 19% since 2014

- Cost $700M/year

- One half (if not more) occur in persons aged 15 to 24 years.

Why Are STI Rates on the Incline?

- Drug Use- Opioid epidemic
  - Directly to shared drug paraphernalia use
  - Associated lifestyle

- Limited access to care for disenfranchised populations

- Budget cuts/financial constraints placed on STD programs. Limits Tx, Screening and Follow-up

- Reduced safe sex practice and condom use in vulnerable populations
How to Correct This?

- Identification of infected persons: Screening
- Evaluation, Tx and Counseling of partners: EPT
- Pre-Exposure Prophylaxis and Immunization
- Effective Dx and Tx (Threatened by resistant organisms)

2015 CDC STD Screening Recommendations

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Special Populations

- **Pregnancy**: Routinely screen:
  - HIV. retest 3rd tri. if high risk, and rapid HIV in labor w/o documentation
  - Syphilis. retest 3rd tri. if high risk
  - Hep B. Retest at admission for L&D if high risk (mult partners, IVDA, other STIs, partner with Hep etc.)
  - Ng. retest 3rd tri. if high risk and if tx’d early in preg.
  - Ct. retest 3rd tri. if high risk, <25 and if tx’d early in preg.
  - Pap. as indicated per screening guidelines (?HPV)
  - Hep C. if high risk - IVDA, Transfusion or Transplant <92

Special Populations cont’d

- **Female Adolescents**: (Demographic with highest rate of Ct and Gc. Very high if not highest for HPV)
  - Confidential care for STIs can be provided in all states. (dependents in health insurance plans may not remain confidential)
  - Yearly screening for Ct. <25
  - Yearly screening for Ng. <25 at risk. (age being a risk)
  - HIV should be discussed

Partner Management: Expedited Partner Therapy (EPT)

- Data limited for benefit of reducing prevalence/incidence w/ partner notification
- When partners are tx’d patients have reduced re-infection rate
- EPT: Partners are tx’d without evaluation or counseling
- Evidence for Ct. reduced by 20% and Gc. by 50% with EPT. ? Benefit for TV.
Pre-Exposure Strategies

- **PrEP.** Although evidence is can backfire: providers withhold, fearing increase # partners or reduce barrier contraception efforts
- **HAART to undetectable VL** U=U
- **HPV Vaccine:** Nonavalent vaccine approved for females and males 9-26-45
- **Hep B Vaccine** for all uninfected pts evaluated for STIs.
- **Hep A & B vaccine** for MSM, IVDA and HIV
AMR: Antimicrobial Resistance

• WW 10 Million Deaths in 2050, $100Trillion
• 35,000 deaths/yr in US currently (increasing)
• Stewardship on Abx guidance in agriculture, aquaculture, industry, manufacturing, sewage/disposal and healthcare
• Global awareness on infection control, advances in hygiene, improved vaccination and diagnostics, appropriate provision
• R&D on future Anti-Biologics
  – Support, collaboration and recruitment scientists
• Awareness

CDC: Antibiotic Resistance Threat

• Highest Risk:
  – *Clostridioides difficile*
  – *Acinetobacter*
  – Candida auris
  – *Enterobacteriaceae*
  – *Neisseria gonorrhoeae*
• Serious Threats:
  – *MRSA*, S pneumoniae, M tuberculosis, Salmonella, *VRE*, *P aeruginosa*, Shigella, Campylobacter
• Potential Risks:
  – Aspergillus, *M genitalium*, B pertussis, GAS, GBS

Antibiotic-Resistant N. gonorrhoeae (ARNG)

• Sulfa, PCN, 1st Ceph, Tetracycline, Macrolides all Hx.
• CDC had recommended single dose quinolones beginning 1993.
• By 2006, resistance or intermediate resistance had increased to 14% (compared with 2% in 2000) for United States
• 2007 Quinolones no longer recommended
Antibiotic-Resistant N. gonorrhoeae (ARNG)

- Gonococcal isolate Surveillance Project (GISP)
- 2014-2017 Ng isolates with elevated MIC
  Azithro doubled 2.5-4.4%
- 2017: 0.2% Ng isolates with elevated MIC to Ceftriaxone
- Oral cephalosporin Tx failures reported in Asia
- Because of concern 250 mg Ceftriaxone is recommended dose.

Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum*

**Recommended Regimens**

Ceftriaxone 250 mg in a single intramuscular (IM) dose

OR, IF NOT AN OPTION

Cefixime 400 mg in a single oral dose

PLUS

Azithromycin 1 gm po

Dual therapy recommended even if Ct negative for greater effectiveness with possible resistance.

N. gonorrhoeae

- Follow-up – If diagnosed with uncomplicated gonorrhea and treated with recommended regimens, no test of cure routinely needed.
  Retest at 3 months for re-infection (not failed therapy).
- **Any person should be rescreened 3 mos. After Tx for Gc, Ct, Tv.**
  (If pregnant TOC and retest3rd trimester)
- Partners –EPT: Dual therapy with oral agents (Cefixime and Azithro) or Instruct patients to refer partners for evaluation, testing, and treatment.
**N. gonorrhoeae: What if?**

- **Severe allergy**
  - Gentamicin 240 mg IM + azithromycin 2 g PO, or
  - Gemifloxacin 320 mg PO + azithromycin 2 g PO

- **Increasing resistance?**
  - Zoliflodacin
  - Gepotidacin
  - Solithromycin
  - Delafloxacin
  - Fosfomycin

---

**Gonorrhea Tx**

- Zoliflodacin- Inhibits DNA synthesis
- **RCT 179** & **69** received 1500 or 3000 mg
  - **Microbial eradication**
    - 96% uro-gen
    - 50% pharyngeal
    - 100% rectal

- All 3 regimens cured 13 pts with anorectal Ng
- However Pharyngeal site: 67% 2 g zol, 78% 3 g zol, 100% Ceft

- In phase III testing

---

**Gonorrhea Tx**

- Gepotidacin: Bacterial Topoisomerase inhibitor
- **RCT 69** & **69** received 1500 or 3000 mg
  - Microbial eradication
    - 96% uro-gen
    - 50% pharyngeal
    - 100% rectal

- All of the Tx failures were Resistant to Cipro and harbored mutations for abx binding site
- In phase III studies
Gonorrhea Tx

- **Solithromycin**: fluoroketolide w activity against Ng, Ct, and M gen.
- Phase 2 study with 100% efficacy in urogen/rectal and oral sites.
- Limiting liver effects and infusion site infection
- NIAID phase III study revealed no difference compared to Ceftriaxone/Azithro

---

Gonorrhea Tx

- **Ertapenem**: Carbapenem
- Comparable efficacy to Ceftriaxone and Cefixime
- Ongoing phase III study comparing Ertapenem/Fosfomycin/Gentamycin/Ceftriaxone for anogenital Ng
- Concern for exposure to non-target organisms and resistance

---

Gonorrhea Tx

- **Fosfomycin**
- Encouraging In-Vitro activity against multi-drug resistant Ng.
- Has led to resistant Gram-negative organisms when used as monotherapy
- Ongoing studies for combination use with Cipro and Azithro
Gonorrhea Tx

- Spectinomycin: originally used in 60s but resistance evolved and its use D/Cd
- New class Aminomethyl Spectinomycin has demonstrated greater efficacy for Ng and also Ct and being tested

Prevention Developments

- NIH renewing interest and resources for Vaccine development.
  - 2018 $9M RFA for 3-5 awards
- PrEP and PEP for other STIs

Doxycycline

- Pilot study demonstrating efficacy as STI-PrEP
- Small study 30 MSM and Transgender Women
- 70% decrease in Tx group for Tp/Ct/Gc

- Substudy of Ipergay with Post exposure Doxy:
  - 232 MSM, Tx group 200 mg Doxy after episodes
  - 70% decrease in Tp/Ct but not Ng
Doxycycline

- BC CDC
  - Study using Doxy PrEP for Syphilis in HIV negative MSM also on HIV-PrEP
  - Study using daily Doxy for Syphilis prevention in 288 MSM HIV+
- Australia
  - Study using 100mg Doxy daily in 125 MSM or BM to reduce Tp/Gc/Ct

Vaccine Research

- Retrospective case-control study of 15,000 young adults received MnB vaccine during an epidemic and were 31% less likely to be Dxd with Ng compared to Ct.
  - Same study demonstrated 45% decrease compared to Non-vaccine recipients
- Research at OHSU have identified proteins from cell envelope and cytoplasm that are present in all resistant strains of Ng and using these as targets for new therapies

Vaccine Research

- Researchers believe natural Ct infection can lead to immunity and explains why adolescents have higher infections rates than older persons
- Some data show young women with spontaneous clearance are resistant to re-infection
- Potential promise with Chlamydial antigen BD584 as vaccine candidate
Vaccine Research

- UK has several phase I chlamydial vaccine trials.
- Efforts have identified common antigens on Treponema outer membrane which are preserved across strains and may serve as a vaccine target.
- Cross protection among syphilis strains seems to be lacking and previously infected individuals are susceptible to future infection with different strains.
LARC AND BIRTH OUTCOMES

Stephanie Teal, MD, MPH
Professor of Obstetrics and Gynecology and Pediatrics
University of Colorado School of Medicine

Why is a Professor of Family Planning giving an OB talk?

Outline of presentation

- What is the relationship between birth spacing and birth outcomes?
- Is there unmet need for improved birth spacing?
- Does improved access to highly effective contraceptives
  - increase interpregnancy intervals?
  - Time to first pregnancy?
  - Reduce unintended pregnancy?
- Does improved access to highly effective contraceptives
  improve birth outcomes?
Short interpregnancy interval and perinatal outcomes

- Multiple studies show association of short IPI and:
  - delayed PNC, preterm birth, neonatal morbidity, low birthweight
- Retrospective study of primiparous women with singleton gestation delivering in US
  - N=1,964,000
  - Short IDI associated with PTD, SGA, low Apgar, NICU admission


Unintended pregnancy, birth spacing and birth outcomes

- Regardless of birth interval, unintended pregnancies have greater risk of adverse outcomes
  - preterm birth (PTB) and delivery of LBW infants
- The link between unintended pregnancy and poor birth outcomes is likely multifaceted,
  - maternal socioeconomic risk factors,
  - inadequate prenatal care, and
  - preconceptual and prenatal maternal behavioral risk factors


Is there an unmet need for improved birth spacing?

- 33% of US pregnancies have interpregnancy interval of <18 months
- 9% have interdelivery interval of <18 months
- Half of postpartum women resume intercourse within 6 weeks of delivery
- 117,000 postpartum Medicaid recipients in CA:
  - 60% did not have a contraceptive claim within 3 months postpartum
- 13% received contraception at first postpartum visit: significantly more likely to have an adequate IPI
- Infant <9 months is a risk factor for abortion in next pregnancy
Does improved access to LARC increase IPI?

- 2006-2010 NSFG data
- Contraceptive use at 0, 3, 6, 12, 18 months
- Pregnancy within 18 months
  - Hormonal method users=12.6%
  - LARC users=0.5%
- At least 70% of pregnancies within 12 months were unintended

Contraception for young mothers

- 12 to 49% of adolescent mothers are pregnant again within one year (RRP)
- A second child in adolescence predicts a high risk of negative outcomes
- Teens have the highest rate of PTB by age group
- Many different interventions with limited success
- Norplant associated with prevention of RRP in adolescents

Immediate post-partum implants

- All adolescents in CAMP delivered 6/1/08-11/30/09
- Prenatally, offered immediate PP implant
- Immediate PP IUDs not available
- Records reviewed; phone interviews for missing data
- Variables: demographic, reproductive, contraceptive use, discontinuation/re-initiation of contraceptives, pregnancy
- Consistent Contraception
- Using one or more contraceptive method(s) for 80% of the year of observation
Participation

<table>
<thead>
<tr>
<th>Group</th>
<th>N=396</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravid</td>
<td>253</td>
<td>18.6 ± 1.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>171</td>
<td>35.6%</td>
</tr>
<tr>
<td>Black</td>
<td>161</td>
<td>89.5%</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.3</td>
<td>48.6%</td>
</tr>
<tr>
<td>Underweight</td>
<td>153</td>
<td>56.8%</td>
</tr>
<tr>
<td>Average weight</td>
<td>218</td>
<td>43.1%</td>
</tr>
<tr>
<td>Overweight / obese</td>
<td>153</td>
<td>94.2%</td>
</tr>
</tbody>
</table>

Controls

<table>
<thead>
<tr>
<th>Group</th>
<th>N=225</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravid</td>
<td>142</td>
<td>14.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>123</td>
<td>42.7</td>
</tr>
<tr>
<td>Black</td>
<td>113</td>
<td>56.8%</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.5</td>
<td>34.6%</td>
</tr>
<tr>
<td>Underweight</td>
<td>107</td>
<td>60.7%</td>
</tr>
<tr>
<td>Average weight</td>
<td>136</td>
<td>34.6%</td>
</tr>
<tr>
<td>Overweight / obese</td>
<td>107</td>
<td>94.6%</td>
</tr>
</tbody>
</table>


Implant Continuation

<table>
<thead>
<tr>
<th>Reason for discontinuation</th>
<th>n=46</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregular bleeding</td>
<td>19</td>
</tr>
<tr>
<td>Headache</td>
<td>5</td>
</tr>
<tr>
<td>Moodiness</td>
<td>4</td>
</tr>
<tr>
<td>Weight gain</td>
<td>4</td>
</tr>
</tbody>
</table>


Repeat Pregnancy

<table>
<thead>
<tr>
<th>Group</th>
<th>n=91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravid</td>
<td>18.6%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>46.2%</td>
</tr>
<tr>
<td>Black</td>
<td>2.6%</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

Cost-effectiveness

■ Costs estimated using Colorado Medicaid payments
  – Implant device, insertion, removal, ectopic, SAB, NSVD, C/S
■ Outcomes estimated using results of CAMP IPI project


Annual costs/1000 women


Cost-effectiveness

For every dollar spent $0.79, $3.54, and $6.50 would be saved at 12, 24, and 36 months.
LARC and Birth Outcomes

1/24/20

STRATEGY & TACTICS

INCREASE USE OF LARC

- Eliminate and/or Reduce Cost to Women
- Expand Marketing and Outreach About Methods
- Educate and Train Providers
- Counsel Patients

---

STRATEGY & TACTICS

PROMOTE HEALTHY DECISIONS & PLANNING

- Normalize Conversations About Sexual Health
- Engage Schools, Parents, and Communities
- Strengthen Outreach to Specific Audiences
- Connect Clinics, Mobiles, and Social Workers

---

STRATEGY & TACTICS

IMPROVE PUBLIC POLICY & PRACTICES

- Partner with State and County Government to Lead Public Health Improvements
- Integrate Public Health and Social Service Programs
- Enhance Medicaid Coverage for Contraceptive Services
- Advance State and School Policies
Between 2009-2013, the abortion rate fell by 42% for those aged 15-19 and 18% for those aged 20-24.

Unintended Pregnancy Rate

Average age at first birth, Colorado, 1990-2014
Does LARC really reduce unintended pregnancy in teens?
Pregnancy Rates among Sexually Experienced U.S. Adolescents, as Compared with CHOICE Participants


In the realm of PTB prevention, these numbers are more impactful than all of the previous efforts with tocolytics and progesterone... (nationwide the) downstream impact would be prevention of more than $1 billion in health care expenditures... A. Caughey, Obstet Gynecol Survey
Effect on low birthweight & preterm birth

Adjusted for: maternal age, race/ethnicity, BMI, education, income, marital status, prenatal care, smoking status, history of gonorrhea, history of chlamydia, history of congenital anomaly, and interpregnancy interval.

Direct link between LARC use and reduced PTB

- N=112,000 Medicaid births in California, second order or higher (2011)
  - How long ago was the prior birth?
  - Was the birth preterm?
  - Contraceptive method after the prior birth?
- 9.75% of births preterm
- For each additional month of contraceptive use, odds of PTB ↓ 1.1%
- Mean contraceptive coverage duration was greatest with IUD and implants

Missed opportunities

- Patients with too little info to request LARC
- Providers perceive disinterest
- Missed opportunity to increase LARC awareness and knowledge
- Providers uncertain of suitability of LARC
Colorado results

- LARC initiation and use is very high in Colorado
- This results in reductions in:
  - Teen births
  - Abortions
  - Unintended pregnancies
  - Rapid 2nd births
  - Preterm births
  - Low birth weight
  - Costs
- Same-day initiation is important and reasonable
- Patients know what they want, are confident in their choices, and continue use

Your questions!
Bundles, Bundles, Bundles: Improving Surgical Outcomes

Saketh R. Guntupalli, MD, FACOG, FACS
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Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
University of Colorado School of Medicine- Denver

Disclosures

• I have no relevant disclosures for this talk.

Surgical Bundles

• A grouping of best practices that individually improve care, but when applied together result in substantially greater improvement.

• Science behind the bundle elements is well established – the standard of care.

• Bundle element compliance can be measured as “yes/no” for audit.
Surgical Bundles

Key components of bundles and protocols
• Easy to implement
• Easy to replicate
• Compliance rate is high (> 90%)
• Easy to identify “failures” or issues with compliance
• Compliance can be measured as “yes/no” for audit

Surgical Bundles- Top 3

The are many different types of bundles but the three that generally have the most impact in surgical practice...

• Prevention of Surgical Site Infections
• Prevention of Catheter Associated Urinary Tract Infection (CAUTI)
• Prevention of Venous Thromboembolism

Surgical Site Infection Control

• Infections are the leading cause of morbidity associated surgery.
• These infections have a substantial effect on surgical outcomes
  • Long term prognosis of the patient
  • Cost to the health care system
Surgical Site Infection Control

- Purulent discharge, abscess or spreading cellulitis at surgical site up to one month after surgery.
- 3rd most common hospital infection
- Incidence: 0.5 – 15%
  - Incisional
    - Superficial
    - Deep
  - Organ Space
    - Generalized (peritonitis)
  - Abscess

Risk factors for the development of SSI

- Diabetes mellitus
- Hypoxemia
- Hypothermia
- Leukopenia
- Nicotine (tobacco smoking)
- Immunosuppression
- Malnutrition
- Poor skin hygiene

Surgical Site Infection – Wound Classification

- Class 1 = Clean
- Class 2 = Clean contaminated
- Class 3 = Contaminated
- Class 4 = Dirty infected

Bundles, Bundles, Bundles: Improving Surgical Outcomes

SSI Definitions

- Superficial
  - Purulent drainage from wound
  - Positive wound culture
  - Pain, redness, swelling
  - Diagnosis by surgeon

- Deep
  - Purulent drainage from deep aspect of the wound
  - Dehiscence
  - Abscess on exam or CT scan

- Organ Space
  - Infection in the surgical cavity (abdomen)

What are the costs associated with surgical site infection?

- 313 million
- 38%
- $1 billion
- 3-20 days
- 1 in 2

SSI Bundles

- Appropriate preoperative antibiotics given at right time
- Surgical clipping of the area
- Correct identification of type of surgery (clean, contaminated etc.)
- Appropriate closure of wound

BUNDLES in Electronic Health Record

- Correct type of wound description
- This initiates an order set for antibiotic therapy IF INDICATED
- Drain placement?
- Type of wound closure
Bundles for prevention of surgical site infections - Clipping

• Clipping should always be done outside the OR whenever possible
• Removal of stray hairs from clipping should be done using current methods (tape and/or suction), while clipping on top of a disposable underpad
• Remove and dispose of single-use clipper head immediately after use and clean the clipper unit according to manufacturer instructions before storing
• In cases of excessive amounts of hair, use vacuum assisted suction device and associated single-use disposable tubing

Surgical Site infection - antibiotics

• Antibiotic therapy for various gynecologic procedures
• Key to this is using the correct antibiotics for the right procedure. AND
• Continuing the antibiotic for the right amount of time
• Prolonged therapy has its consequences...
Johns Hopkins Hospital Antibiotic Poster
Perioperative Antibiotic Prophylaxis To Prevent Surgical Site Infection

Urinary Tract Infection - Background

• Urinary tract infection is the most common health care-associated infection the United States (40% of 1.7 million cases)
• 40% of urinary tractions infections are catheter associated urinary tract infections (CAUTI)
• Up to 25% of all hospitalized patients have a urinary catheter at some point during their stay

National Costs

• CAUTI increases hospital stay 2-4 days on average
• Estimated 13,000 deaths annually from CAUTI (mortality rate 2.3%)
• National economic cost of CAUTI estimated at $400 million annually
• Since 2008 hospitals have been unable to classify CAUTI within a higher diagnosis related group in order to receive additional reimbursement from Medicare
CAUTI Risk Factors

- Prolonged catheterization
- Female sex
- Older age
- Diabetes
- Lower training of inserter
- Placement of catheter outside of OR

- Impaired immunity
- Renal dysfunction
- Orthopedic and neurologic services
- Disconnection of closed drainage system

CAUTI-Prevention

Study Design –Prevention of CAUTI

- Single-site randomized control trial
- Patients enrolled and randomized within 24 hours of surgery
- Randomization performed by computer algorithm via RedCap
- Goal enrolment of 100 patients per arm to detect a 50% reduction in UTI rates in the intervention group (alpha 0.05 and power 0.84)
Treatment Groups

- Arm 1: Standard of Care Technique
  - Catheter placed on surgical field after vaginal prep by resident or attending physician using standard aseptic technique
- Arm 2: Enhanced Aseptic Technique
  - Same steps as SOC, with addition of banding the protective plastic sheath to the catheter and dipping the tip of the catheter in betadine prior to insertion
  - Plastic sheath remains in place until removal of catheter

Assessment

- Urine dipstick within 24 hours post-operatively
- Urine dipstick and patient satisfaction survey at 2 weeks post-operative visit
- If positive nitrates or leukocyte esterase on urine dipstick, then reflex to formal laboratory urinalysis and urine culture
- UTI defined as 10⁵ of a single bacterial organism on urine culture
  - Treated with antibiotic of physician’s choice

Outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Enhanced Aseptic (N=40, 49%)</th>
<th>Standard of Care (N=42, 51%)</th>
<th>Total (N=82)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture confirmed UTI</td>
<td>Yes 4 (10%) 6 (14%) 10 (12%)</td>
<td>No 36 (90%) 36 (86%) 72 (88%)</td>
<td>0.599</td>
<td></td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>Yes 24 (60%) 22 (52%) 46 (56%)</td>
<td>No 16 (40%) 20 (48%) 36 (44%)</td>
<td>0.487</td>
<td></td>
</tr>
<tr>
<td>Surgery time (mean minutes)</td>
<td>181.7 (56-349) 204 (86-376) 193.1 (56-376)</td>
<td>0.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic @ 24 hours</td>
<td>n/a</td>
<td>Yes 0 (0%) 0 (0%) 0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(+) UA at 24 hours</td>
<td>Yes 0 (0%) 1 (2%) 1 (1%)</td>
<td>No 40 (100%) 41 (98%) 81 (99%)</td>
<td>1.00</td>
<td></td>
</tr>
</tbody>
</table>
Bundles, Bundles, Bundles: Improving Surgical Outcomes

Bundles to prevent CAUTI

• Ensure patients who don’t need a catheter don’t get one (diagnostic l-scopes, simple BSO)
• You can always put in a Foley later if your case goes longer
• Initiate antibiotic prophylaxis if patient is at high risk
• Use sterile technique in placement of Foley catheters

Venous Thromboembolism Prevention

• 350,000 to 650,000 with VTE per year
• 100,000 to > 200,000 deaths per year
• About half are hospital related.
  • VTE is primary cause of fatality in half of post surgical patients
  • More than HIV, MVA’s, Breast CA combined
  • Equals 1 jumbo jet crash / day
• 10% of hospital deaths
• PE among top sources of preventable hospital related death
• Huge costs and morbidity (recurrence, post-thrombotic syndrome, chronic PAH, anticoagulation)

Venous Thromboembolism in OBGYN

• Pregnant patients are at particularly high risk for the development of VTE
• Hypercoagulable state of pregnancy
• Lack of mobility as pregnancy progresses
• Prolonged hospitalisation if patients are admitted
  • Pre-Eclampsia
  • PPH
  • Other chronic conditions
One of the most common causes of mortality from extensive surgical debulking in women with gynecologic cancer continues to be venous thromboembolism (collectively deep venous thrombosis and pulmonary embolism).

Rates of VTE after surgery for gynecologic cancer are as high as 26% for deep venous thrombosis (DVT) and 9% for pulmonary embolism (PE) without prophylaxis.

Based on this data, the American College of Chest Physicians recommends the use of preoperative heparin, sequential compression devices (SCD) during surgery, and post-surgical DVT prophylaxis for women undergoing pelvic surgery who are at moderate risk for the development of VTE.

- Low Risk: Minor surgery in mobile patients. Medical patients who are fully mobile. Observation patients with expected hospital stay < 48 hours. No prophylaxis, reassess periodically, ambulate.
- Moderate Risk: Most general, thoracic, open gynecologic or urologic surgery patients. Medical patients, impaired mobility from baseline or acutely ill. UFH or LMWH prophylaxis.
- High Risk: Hip or knee arthroplasty, hip fracture surgery, multiple major trauma, spinal cord injury or major spinal surgery, Abdominal-pelvic surgery for cancer. IPCD AND LMWH or other anticoagulant.

For those at moderate or high risk and contraindications to anticoagulation, use IVC filters.

VTE Bundle Screening
VTE Bundles

- Necessary to prevent life threatening complications
- Easy to use in an electronic health record
- Risk stratifying patients is key
  - Open of MIS surgery?
  - Cancer or No cancer?
  - Length of the procedure?
  - Immobility following the procedure

Our VTE Bundle

- Bundle used in our practice....(order set in EPIC)
  - All patients risk stratified as low moderate and high risk
  - Moderate and high risk patients
    - Sequential compression devices at intubation and throughout case
    - Preoperative heparin 5000 units SQ at incision
    - Post operatively:
      - 5000 units SQ q 6 hours x 24 hours (begin 6-12 hours after surgery completed)
      - Within 24 hours convert to SQ enoxaparin if H/H stable
    - If high risk or cancer- continue anticoagulation for 28 days per ACCP recommendations
    - If moderate risk tailor to patient

Study Design

- Prospective Randomized Open-Blinded End-point (PROBE) study for safety with N=400
- Previous presentation for interim safety analysis was presented at the 2017 Society of Gynecologic Oncology annual meeting
- This data represents the final report for safety and efficacy
- Recruitment occurred at two sites:
  - University of Colorado Hospital, USA
  - University of Southern California, USA
Study Design

- Participants were randomized to:
  - Oral apixaban 2.5 mg tablet BID for 28 days post surgery OR
  - Subcutaneous enoxaparin 40 mg QD for 28 days post surgery
- Followed for 90 days post-operatively

Study Design

Screening Visit
- Suspected/confirmed Gyn-Onc malignancy
- No history VTE
- No bleeding disorders
- Not on anticoagulant or NSAIDS or SSRIs

Gyn. Surgery
- 5,000 units Heparin SQ
- Compression devices
- Heparin 5,000 units SQ TID post-op
- Observed for no bleeding 12-24 hrs. post-surgery
- Epidural had been d/c as intended

Open Cases
MIS (<20%)
Bundles, Bundles, Bundles: Improving Surgical Outcomes

Study Design

Randomization: 1:1

Post-surgery day 1-7

Screening Visit
- Suspected/confirmed Gyn-Onc malignancy
- No history of VTE
- No bleeding disorders
- Not on anticoagulant or NSAIDS/SSRIs

Gyn. Surgery
- 5,000 units Heparin SQ
- Compression devices
- Heparin 5,000 units SQ TID post-op

Open Cases
- No observed bleeding for 12-24 hrs. post-surgery

Visit 3
- Post-op check 10-18 days post-surgery
- Assessment of bleeding
- Wells criteria and physical assessment for VTE
- Collection of AEs
- Medication adherence

Visit 4
- Study day 24-32
- Assessment of bleeding
- Wells criteria and physical assessment for VTE
- Collection of AEs
- Medication adherence
- Satisfaction and QOL
**Study Design**

- **Screening Visit**
  - Gyn-Onc malignancy
  - No history of VTE
  - No bleeding disorders
  - Not on anticoagulant or NSAIDS/SSRIs

- **Gyn. Surgery**
  - 5,000 units Heparin SQ
  - Compression devices
  - Heparin 5,000 units SQ TID post-op

- **Open Cases**
  - Apixaban 2.5mg BID for 28 days
  - Enoxaparin 40mg SQ for 28 days

- **MIS (≤20%)**
  - Apixaban 2.5mg BID for 28 days
  - Enoxaparin 40mg SQ for 28 days

- **Visit 3**
  - Post-op check 10-18 days post-surgery
  - Assessment of bleeding
  - Wells criteria and physical assessment for VTE
  - Collection of AEs
  - Medication adherence

- **Visit 4**
  - Study day 24-32
  - Assessment of bleeding
  - Wells criteria and physical assessment for VTE
  - Collection of AEs
  - Medication adherence
  - Satisfaction and QOL

- **Visit 5**
  - Study day 76-104
  - Assessment of bleeding
  - Wells criteria and physical assessment for VTE
  - Collection of AEs

---

**Primary Outcome - Safety Evaluation**

- One major bleeding event in each arm
  - 0.5% vs. 0.5%, OR=1.05, 95% CI 0.07-16.76, \(P=1.00\)
  - 12 CRNM bleeding events in the apixaban arm and 19 in the enoxaparin arm
  - 5.4% vs. 9.7%, OR=1.88 95%, CI 0.87-4.1, \(P=0.11\)

  No significant difference in major bleeding or CRNM

---

**Secondary Outcome: Venous Thromboembolism**

- 5 VTE events occurred during the study period
  - 2 in the apixaban arm and 3 in the enoxaparin arm
  - 1.0% vs. 1.5%, OR=1.56 95% CI 0.26-9.50, \(P=0.68\)
  - 13 additional patients evaluated for suspected VTE (3.2%)
  - Underwent lower extremity ultrasonography or CT angiography
  - All determined to be negative for VTE

  No difference in VTE events
Bundles for Improvement of Quality

- Bundles can improve the quality of surgical health care delivery in selected patients in both obstetrics and gynecology.
- Bundles should be implemented in systems that have a high degree of reproducibility and oversight.
- Identification of key quality outcomes for improvement are key to bundles systems to work.

Thank you!
LEARNING OBJECTIVES

• Implement effective office introduction to aneuploidy screening
• Perform timely referral for follow-up of abnormal or unusual results
• Effectively counsel on cfDNA/NIPT technology, indications, and limitations
• Identify some cfDNA/NIPT pitfalls using case examples

DISCLOSURES

• I have no relevant financial relationships or conflicts of interest.

THE PRENATAL TESTING PARADIGM

Prescreen /Pretest  Counseling  Postscreen/ Posttest
Genetic/MFM  Counseling  Procedure/ Diagnosis
Maternal Decisions  Counseling  Termination/ Continuation

WHAT DOES YOUR PATIENT WANT TO KNOW?

- Lethal abnormalities only?
- Severe structural anomalies?
- Any abnormalities?
- Informational/planning only?
- Nothing?
- Everything?

PREVALENCE OF CHROMOSOMAL ABNORMALITIES

Percent of Reported Chromosome Abnormalities

- T21
- T18
- T13
- 45,X
- Sex trisomy
- Other rare
DETECTION OF DOWN SYNDROME: IMPROVEMENTS

DETECTION RATES FOR SEQUENTIAL SCREENING

PRENATAL SCREENING OPTIONS – RISK SCORE

Down Syndrome Testing with 5% Screen Positive Rate
Detection Rate (%)
1st Trimester NT Ultrasound 64-70
1st Trimester First trimester blood screen NT Ultrasound 82-87
2nd Trimester Triple Screen 69
2nd Trimester Quadruple Screen 81
Integrated Screen 51-60
Integrated Serum 51-60
CELL FREE FETAL DNA

- Access fetal DNA in maternal blood
- Measures placental DNA fragments
- Up to 10% of DNA in maternal plasma is FETAL
- 10 weeks GA detection
- Rapidly degraded after delivery
- First available 2011
- High detection rate and low false positives

METHODS

CELL FREE FETAL DNA FOR T21: META-ANALYSIS
CELL FREE FETAL DNA FOR OTHER ANEUPLOIDIES

<table>
<thead>
<tr>
<th>Aneuploidy</th>
<th>Detection Rate</th>
<th>False Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 18</td>
<td>97%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>87%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Sex Chromosomes</td>
<td>86%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Gil et al. (2017)

CELL FREE FETAL DNA

- Trisomy 21
  - 99% detection
  - 0.2% false positive
- Trisomy 18, Trisomy 13
  - 80-98% detection
  - 1% false positive
- Sex chromosomes
  - Y and aneuploidy
- Microdeletion/duplication
- Copy number variants >7Mb
- Rh typing
- Chorionicity
- Paternity testing
- Single gene disorders


• Trisomy 21
  • 99% detection
  • 0.2% false positive
• Trisomy 18, Trisomy 13
  • 80-98% detection
  • 1% false positive
• Sex chromosomes
• Y and aneuploidy
• Microdeletion/duplication
• Copy number variants >7Mb
• Rh typing
• Chorionicity
• Paternity testing
• Single gene disorders

EVER EXPANDING UNIVERSE

Available panels currently screen for T9 and T16 and 5 microdeletion regions.
WHAT WOULD YOU DO?

21yo G1P0 at 12 weeks wants "the gender test" for prenatal aneuploidy screening. You discussed cfDNA, sequential screen, CVS, and amniocentesis.

cfDNA is screen positive for Trisomy 13.

What’s next?

16

WHAT WOULD YOU DO?

A. First trimester anatomy and NT
B. Detailed anatomy at 17 weeks
C. Refer to MFM and recommend diagnostic testing
D. Resend cfDNA
E. Send Quad Screen

17

WHAT WOULD YOU DO?

A. First trimester anatomy and NT
B. Detailed anatomy at 17 weeks
C. Refer to MFM and recommend diagnostic testing
D. Resend cfDNA
E. Send Quad Screen

18
WHAT WOULD YOU DO?

She made an appointment at Planned Parenthood for termination.
She did not see MFM or have diagnostic confirmation.
POCs show normal karyotype 46, XY

LIMITATIONS OF CF DNA

• False positives (such as placental mosaicism)
• True mosaic positives
• Vanishing twin
• Maternal abnormalities
  • Copy number variants
  • Chromosome abnormality
• Mosaicism (e.g., 45 X,0)
• Higher false positives for conditions other than T21, T18 and T13
• No-call results
• Lower PPV in low risk populations
• Does not screen for ONTD
• Insurance coverage?
• Rapid change (sales validation)

There will always be false positives and negatives.
STILL JUST SCREENING: FALSE POSITIVES AND NEGATIVES

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21</td>
<td>93%</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>64%</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>44%</td>
</tr>
<tr>
<td>45, XO</td>
<td>38%</td>
</tr>
<tr>
<td>Total</td>
<td>67%</td>
</tr>
</tbody>
</table>


REASSURE ON INVASIVE DIAGNOSTIC TESTING RISK

- Stratified by risk profile, there is NO risk for CVS or amniocentesis.
- CVS 0.2% and Amnio 0.12% procedure related loss.


Effect of Cell-Free DNA Screening vs Direct invasive Diagnosis on Miscarriage Rates in Women With Preganacies at High Risk of Trisomy 21

- First Tri Screen positive → randomized to cfDNA → invasive testing if positive.
- Or immediate invasive testing.
- No difference in miscarriage rate (0.0%) for pregnancy at risk of Trisomy 21.

Updates on Prenatal Genetic Screening

Cell-free DNA Analysis for Noninvasive Examination of Trisomy

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Positive predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire cohort (mean age 30.7 yrs)</td>
<td>83%</td>
</tr>
<tr>
<td>Maternal age &lt;35 yo</td>
<td>70%</td>
</tr>
<tr>
<td>Low risk trimester TTS (c1/270)</td>
<td>50%</td>
</tr>
</tbody>
</table>

POSITIVE PREDICTIVE VALUES

ONLINE PPV CALCULATORS

- Perinatal Quality Foundation (PQF)
  - http://www.perinatalquality.org/Vendors/NSGC/NIPT
  - Also includes microdeletion calculator, but need to get sensitivity/specificity for these from test report.
  - Can be adapted as smartphone app.

- UNC Calculator
  - https://www.med.unc.edu/mfm/nips-calc/ (after testing)
  - Lets you set which company’s test is being used
  - Standard assumptions
  - Adjust maternal age and GA, or from a priori risk

High Risk: 35yo, sono abnormalities, prior aneuploid child, parental chromosomal problems (T13, 21), positive maternal serum screening.
PPV/NPV CALCULATOR: WWW.PERINATALQUALITY.ORG

NIPT/Cell Free DNA Screening Predictive Value Calculator

Updates on Prenatal Genetic Screening
CFDNA VS SEQUENTIAL SCREENING: GENERAL POPULATION

- Compared sequential vs cffDNA in large California cohort (n = 453K)
- 2575 (0.6%) had a chromosomal abnormality; 50% T21
- Sequential screening detected 83% that were potentially also detectable by cffDNA
- A chromosome abnormality undetectable by cffDNA was present in 2% of sequential-screen positive pts
- Overall detection rate for “others” (n = 601) higher for SS (54% v 6)
- “No result” cffDNA seen in 3.3%, 10.3%, 12.5%, 17% of T21, T13, T18, and 45, XO
- cffDNA has lower detection than sequential screen for T18 (86 v 93%) and 45X (74 v 80%)
- cffDNA has higher detection than sequential screen for T21 (96 v 93%)
- Overall detection rate for all aneuploidies is higher for SS (82% v 71%)

ACOG GUIDELINES FOR CFDNA

- Committee Opinion 2012
  - Patients at increased risk for aneuploidy
    - early pregnancy
    - advanced maternal age
    - family history
    - abnormal serum testing
    - abnormal ultrasound findings
- Committee Opinion 2015
  - Discuss screening and diagnostic tests with all patients
  - Use conventional serum screening for general population
  - Do not test with multiple technologies
  - Do not perform routine microdeletion screening
- Practice Bulletin 2018
  - Sensitivity and specificity are similar in unaffected and high risk populations
  - PPV is lower due to prevalence
  - Okay to follow maternal serum screening with cffDNA but causes delay
  - No termination without diagnostic testing
  - Regard “no call” with caution
  - Microdeletion testing not recommended
  - MSDAP testing is still recommended
  - Abnormal maternal serum screen with normal cffDNA is 3% residual risk
SMFM GUIDELINES

- With negative cfDNA, first trimester ultrasound NT not recommended
- Invasive/diagnostic testing not recommended for isolated soft sonographic marker with negative cfDNA
- Isolated soft marker and normal maternal serum 1st or 2nd trimester screening, the finding is "not clinically significant" or "normal variant"
- Any fetus with structural abnormality, offer diagnostic testing and microarray
- Do not perform routine cfDNA screening for microdeletions

WHAT WOULD YOU DO?

34yo G2P1 at 20w for routine fetal anatomy survey. First tri ultrasound was normal with normal NT. cfDNA negative for T21, 18, 13, XX

Ultrasound shows normal male genitalia

What’s next?

WHAT WOULD YOU DO?

A. Quad screen
B. Repeat cfDNA
C. Refer to MFM
D. Detailed ultrasound
E. Amniocentesis
F. Maternal karyotype
Updates on Prenatal Genetic Screening

WHAT WOULD YOU DO?
A. Quad screen
B. Repeat cfDNA
C. Refer to MFM
D. Detailed ultrasound
E. Amniocentesis
F. Maternal karyotype

DIFFERENTIAL
Lab error/ mix up
False-negative (<1%)
XX sex development disorder
SRY, CAH, others
Sex chromosome anomaly or mosaic

OUTCOME
Normal male
SRY translocation
Extremely rare disorder

DOES NT MEASUREMENT HAVE ADDED VALUE IN NIPT TESTING?
- 25,057 singleton pregnancies, 1st trimester combined testing
- 225 fetuses (0.9%) with NT >3.5mm → 211 karyotyped
  → 103 chromosomal anomalies
    - 79/225 with T13, T18, or T21
    - 24/225 chromosomal anomaly other than T13, T18, or T21
      was detected
    - 11/225 fetal demise
    - 10/225 fetal anomalies
    - 3 fetuses with normal US
- So 3 (0.01%) chromosomal anomalies would have been missed using NIPT and fetal ultrasound that would have been detected on first tri NT measurement
- Also... Dating, number, and chorionicity

REFERENCES
First trimester dating and 18/13 (Down) sequencing cfDNA testing or diagnostic testing
cfDNA if abnormal sequential screening
Detailed fetal anatomy survey (20w): Amnio if anomaly

First tri anatomy Dating and NT (13w) Sequential cfDNA screen or diagnostic testing
WHAT WOULD YOU DO?

37 yo G3P0 at 12 weeks with IVF pregnancy. Twin demise at 7 weeks. Patient wants “the gender test.”

cfDNA is unreportable.

At 18 weeks, a different cfDNA test is sent. Result is triploidy.

What’s next?

WHAT WOULD YOU DO?

A. Repeat one more cfDNA test with a third company
B. Suggest amniocentesis and refer to MFM
C. Perform a detailed fetal ultrasound
D. Perform second trimester serum screening

WHAT WOULD YOU DO?

A. Repeat one more cfDNA test with a third company
B. Suggest amniocentesis and refer to MFM
C. Perform a detailed fetal ultrasound
D. Perform second trimester serum screening
OUTCOME
Counseled 3x by 2 MFM's
Declined amniocentesis due to risk of procedure
Decided to ignore the cfDNA result

FETAL FRACTION
• After 10 weeks gestation, average fetal fraction is 4-30% (average 10-12%)
  • Obesity
  • Early gestational age
  • Sample collection error
  • Aneuploidy (T18, Triploidy)
  • Low molecular weight heparin
  • IVF
  • Twins
  • Homozygosity due to consanguinity or uniparental disomy

cfDNA Failure Rates

Updates on Prenatal Genetic Screening

**CFDNA FOR TWINS: LIMITED DATA**

<table>
<thead>
<tr>
<th></th>
<th>Detection Rate</th>
<th>False Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21</td>
<td>98% (81-99)</td>
<td>0.05% (0.01-0.3)</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>89% (65-97)</td>
<td>0.03% (0-0.3)</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>67% (2 of 3)</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

- 997 included pregnancies
- 86% dichorionic
- 14% monochorionic
- Pooled singleton detection for T21, T18, T13 is 99%+
- Pooled singleton false positive rate for T21, T18, T13 is 0.04%
- Better than maternal serum screening?

**Sonography and cfDNA for chorionicity**

- **Age Appropriate**: 83.0%
- **Incorrect Diagnosis**: 17.0%
- **Increased Cost**: 1.0%

**WHAT WOULD YOU DO?**

28yo G2P1 at 12 weeks with history of anti-D alloimmunization (1:2000) and prior child required repeat transfusions.

Father is heterozygous.

First trimester anatomy and NT are normal.

What’s next?
WHAT WOULD YOU DO?
A. Recommend serial MCA Dopplers for fetal anemia
B. Check serial anti-Rh titers
C. Extra dose of Rhogam
D. Refer to MFM for amniocentesis
E. Refer to MFM for genetic consult
F. Refer to MFM for cfDNA Rh typing

OUTCOME
50% chance of Rh negative fetus

cfDNA testing was Rh negative

Returned to low risk OB care with no special surveillance
RH(D) TESTING WITH CFDNA

• 30 studies, >10,000 tests
• Rh(D) and fetal sex are virtually diagnostic
• >99% sensitive/specific

WHAT WOULD YOU DO?

35yo G-4P3 at 12 weeks. First trimester ultrasound and NT are normal. She wants cfDNA.

cfDNA: high risk for trisomy 21, 18, 13. XY.
The patient was unsurprised and said this happened in her last pregnancy, too.

What’s next?
Updates on Prenatal Genetic Screening

WHAT WOULD YOU DO?
A. Repeat cfDNA
B. Refer for CVS
C. Refer for genetic counseling
D. Routine care

OUTCOME
CVS was normal 46, XY
16 week early anatomy normal
Genetic counseling showed FH early colon cancer
MRI abdomen/pelvis
Mass biopsied
Colon cancer diagnosed
MATERNAL DETECTION ON CFDNA SCREEN

- Multiple aneuploidy or single autosomal monosomy, consider malignancy.
- 20-40% risk of maternal malignancy with multiple aneuploidy detection.
- Detection rates variable.

<table>
<thead>
<tr>
<th>Type of Aneuploidy</th>
<th>Total No. of Samples</th>
<th>No. of Cases Maternal Malignancy</th>
<th>Maternal Malignancy OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single trisomy*</td>
<td>2955</td>
<td>7 (0.2, 0.4)</td>
<td>3.0 (1.4 - 6.3)</td>
</tr>
<tr>
<td>Single SCNA*</td>
<td>710</td>
<td>6 (0.4, 0.8)</td>
<td>1.2 (0.6 - 2.6)</td>
</tr>
<tr>
<td>Single trisomy + SCNA</td>
<td>30</td>
<td>6 (0.4, 0.8)</td>
<td>1.6 (0.9 - 3.0)</td>
</tr>
<tr>
<td>Single monosomy</td>
<td>98</td>
<td>1 (0.0, 0.5)</td>
<td>0.9 (0.1 - 6.8)</td>
</tr>
<tr>
<td>Multiple aneuploidy*</td>
<td>39</td>
<td>7 (2.7, 19.0)</td>
<td>3.5 (0.9 - 13.3)</td>
</tr>
<tr>
<td>Risk of overall NICU</td>
<td>573</td>
<td>4 (0.3, 3.0)</td>
<td>0.7 (0.1 - 4.3)</td>
</tr>
</tbody>
</table>

WHEN TO REFER? IT’S NOT QUICK COUNSELING!

- Diagnostic testing risks and benefits.
- Maternal causes of positive cfDNA screening.
- Vanishing twin.
- Zygosity testing and monochorionic twin follow up.
- Low fetal fraction or repeat no call.
- IVF, donor egg.
- Transplant patient, bone marrow transplant.

FETAL ANEUPLOIDY SCREENING: SOME KEY POINTS

- No screening is okay.
- Discuss screening versus diagnostic testing with all patients early in pregnancy.
- Choice of test depends on goals and values.
- Discuss risks and benefits of the tests.
- Emphasize PPV/NPV rather than sensitivity/specificity.
- If negative screening, do not offer additional screening.
- Repeat cfDNA if desired for no call results but remember the risk of aneuploidy is higher.
FETAL ANEUPLOIDY SCREENING: SOME KEY POINTS

- Abnormal NT or cystic hygroma → refer for counseling and diagnostic testing.
- Don’t forget maternal serum AFP screening with cfDNA.
- Twin screening with NIPT can be difficult to interpret and is always less accurate than for singleton.
- Mention risk of maternal findings.
- Do screen IVF patients who had preimplantation genetic testing.
- Any unusual results may be worth MFM referral/ultrasound.
- If you sent cfDNA screening, please send MFM the report.

THANK YOU!
### Quick Reference: Positive Predictive Values

#### Trisomy 18 positive predictive value (%)

<table>
<thead>
<tr>
<th>Maternal age in years</th>
<th>20</th>
<th>25</th>
<th>30</th>
<th>35</th>
<th>40</th>
<th>45</th>
<th>50</th>
<th>55</th>
<th>60</th>
<th>65</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>10.0</td>
<td>11.0</td>
<td>12.0</td>
<td>13.0</td>
<td>14.0</td>
<td>15.0</td>
<td>16.0</td>
<td>17.0</td>
<td>18.0</td>
<td>19.0</td>
</tr>
<tr>
<td>17</td>
<td>9.9</td>
<td>11.0</td>
<td>12.0</td>
<td>13.0</td>
<td>14.0</td>
<td>15.0</td>
<td>16.0</td>
<td>17.0</td>
<td>18.0</td>
<td>19.0</td>
</tr>
<tr>
<td>18</td>
<td>9.8</td>
<td>10.9</td>
<td>11.9</td>
<td>12.9</td>
<td>13.9</td>
<td>14.9</td>
<td>15.9</td>
<td>16.9</td>
<td>17.9</td>
<td>18.9</td>
</tr>
</tbody>
</table>

**PPV Calculator:** [https://www.perinatalquality.org/Vendors/NSGC/NIPT/](https://www.perinatalquality.org/Vendors/NSGC/NIPT/)

### Quick Reference: Positive Predictive Values

#### Trisomy 13 positive predictive value (%)

<table>
<thead>
<tr>
<th>Maternal age in years</th>
<th>20</th>
<th>25</th>
<th>30</th>
<th>35</th>
<th>40</th>
<th>45</th>
<th>50</th>
<th>55</th>
<th>60</th>
<th>65</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>6.3</td>
<td>7.3</td>
<td>8.3</td>
<td>9.3</td>
<td>10.3</td>
<td>11.3</td>
<td>12.3</td>
<td>13.3</td>
<td>14.3</td>
<td>15.3</td>
</tr>
<tr>
<td>17</td>
<td>6.2</td>
<td>7.2</td>
<td>8.2</td>
<td>9.2</td>
<td>10.2</td>
<td>11.2</td>
<td>12.2</td>
<td>13.2</td>
<td>14.2</td>
<td>15.2</td>
</tr>
<tr>
<td>18</td>
<td>6.0</td>
<td>7.0</td>
<td>8.0</td>
<td>9.0</td>
<td>10.0</td>
<td>11.0</td>
<td>12.0</td>
<td>13.0</td>
<td>14.0</td>
<td>15.0</td>
</tr>
<tr>
<td>19</td>
<td>5.9</td>
<td>6.9</td>
<td>7.9</td>
<td>8.9</td>
<td>9.9</td>
<td>10.9</td>
<td>11.9</td>
<td>12.9</td>
<td>13.9</td>
<td>14.9</td>
</tr>
</tbody>
</table>

**PPV Calculator:** [https://www.perinatalquality.org/Vendors/NSGC/NIPT/](https://www.perinatalquality.org/Vendors/NSGC/NIPT/)
The Role of Gynecology in Transgender Care

At the conclusion of this presentation, learner should be able to:

1. Gain understanding of gender correct terms
2. Discuss routine gynecologic care for transgender patients
3. Identify options for contraception and menstrual suppression in transgender men
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5. Discuss post-surgery bone health and long-term impact of ovarian removal

Healthcare Barriers and Unique Needs in LGBTQ Care

- Transgender and non-binary individuals face double the poverty rate and 9x rate of attempted suicide in US
- Targets of violence: 50% reporting physical violence and 26% sexual violence
- Only 50-60% report receiving routine medical care given fear of mistreatment
- Lack of provider education: Survey of practicing gynecologists — only 50% felt comfortable treating transgender men and 80% reported no residency training in transgender patient care
Gender Terminology

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisgender</td>
<td>Those whose gender identity and/or gender expression align with their sex assigned at birth</td>
</tr>
<tr>
<td>Transgender</td>
<td>Encompasses those whose gender identity and/or gender expression differs from their sex assigned at birth</td>
</tr>
<tr>
<td>Transman</td>
<td>Sex assigned at birth is female but gender identity is male or masculine</td>
</tr>
<tr>
<td>Transwoman</td>
<td>Sex assigned at birth is male but gender identity is female or feminine</td>
</tr>
<tr>
<td>Cross-sex hormone therapy</td>
<td>Hormone treatment for those who want to adapt their bodies to align with their gender identity</td>
</tr>
<tr>
<td>Gender non-binary</td>
<td>Those who may identify themselves as both or alternatively male or female, as neither male nor female, or a gender outside the male-female binary</td>
</tr>
</tbody>
</table>
Is there a name you go by other than your legal name?
What name do you go by?
What would you like me to call you?

Hello, my name is Dr. __________, I use she / her / hers pronouns. What do you prefer?

Don’t assume… just ask!

Gender Identity
How do you identify your gender?
There are lots of ways people think of their gender identity – how do you think of yours?

Sexual Orientation
Who are you attracted to – boys, girls, both or neither, other?
Gender Neutral Terminology During Pelvic Exam

<table>
<thead>
<tr>
<th>Gendered</th>
<th>Less Gendered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulva</td>
<td>External pelvic area, Outer parts</td>
</tr>
<tr>
<td>Labia</td>
<td>Outer folds</td>
</tr>
<tr>
<td>Vagina</td>
<td>Genital opening</td>
</tr>
<tr>
<td>Uterus, Ovaries</td>
<td>Internal/reproductive organs</td>
</tr>
<tr>
<td>Breasts</td>
<td>Chest</td>
</tr>
<tr>
<td>Pap smear</td>
<td>Cancer screening</td>
</tr>
<tr>
<td>Bras/panties</td>
<td>Underwear</td>
</tr>
<tr>
<td>Pads/Tampons</td>
<td>Absorbent garments</td>
</tr>
<tr>
<td>Period/menstrual</td>
<td>Bleeding</td>
</tr>
</tbody>
</table>

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Trans Men
Female to Male Transgender Patients
### Common Myths and Facts about Sexual Activity

<table>
<thead>
<tr>
<th>Topic</th>
<th>Myth</th>
<th>Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex partners/sexual behavior for trans community</td>
<td>• Have few sex partners • Never engage in penis-in-vagina sex (PIV) • Do not have sex with cisgender men</td>
<td>• Have diverse sex partners across their lifetime • Engage in a wide variety of sexual behaviors</td>
</tr>
<tr>
<td>Acquisition of HPV and other STIs</td>
<td>• Have minimal risk for acquiring HPV and other STIs if no history of PIV sex</td>
<td>• HPV and other STIs can be transmitted via all types of sexual contact, including use of shared sex toys</td>
</tr>
<tr>
<td>Screening for STIs</td>
<td>• Not necessary if no history of PIV sex</td>
<td>• Should be performed if there is any history of sexual contact</td>
</tr>
<tr>
<td>Cervical cancer screening</td>
<td>• Unnecessary if an individual has not had PIV sex • Must be completed prior to initiating cross sex hormone therapy</td>
<td>• Indicated for individuals with a history of any type of sexual activity, cross-gender hormone treatment should not be contingent on pap smear screening</td>
</tr>
</tbody>
</table>

---

### Gynecologic Care

- Cervical cancer screening + vaccination same as cisgender women
- Sexual history + STI Screening

---

### Gynecologic Care

- Annual clinical breast exam
  - Start at age 25+
  - Stop after mastectomy
- Annual mammography
  - Start at age 40
  - Stop after mastectomy

**High risk patients – follow same high-risk guidelines**

1. ACOG Comm Opin Care of TG Adolescents 2017
2. ACOG Practice Bulletin Breast Cancer Screening 2017
3. Hembree J Clin Endocrinol Metab 2017
4. ACOG Comm Opin Care of TG Adolescents 2017
5. Bentsianov Contraception 2018
Trans Women
Male to Female Transgender Patients

Gynecologic Care
- Sexual history and STI counseling
- Neovaginal care after surgery
- Maintenance vaginal dilation

Lack of consensus among organizations given limited evidence
1. ACP, Fenway Guide to LGBTQ
   Annual at age 50 and ≥ 5 years Estrogen, BMI > 35 or FMH Breast cancer
2. Center for Excellence for TG Health, UCSF
   Annual or Biennial at age 50 and ≥ 5 to 10 years of E
3. Endocrinology Societies
   Screen all transgender women identical to cisgender

1. ACOG Comm Opin Care of TG Adolescents 2017
2. ACOG Practice Bulletin Breast Cancer Screening 2017
3. Hembree J Clin Endocrinol Metab 2017
4. Bentsianov Contraception 2018
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Contraception

- Contraception rates 30-65% with majority using condoms as primary form
- 52% of users discontinued: 32% due to fear of hormone effects
- 56% reported using T as contraception with 5.5% reporting provider told them to do so!

Unplanned Pregnancy

- Intended and unintended pregnancies occur
  - Self-reported survey of 41 transmen
    - 76% reported resumption of menses within 3 months of stopping T
    - 20% conceived while amenorrheic
    - 32% were unplanned and on testosterone
Contraception Counseling

At risk for unintended pregnancy during and after testosterone therapy

Testosterone therapy has teratogenic potential in pregnancy

Contraception should be discussed and encouraged among transgender men engaging in receptive vaginal intercourse

Bentsianov. Contraception 2018
Cipres. Contraception 2017

Contraceptive Options

Menstrual bleeding

Menstrual bleeding often worsens dysphoria
- 66% felt unsafe in men’s restrooms
- 67% take special measures to avoid public restrooms
- 40% tried menstrual suppression

2. Ahmad. Transgend Health 2016
Testosterone therapy is associated with reduced estrogen and gonadotropins and decreased menstrual bleeding

Effects of Three Different Testosterone Formulations in Female-to-Male Transsexual Persons

- 138 transgender men
- 3 different doses of IM testosterone enanthate ranging from 125 mg every 2 weeks to 250 mg every 2 weeks
- Cessation of menses in 86–97% of subjects by 6 months

Nakamura. Endocrine Journal 2013

- 25

Menstrual Bleeding after Testosterone

- 45 transgender men
- Randomly assigned IM testosterone or testosterone gel
- Time to amenorrhea from 30-41 weeks
- All amenorrheic at 12 months


- 26

Evaluation

<table>
<thead>
<tr>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-injection testosterone level</td>
</tr>
<tr>
<td>Pregnancy test</td>
</tr>
<tr>
<td>STI testing</td>
</tr>
<tr>
<td>Pelvic exam</td>
</tr>
<tr>
<td>Pelvic ultrasound</td>
</tr>
<tr>
<td>Endometrial biopsy if risk factors</td>
</tr>
</tbody>
</table>

Schwartz. Obstet Gynecol 2019

- 27
Menstrual suppression

- Treatment options
  - Adjust testosterone dose if low or low-normal
  - Supplement with Progesterone
  - Norethindrone acetate 2.5-5mg
  - Provera 5-10mg
  - Levonorgestrel IUD
  - Aromatase inhibitor
  - GnRH agonist

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Gender Nonconformity ≠ Gender Dysphoria

Gender Nonconformity is Not the Same as Gender Dysphoria

Gender nonconformity refers to the extent to which a person’s gender identity, self-identification, and gender expression differ from the culturally normed gender for people of a particular sex. Gender dysphoria, on the other hand, is the discomfort or distress that occurs when a person’s gender identity and/or gender expression is inconsistent with their assigned sex at birth.
### Surgical Preferences for Transgender Males

<table>
<thead>
<tr>
<th>Type of Procedure</th>
<th>Have had it</th>
<th>Want it some day</th>
<th>Not sure if they want this</th>
<th>Do not want this</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest surgery reduction or reconstruction</td>
<td>21%</td>
<td>52%</td>
<td>17%</td>
<td>10%</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>8%</td>
<td>44%</td>
<td>28%</td>
<td>19%</td>
</tr>
<tr>
<td>Metoidioplasty</td>
<td>1%</td>
<td>15%</td>
<td>37%</td>
<td>47%</td>
</tr>
<tr>
<td>Phalloplasty</td>
<td>1%</td>
<td>11%</td>
<td>31%</td>
<td>56%</td>
</tr>
<tr>
<td>Other</td>
<td>3%</td>
<td>7%</td>
<td>13%</td>
<td>77%</td>
</tr>
</tbody>
</table>

2015 US Transgender Survey

### Surgical Preferences for Transgender Females

<table>
<thead>
<tr>
<th>Type of Procedure</th>
<th>Have had it</th>
<th>Want it some day</th>
<th>Not sure if they want this</th>
<th>Do not want this</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hair removal or electrolysis</td>
<td>41%</td>
<td>59%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Voice therapy</td>
<td>11%</td>
<td>66%</td>
<td>19%</td>
<td>24%</td>
</tr>
<tr>
<td>Vaginoplasty</td>
<td>10%</td>
<td>45%</td>
<td>23%</td>
<td>22%</td>
</tr>
<tr>
<td>Augmentation mammoplasty</td>
<td>8%</td>
<td>36%</td>
<td>31%</td>
<td>24%</td>
</tr>
<tr>
<td>Unipolar (Vaginal)</td>
<td>9%</td>
<td>40%</td>
<td>24%</td>
<td>26%</td>
</tr>
<tr>
<td>Facial Feminization</td>
<td>9%</td>
<td>40%</td>
<td>30%</td>
<td>25%</td>
</tr>
<tr>
<td>Tracheal Shave</td>
<td>4%</td>
<td>25%</td>
<td>29%</td>
<td>26%</td>
</tr>
<tr>
<td>Silicone Injections</td>
<td>2%</td>
<td>8%</td>
<td>27%</td>
<td>61%</td>
</tr>
<tr>
<td>Vaginoplasty</td>
<td>1%</td>
<td>18%</td>
<td>32%</td>
<td>51%</td>
</tr>
<tr>
<td>Other</td>
<td>5%</td>
<td>13%</td>
<td>10%</td>
<td>67%</td>
</tr>
</tbody>
</table>

2015 US Transgender Survey

### Gender Confirmation Surgery

“Bottom Surgery”

- Hysterectomy +/- oophorectomy
- Age ≥ 18
- Minimum of 12 months on testosterone
- WPATH recommends mental health evaluation and two letters to surgeon prior to GCS

- Primary care provider
- Behavioral health specialist
Surgical Outcomes

Complication Rates and Outcomes After Hysterectomy in Transgender Men

- 159,736 hysterectomies, 521 for gender dysphoria
- Mean age 23.9 years
- Complications rates comparable 3.4% cis-gender vs. 3.3% transgender, p=0.92

At the conclusion of this presentation, learner should be able to:

- Gain understanding of gender correct terms
- Discuss routine gynecologic care for transgender patients
- Identify options for contraception and menstrual suppression in transgender men
- Review surgical pre-requisites and surgical outcomes for gender-affirming hysterectomies
- Discuss post-surgery bone health and long-term impact of ovarian removal

Bone Health – Trans women

Bone Density Changes in Trans Women on Gender-Affirming Hormone Therapy
Bone Health – Trans men

Bone Density Changes in Trans Men on Gender-Affirming Hormone Therapy

Bone Health – Pubertal Blockade?

- Recent study of 34 teens treated with GnRH blockade,
- followed by cross-sex hormones

Figure 1. Longitudinal z-score (mean ± SD) development of the LS from start medical treatment until the age of 22 years...

Bone Density Screening

Endocrine Society Clinical Practice Guidelines for Gender Dysphoria recommends checking bone density in patients with risk factors for osteoporosis or those who stop cross-sex hormones after gonadectomy
What about the ovaries?

- The long-term outcomes of performing oophorectomy at the time of hysterectomy in transgender men are unknown.
- Histologic data show that testosterone exposure to the ovaries induces morphologic changes similar to polycystic ovaries.
- Testosterone alone may increase the likelihood of developing cardiovascular risk factors - hypertension, hyperlipidemia and polycythemia.
- Hormone profile of transgender men exposed to testosterone therapy is markedly different than that of cisgender women and more closely resembles that of cisgender men.
- Adverse effect of oophorectomy for cisgender women is hypothesized to differ for transgender men. It’s unknown whether transgender men experience the same increase in all-cause mortality and cardiovascular risks from removal of ovaries.
- If oophorectomy is chosen, options for fertility preservation must be discussed.

What about the ovaries?

**BENEFITS**

- Congruence with gender identity
- Decreased testosterone dose
- Negates need for future pelvic exams
- No change in vasomotor symptoms
- No bone density loss

**RISKS**

- No biologic offspring without fertility preservation
- Unknown cardiovascular risks??

Services

- TRUE Center at Children’s Hospital Colorado, 720-777-8283
- UC Health Integrated Transgender Program, 720-848-2650
- Denver Health LGBTQ Center of Excellence, 303-602-6760
Thursday
Surgical Considerations in the Morbidly Obese Patient

Ritu Salani MD, MBA
Professor
The Ohio State University

Objectives
1. Discuss pre-operative optimization
2. Describe tools for intra-operative surgical management
3. Identify methods to address obesity management
4. Review the impact of obesity on overall health and the economy

Disclosures
- Advisory board/Consultant
  - Clovis
  - AstraZeneca
  - Iovance
- Data monitoring committee
  - Genentech
Introduction

Currently, in the United States
- 39.6% of all adults are obese
- 41.6 million women (38.3%) are obese
- 40.2% of middle aged and 37% 60 and over
- 6.6% are morbidly obese (BMI over 40)

CDC.Gov (1/11/20)
Go. American Heart Association2013.

Obesity Trends 2018

The impact of obesity in the US

- Associated with ~280,000-400,000 deaths/year
- 2nd most common cause of preventable death
- Life expectancy
  - Rate of death is 20-50% higher in the overweight
  - 6-7 years lower in obese vs non- overweight
  - 30% increase in overall mortality for each 5 kg/m²
    increase in BMI

Surgical Considerations in the Morbidly Obese Patient

The morbidity of obesity
- Psychosocial dysfunction
- Stroke
- Dementia
- Sleep apnea
- Asthma
- Diabetes mellitus
- Kidney disease
- Dyslipidemia
- Incontinence
- Infection/skin changes
- Osteoarthritis
- Cancer
- Fatty liver/cholelithiasis
- Pregnancy complications
- Anovulation/Infertility
- Circulatory/thromboembolic disease
- Gout
- Heart disease/hypertension
- Obesity-related:
  - Breast
  - Colorectal
  - Esophageal
  - Endometrial
- Malignant obesity
  - 357,900 estimated cases of US cancers that are preventable each year
Surgical Considerations in the Morbidly Obese Patient

Malignant obesity
- Obesity increases the likelihood of dying from cancer overall.
- Accounts for 20% of cancer deaths in women.

Surgical considerations and challenges

Preoperative considerations
- Is surgery necessary?
- Are there alternative options?
- Can surgery be delayed to allow for pre-operative optimization?
- Specific risks
  - Discuss priorities of procedure
    - E.g. omitting lymph node dissection
  - How do we address obesity after surgery?
Surgical Considerations in the Morbidly Obese Patient

Cardiac Considerations

- Coronary disease
  - 20% increased risk for each 5 kg/m² higher BMI
  - Higher risk with ↑ waist circumference and waist-to-hip ratio
- Heart failure in women
  - Obesity attributes to 14% of cases
  - Risk increases 7% in women for each 1 kg/m² in BMI >30
- Arrhythmias

Post-operative Myocardial Infarctions

<table>
<thead>
<tr>
<th>Type of Procedure</th>
<th>Risk of MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor surgery</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Uncomplicated abdominal surgery</td>
<td>1-5%</td>
</tr>
<tr>
<td>Emergent/complicated surgery</td>
<td>&gt;5%</td>
</tr>
</tbody>
</table>
Airway/pulmonary management

- Difficult intubation/ventilation
  - May be exacerbated by surgical approach/positioning
  - Decreased neck mobility, narrowing of pharyngeal space
- Respiratory complications
  - Obstructive sleep apnea (OSA)
  - Rate of OSA is ~43% in patients with a BMI > 40
  - Associated with respiratory complications

Pulmonary management

- In general, consider supplemental oxygen in high risk patients
  - BMI > 40
  - ASA score of 3 or higher
  - Snoring history
- Unknown benefit of screening for sleep apnea
- Routine pulmonary function tests are not recommended

Diabetes mellitus

- Over 80% attributable to obesity
  - 2.5x risk with weight gain of 5-10 kg
  - 61x risk with BMI > 35
  - Tight glycemic control can reduce hospital stay
  - Consider pre-operative hemoglobin A1C
    - In diabetics or high risk patients


Surgical Considerations in the Morbidly Obese Patient

Miscellaneous preoperative considerations

- Possible need for intensive care or stepdown unit
- Physical deconditioning
  - Discuss physical activity prior to surgery
  - Plan for rehabilitation postoperatively

Intra-operative considerations

Antibiotic prophylaxis

<table>
<thead>
<tr>
<th>Group</th>
<th>Cefazolin (mg)</th>
<th>Tissue level (µg/g)</th>
<th>Bactericidal activity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Incision</td>
<td>Colon</td>
</tr>
<tr>
<td>Control</td>
<td>1 g IV</td>
<td>6.0</td>
<td>4.1</td>
</tr>
<tr>
<td>Obese</td>
<td>1 g IM</td>
<td>1.7</td>
<td>1.88</td>
</tr>
<tr>
<td>Obese</td>
<td>1 g SQ</td>
<td>0.96</td>
<td>1.74</td>
</tr>
<tr>
<td>Obese</td>
<td>1 g IV</td>
<td>4.0</td>
<td>2.63</td>
</tr>
<tr>
<td>Obese</td>
<td>2 g IV*</td>
<td>7.2</td>
<td>4.1</td>
</tr>
</tbody>
</table>

* 2 g over 80 kg and 3 g over 120 kg (cefazolin)
Surgical Considerations in the Morbidly Obese Patient

Surgical approach

- **Vaginal approach**
  - Better outcomes/Fewer complications
  - Lowest risk, recommended
  - Exposure/access may be impeded

ACOG committee opinion 619;2015

- **Laparotomy**
  - Selection of the incision
  - Midline/Transverse
  - Skin traction
  - Avoid area under panniculus
  - Concomitant panniculectomy


- **Minimally invasive approach**
  - Comparable outcomes
  - Decreased perioperative complications
  - Increased procedure time
  - Increased cardiopulmonary management challenges
  - Use bony landmarks

Surgical Considerations in the Morbidly Obese Patient

**Surgical positioning**
- Know the table capacity
- Have patient position herself
- Adequate padding
  - Reduce risk of pressure ulcers
  - Don’t forget about the arms
- Trendelenberg position
  - Base/pad to stabilize patient
  - Slow tilt will allow the body to acclimate to ventilation

**Surgical positioning devices**
- Pink pad®
- TrenGuard®

**Lithotomy positioning**
- Candy cane-shaped stirrups
  - More operating space
  - May lead to extreme knee and hip abduction
- Boot-type stirrup (Bariatric stirrups)
  - Better lower extremity alignment and safety
  - Less maneuverability
  - Decreased surgical site access
- Use additional padding to avoid neural injuries
Surgical Considerations in the Morbidly Obese Patient

Surgical instruments
- Instrument mobility may be affected by thickness of the abdominal wall
- Optimize exposure

Abdominal wall complications
- Obesity has higher rates of the following:
  - Surgical site infections
  - Wound separations
  - Hernias
  - Fascial closure
    - Continuous mass closure favored over interrupted
    - Less wound complications
    - Decreased operative time

Subcutaneous/skin complications
- Subcutaneous closure during C-section
  - Wound disruption 14.5% versus 26.8%
  - Seroma 5.1% versus 17.2%
- Drain placement
  - Inconclusive results but likely no difference
- Skin closure (suture versus staples)
  - Suture closure was associated with a 57% decrease in wound complications
  - Overall, inconclusive studies

Surgical Considerations in the Morbidly Obese Patient

Post-operative considerations

Surgical site infections
- Approximately 274,000-600,000 cases/year
  - Longer hospital stays
  - Higher readmission rates
  - Excess cost of ~$10,000/patient
  - Intra-operative efforts to reduce rates
    - Preoperative antibiotics
    - Skin antiseptic agents
      - Chlorhexidine-alcohol

Prevention/reduction techniques
- Perioperative glycemic control
  - Increased risk with every 40 point increase
- Perioperative normothermia
- Decreased wound infection and lower length of stay
- Perioperative oxygenation
- Improved infection rate with FiO2 of 80% compared to 35%
- Proper post-operative wound care

**Surgical Considerations in the Morbidly Obese Patient**

---

**Negative pressure wound therapy**
- Applied over a closed incision
- Lower rate of wound dehiscence and infections
- Only small studies/case reports published
- Cost of care: 33% rate reduction for benefit


---

**Venous thromboembolic disease**
- Prophylaxis in moderate risk patients
- Obesity
- Gynecologic surgery >45 minutes
- Not at major risk for bleeding
- Recommended regimens
  - Low molecular weight heparin
  - Low-dose unfractionated heparin OR
  - Mechanical prophylaxis with intermittent pneumatic compression

ACOG committee opinion 619; 2015

---

**Managing obesity**
- Address with patients as early as possible
  - BMI >25
- Assess the patient’s readiness
- Build a partnership to promote change
- Discuss medical benefits
  - Cancer is a teachable moment
- Provide resources and encouragement
Online resources
- [www.cancer.org/healthy/eathealthygetactive](http://www.cancer.org/healthy/eathealthygetactive/)
- [www.acefitness.org/acefit/](http://www.acefitness.org/acefit/)
- [www.heart.org/HEARTORG/GettingHealthy/PhysicalActivity/](http://www.heart.org/HEARTORG/GettingHealthy/PhysicalActivity/)
- [www.cdc.gov/physicalactivity/everyone/guidelines](http://www.cdc.gov/physicalactivity/everyone/guidelines)
- [www.choosemyplate.gov](http://www.choosemyplate.gov)
- [www.eatright.org](http://www.eatright.org)
- [www.livestrong.org](http://www.livestrong.org)
- [www.aicr.org](http://www.aicr.org)

Addressing obesity
- Discuss potentially protective interventions
- Contraceptive counseling
  - Birth control pills
  - Levonorgestrel intra-uterine device

Addressing Obesity
- Surgical intervention: Bariatric surgery
  - Candidates
    - BMI > 40 kg/m² or ≥ 35 kg/m² with comorbidities
    - Failed attempts at diet and exercise
    - Free of psychological disease
    - Well informed and motivated
Bariatric surgery
- In 2008, 220,000 people had weight loss surgery
  - Less than 1% of eligible candidates
  - Complication rate ~20%, mortality rates 0.1%-1.1%
  - Most successful method of weight loss
  - Results in improvement/resolution of co-morbidities (60-80%)
  - Improved quality of life

Impact of bariatric surgery on Ob/Gyn
- Pregnancy outcomes
  - Should wait until stabilization of weight loss
  - Lower rates of gestational diabetes
  - Ensure nutritional supplementation (reports of neural tube defects)
- Fertility outcomes
  - Improved fertility rates (contraceptive counseling)
  - Improved outcomes associated with assisted reproductive technology

Impact of bariatric surgery on Ob/Gyn
- Urogynecology outcomes
  - Improvement in urinary incontinence and quality of life
- Oncology outcomes
  - After bariatric surgery, 71% reduced risk for uterine malignancy

References:
Knoepf, Urology 2013.
The cost of obesity

- Overall economic impact is ~$200 billion/year
- ~10% of all health care costs
- Increased cost in obese population
  - Inpatient
  - Outpatient
  - Pharmaceutical
  - Disability/sick leave

Facilities and equipment

- Per hospital, accommodating the obese can cost $500,000/year
  - Specialized equipment (OR tables, instruments)
  - Remodeling facilities (doorways, furniture, etc.)
  - Increased storage space
  - Widened doorways and hallways
  - Operating room tables/motorized lifts

Impact of obesity on health care personnel

- Occupational injuries

  - Higher incidence of back, shoulder, and neck injuries among obese

  - Increased workers' compensation claims

  - Higher incidence of musculoskeletal disorders and injuries
Impact of obesity on health care personnel

- Specialized lift equipment/minimal lift policies
  - Designated lift teams
  - Use of mechanical lifts
- Decreased injury rate by over 41%
- Improved patient satisfaction rates

Franasiak. Gynecol Oncol 2012
Ruitenburg. Int Arch Occup Environ Health 2013

Impact of obesity on surgeons

- Operating room/Surgeon impact
  - Prolonged standing/retraction
  - Fixed and awkward positioning
  - Longer cases
  - Moving patients
- Consider exercises breaks in the operating room
  - 60 second stretches every hour

Hunter. Nurs Econ 2010
Franasiak. Gynecol Oncol 2012

Economic impact of obesity on the surgeon

- Obese patients=increased workload
  - Less cases=less RVUs
  - Reimbursement are based on complexity of procedure
    - With patient satisfaction
  - Obesity doubled during this time frame
  - Bundled payments will reduce reimbursements even more
  - Surgeons are getting paid less for more work!

We need to be involved in health care policy!
Summary
- Obesity contributes to preventable health sequelae and death
- Surgical intervention requires an understanding of potential risks and "best practices"
- Discuss alternative to surgery and the management of obesity (e.g., weight loss surgery)
- Increasing economic impact of management of obesity needs to be addressed

Thank you!
ritu.salani@osumc.edu
Delivery of Obstetric Telemedicine Services

Terry Harper, MD
Division Chief
Maternal Fetal Medicine
University of Colorado

Acknowledgements: Dr. Bettina Cuneo, Children’s Hospital Colorado and Dr. Curtis Lowery, University of Arkansas

WHAT IS TELEMEDICINE??
The use of electronic information and telecommunications technology to support the delivery of health

Telemedicine is a remote clinical services, telehealth is delivery of remote non-clinical services (CME, provider training) etc.

COMMON USES OF TELEMEDICINE
Bridging the distance for rural areas far from Centers of Excellence

- Mental health consults
- Home monitoring of blood pressure, blood sugars
- Retinopathy screening for diabetes
- Teledermatology
- Otoscope that connects to iPhone
- Telepathology
- Telestroke programs
- Teleradiology
- MFM consult and High risk ultrasound services
LESS COMMON USES!!!
USES IN OBGYN

• mHealth excessive weight gain prevention
• Preterm labor home monitoring
• Preeclampsia home monitoring
• Diabetes blood glucose monitoring
• Obstetrical ultrasound and MFM consultative services
• Postpartum Visits — Mood disorder screen, Breastfeeding support

IMAGING SERVICES FROM A DISTANCE

<table>
<thead>
<tr>
<th>Store and forward</th>
<th>Live and real-time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ultrasound machine, designated location with experienced sonographer</td>
<td>Any ultrasound machine, designated location with experienced sonographer</td>
</tr>
<tr>
<td>Anatomic survey with suspected abnormality</td>
<td>Anatomic survey with suspected abnormality</td>
</tr>
<tr>
<td>Physician reviews at convenient time for MD</td>
<td>Physician reviews at time of visit</td>
</tr>
<tr>
<td>No direct interaction with sonographer or patient; if images are not of diagnostic quality, patient has to return</td>
<td>Direct interaction with sonographer and patient; scanning done under supervision of physician, diagnosis and consult at time of visit</td>
</tr>
<tr>
<td>Hours to days between study and diagnosis/management</td>
<td>Real-time diagnosis and management</td>
</tr>
<tr>
<td>Giving bad news remotely (or by referring provider)</td>
<td>Giving bad news by specialist &quot;in person&quot;</td>
</tr>
<tr>
<td>Can bill for ultrasound read but not consult</td>
<td>Can bill for read and consult</td>
</tr>
<tr>
<td>Equipment cost minimal</td>
<td>Equipment cost increasing but currently additional cost to site</td>
</tr>
</tbody>
</table>

DENVER TO GRAND JUNCTION: ONE EXAMPLE OF TELEMEDICINE
VIDEO OF FETAL ECHO
TELEMED APPOINTMENT

CHALLENGES
- Reimbursement (prior authorizations occasionally required - Aetna)
- Technology infrastructure and support
- Providers must be licensed in the state where the patient is receiving care
- Patient and provider acceptance
- Medical records/documentation

REIMBURSEMENT
PATIENT SATISFACTION

- 2019 metaanalysis reviewed 36 studies from many specialties
- System experience: High levels of satisfaction
- Information sharing: Confidence in communication and confidentiality
- Patient centered professional and emotional support was high
- Overall satisfaction: 81% by participants

Acceptance of Fetal Tele-Echo: the Questionnaire

<table>
<thead>
<tr>
<th>Question</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before exam, you comfort with the intern</td>
<td>4.35</td>
</tr>
<tr>
<td>Comfort of sonographer with the equipment</td>
<td>4.04</td>
</tr>
<tr>
<td>Comfort of MD with the equipment</td>
<td>4.93</td>
</tr>
<tr>
<td>Ease of communication with MD</td>
<td>4.94</td>
</tr>
<tr>
<td>How well did the MD explain the reason for and results of exam?</td>
<td>4.99</td>
</tr>
<tr>
<td>Ease in asking questions of the MD</td>
<td>4.51</td>
</tr>
<tr>
<td>Knowledge and skills of the sonographer</td>
<td>4.72</td>
</tr>
<tr>
<td>Knowledge and skills of the MD</td>
<td>2.5</td>
</tr>
<tr>
<td>How well did the MD explain the results?</td>
<td>4.93</td>
</tr>
<tr>
<td>Understanding and concern shown by MD</td>
<td>4.57</td>
</tr>
<tr>
<td>Quality of interaction</td>
<td>2.55</td>
</tr>
</tbody>
</table>

100% would rather have their visit locally using fetal tele-echo than travelling to Denver

TRAVEL TO DENVER?
CHILD CARE AND TIME OFF WORK

The Bottom Line

The average price of regular and premium gas Denver, CO is $2.36 $2.67/gallon.

Average gas gets 28 miles/gallon. Average to Grand Junction 209 miles $2.67. Round trip 21 gallons = $49.8 per trip for regular and $62.37 per trip for premium.

Average price of hotel in Denver = $110/night.

Average hourly wage = $20.79 (www.bls.gov/oes/2016/oes.html).

Average hourly wage = $20.79 (www.bls.gov/oes/2016/oes.html).

Total: $59 - $62 gas $170 for hotel $1,295 (2 days, 10 hrs) for lost wages = $1,150 - $1,527 per trip.

Since 2018, they have performed 481 consultations and saved $170,000 with no loss in diagnostic accuracy.

The Real Value of Telemedicine

- Drive > 300 miles round trip with your (darling) kids (are we there yet?)
  - Speed 60 mph on gas
  - Speed 75 mph on hotel
  - Lose $100 of wages
- Cross 4000 ft. Pass twice in the snow
- Drive to the big city with all that traffic
- Get the same information in one hour without leaving town?

Priceless!
HOW TO START A PROGRAM?

1. What problem are you trying to solve with a telehealth project implementation?
2. What are the objectives of this project?
3. Who is in the primary target group? (age, gender)
4. Where will the service be located?
5. When will the service be launched (time, in months, if not)?
6. What are the goals you want to achieve (cost-effective, patient centered, etc.)?
7. What are the benefits of telehealth (collaboration, time, cost savings, etc.)?
8. What's the cost ratio for your patient population (insurance, Medicaid, Medicare, self-pay, other)?
9. What staff do you think you'll need to complete a telehealth visit (nurse, MA, MD)?
10. Determine and outline what reimbursement will look like for your telehealth activity.

NATIONAL CONSORTIUM OF TELEHEALTH RESOURCE CENTERS

REFERENCES

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• Systematic review of patient and caregivers’ satisfaction with telehealth video conferencing as a mode of service delivery in managing patients with diabetes. Asian J Endocrinol Metab 2018
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• Fawaz et al. Telemedicine Technologies for Obstetrics in Pregnancy: A Systematic Review and Meta-
  Analysis. Obstet Gynecol 2005
• Cuneo et al. Risk Stratification of Fetal Cardiac Anomalies in an Underserved Population Using
  Telemedicine. A JOGO 2019
• Ming et al. Telemedicine Technologies for Diabetes in Pregnancy: A Systematic Review and Meta-
• Lanssens D et al. Midwives’, obstetricians’ and recently delivered mothers’ perceptions of remote
Objectives

Following this lecture, the learner should be able to
- Define early pregnancy loss and recurrent pregnancy loss
- Identify ultrasound features of early pregnancy loss
- Discuss the evaluation and management options for recurrent pregnancy loss.

Nonviable intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without FHR activity in first 12 6/7 weeks of gestation.

- 10% of all clinically recognized pregnancies
- 80% of all pregnancy losses occur in the first trimester.
- 50% of EPL due to chromosomal abnormalities
- Most common risk factors: Maternal age & prior

<table>
<thead>
<tr>
<th>Maternal Age (years)</th>
<th>Clinically Recognized EPL Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30</td>
<td>19-17%</td>
</tr>
<tr>
<td>35</td>
<td>20%</td>
</tr>
<tr>
<td>40</td>
<td>40%</td>
</tr>
<tr>
<td>45</td>
<td>80%</td>
</tr>
</tbody>
</table>
Recurrent Pregnancy Loss (RPL)
Definitions

- First literature - 1930’s
- Existing guidelines (ASRM, RCOG and ESHRE)
- Occurs in 2-4% of couples
- Loss until 15 weeks (some use 20-24 weeks)
- Recurrent, not sporadic
- Typically defined as two or three consecutive losses
  - Risk of abortion after two losses (30%) is similar to three losses (33%)
- Controversy exists about which to include (only ultrasound or pathology confirmed or home + UPT)
Recurrent Pregnancy Loss (RPL)
Risk of recurrent RPL

- The likelihood of miscarriage increases with increasing numbers of prior miscarriages.

<table>
<thead>
<tr>
<th>Miscarriage number</th>
<th>Likelihood for recurrent losses</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>29%</td>
</tr>
<tr>
<td>4</td>
<td>27%</td>
</tr>
<tr>
<td>5</td>
<td>44%</td>
</tr>
<tr>
<td>6</td>
<td>53%</td>
</tr>
</tbody>
</table>

Causes often discussed for RPL

- Autoimmune
- Uterine anatomic
- Metabolic
- Genetic
- Environmental
- Infectious
- Thrombophilia
- Alloimmune

Antiphospholipid Syndrome (5-20%)

- Diagnosis: International consensus criteria
  - Lab criteria: Test for lupus anticoagulant, anticardiolipin IgG/IgM, beta2glycoprotein IgG/IgM. Repeat in 12 weeks Medium to high positive values only
  - Clinical criteria: DVT/PE, prior sAbx3, prior loss over 10 weeks, prior <34 week preeclampsia or IUGR

- Treatment:
  - Heparin 40 bid + ASA 81 mg daily once viable IUP is diagnosed
  - Low molecular weight heparin comparable efficacy has not been confirmed

Uterine Anatomic Abnormalities (2-38%)

- Diagnosis: sonohysterogram, hysterosalpingogram, 3D ultrasound or MRI
- Treatment: Septum resection conventionally thought to improve outcomes (77-90%) but limited evidence
- Ongoing trial of septum resection for reproductive outcomes Rikeen 2018.

Metabolic disorders

- Diabetes - uncontrolled only
  - check HgA1C or fasting glucose
- Thyroid - poorly controlled hypo or hyperthyroidism
  - check TSH
- Prolactin - prolactin level

Genetic abnormalities (2-5%)

- Diagnosis:
  - Can do POC testing (60% of miscarriages will have sporadic chromosomal anomalies)
  - Maternal and paternal balanced translocation testing

- Treatment:
  - Genetic counseling
  - Preimplantation genetic testing
  - Amniocentesis / CVS
Use of CMA on Products of Conception (99% result)

Most common abnormalities

• Four percent of pregnancies had parental karyotype abnormalities

Environmental

• BMI
• Tobacco
• Alcohol
• Drug use
• Caffeine (over 3 cups coffee/day)

Summary of recommended management

• Test for APLS
• Uterine cavity assessment
• TSH, Prolactin, fasting glucose (or HgA1C)
• Consider POC testing and/or parental karyotype
• Screen for environmental factors
• First trimester psychological support

Expense

Controversies in evaluation/management of RPL

• PCOS- has not been convincingly tied to RPL
• Infectious causes- ureaplasma, mycoplasma, not associated with loss nor are antibiotics associated with improved outcome
• Thrombophilias (genetic)- not associated based on prospective cohort studies
• Alloimmune disorders-HLA typing, neither the cause nor proposed treatment (IVIG) are based on evidence
• Male factors- DNA fragmentation or spermploidy- not recommended for testing
• Luteal phase deficiency…
Luteal phase defect

- **Concept:**
  Progesterone is critical to maintaining a healthy pregnancy and is secreted by the corpus luteum in the second half of the menstrual cycle. If the luteal phase is abnormal, the lining of the uterus may not grow properly.

- **Traditional teaching:** supplement with progesterone through the first trimester

- **PROMISE study: NEJM 2015 study Coomarasamy**
  - Women with 3+ losses
  - 400 mg vaginal micronized progesterone versus placebo
  - Outcome: LB 65.8% in progesterone, 63.3% in placebo, RR 1.04 (0.94-1.15) p 0.45.

Unexplained RPL

- Up to 50%
- Live birth rates are 35-85% in this group

References

- Yousef et al. “Comparison and appraisal of (inter)national recurrent pregnancy loss guidelines.” RBMO. 2019
- Coomarasamy. “A randomized trial of progesterone in women with recurrent miscarriages.” NEJM 2015
- Pasquier et al. “Hydroxychloroquine for prevention of recurrent miscarriage: study protocol for a multicenter RCT.” EMM 2019
- Popescu et al. Recurrent pregnancy loss evaluation combined with 24-chromosome microarray of miscarriage tissue. Human Reprod 2018
- Jaslow et al. Diagnostic factors identified in 1020 women with two versus three or more recurrent pregnancy losses. Fertility and Sterility, 2010
- Ismail et al. J Matern Fetal Neonatal Med 2018

What’s new in RPL?

- Early data on use of hydroxychloroquine for prevention of RPL-results 2023
  - Pasquier et al
  - Pharmacologic properties: antithrombotic, vascular protective, immunomodulatory, lipid lowering, anti-infectious
  - Randomizing 500 women
  - Starting treatment prior to conception through the 10th week

What’s new in RPL?

- Luteal phase defect treatment periconceptionally
  - 2018 Ismail et al. Did RCT of 400 mg progesterone or placebo bid
  - Started in luteal phase until 28 weeks
  - 700 women enrolled
  - Livebirth rate 92% versus 77% (p<0.05)
- Aspirin for prophylaxis in unexplained RPL
  - Blomquist et al 2018
  - RCT of 400 women
  - Live birth rate 83% versus 85.5% (p=0.58) CI 0.89-10.6

Macro for RPL

Recurrent pregnancy loss (RPL): We discussed early pregnancy loss and the definition, diagnosis and management of RPL. The incidence of recurrent pregnancy loss in the general population is about 1%. We reviewed that there are numerous causes for RPL that include parental chromosomal abnormalities (2-5%) and other fetal genetic causes, uterine anatomical factors such as Asherman syndrome or anomalies, autoimmune disease, alloimmune factors (APS; 5-20%), endocrinologic disease (i.e. diabetes, hypothyroidism), and environmental causes (e.g. EtOH, Tob, drugs, excess caffeine), and less commonly teratogen and infectious exposure. However, over 50% of all miscarriages have no known etiology. Discussed that management can begin by screening for hypertension, hormone levels (TSH, prolactin), diabetes (FBG, hemoglobin A1C), renal disease (creatinine), and for maternal APS (anticardiolipin antibodies, lupus anticoagulant, beta-2 glycoprotein antibodies). If any of the laboratory tests are positive for antiphospholipid antibody syndrome, repeat testing would need to be performed in 12 weeks to confirm the diagnosis. Screening for genetic thrombophilias is not indicated without a history of thromboembolism, as a definitive causal relationship between thrombophilias and adverse pregnancy outcomes has not been established (ACOG Practice Bulletin #138, Sept 2013). Discussed uterine cavity assessment and karyotype assessment (POC, parental).
Operating on the challenging patient: Robotic surgery and other tricks

DISCLOSURES

- Disclosure:
  - Consultant for Wright Medical
  - Speaker for Wright Medical
  - Orthopaedic surgery journal
  - No further financial or personal relationships that may be relevant to the interpretation of this work

History of the hysterectomy

- Approx 500,000 hysterectomies are performed per year in the US
- VAGINAL Hysterectomy has declined to about 19%
- LAPAROSCOPIC AND ROBOTIC Hysterectomy have increased to >50% of all hysterectomies performed
- The average Ob/Gyn performs 5 hysterectomies per year in US
Operating on the challenging patient:
Robotic surgery and other tricks

Resident surgical volume
- Residents are required to perform 85 hysterectomies in most ACOG/MAI requirements, including a minimum of 15 TVH and 15 TLH.
- The median number of abdominal hysterectomies has decreased from 39 to 37 per resident (from 2002-2013).
- The median number of laparoscopic hysterectomies has increased from 20 to 43.


Surgical robot
- Accounts for 30-37% of all hysterectomies performed in the US.
- Direct-to-consumer marketing.
- Learning curve to train on robot.
- Aimed to allow the benefit of better visualization, surgical dexterity, less surgical fatigue, fewer complications.

Given this decrease in total number of hysterectomies performed, decrease in training volume, and change in technology, how do we maintain high quality surgery for our patients?
Operating on the challenging patient:
Robotic surgery and other tricks

Pitfalls in the difficult hysterectomy

- Inadequate patient positioning
- Difficult entry
- Adhesions
- Finding the uterus
- Nonfunctional endoscopic equipment
- Endoanesthesia
- Unexpected cancer diagnosis
- Obesity

Patient Positioning

- Use of proper surgical equipment
- Proper use of laser tools
- Use of purse-string sutures
- Adequate exposure before the prep
- Cannula access
- Use of a drapes
- Use of sutures
- RV access running
- Careful use of port openings so you can enter and prevent injury

Patient positioning

- Ideal positioning
- Support on the lowest part of the table
- Side-trip of the mastoid process all the way
- Arms well padded and both tucked at sides
- Pad the anesthesia access
- Face protection
- Knee flexed at 90 degrees or wider
- No hyperflexion at the hip
Need more Trendelenburg!

- Moderate T-burg (15-30 degrees) can be adequate for most cases.
- Steep T-burg (>30 degrees) can be helpful for portions of difficult cases.

Trendelenburg

- Need more Trendelenburg!
- Adequate Trendelenburg (25 degrees)
Perils of Steep Trendelenburg

- Patient slippage
- Abdominal hypertension from steep Trendelenburg position
- Increased intra-abdominal pressure
- Esophageal injury
- Vascular injuries
- Herniation

Trendelenburg Tricks

- Consider coming in and use of steep T. if during the case, you need it
- Open communication with Anesthesiologist
- Increase heart rates with steep T. pressures
- Lower IV fluid administration, etc.
- Try to operate in flat Trendelenburg for the majority of the case until you need it

Difficult Laparoscopic Entry

- Previous surgery (can you review the operative notes to assist positioning to guide you?)
- Hernia or midline incision
- Morbid obesity
- Abdominal wall dehiscence
- Not sure where you want to place your ports
Operating on the challenging patient: Robotic surgery and other tricks

Options for laparoscopic entry

- Veress needle
- Open entry
- Direct entry
- Palmer’s point LUQ entry
- Transvaginal entry

Veress needle entry

- Typically place Veress in umbilicus (even if this is not where your port will be placed) since it is the "shortest distance to the gas"
- Tent up anterior abdominal wall
- Consider inserting Veress with gas insufflated as you can see when a negative intra-abdominal pressure is reached
- If failed two Veress attempts, consider another entry made at risk of injury increased with >2 entry attempts.

Open Hasson entry

- Usually requires 10 mm skin incision and port
- Dissect down to fascia and incise fascia with scissors
- Enter peritoneum
- Can insert the port to the fascia with stay sutures or use a balloon trocar
- Lower risk of vascular injury
- Higher risk of fascial hernia

Mikheal E et al, Laparoscopic Entry Techniques Using a Veress Needle Insertion with and without Concomitant CO2Insufflation: A Randomized Controlled Trial. JMI, v26: 1383-1388.
Operating on the challenging patient:
Robotic surgery and other tricks

Direct entry
- Make incision where you want to place your primary port
- Test up anterior abdominal wall
- Place 0 degree laparoscopic camera into optical laparoscope, clear port and watch the entry into abdomen

Palmer’s point entry
- 1-2 cm anterior to the symphysis
- Take 2 or 3 fingers in to define the stenosis
- Can use Veener needle, direct entry or open entry technique
- Highly unlikely to be a port site for future repair
- May be more approachable if suprapubic will avoid transverse incision repair

Transvaginal entry
- Place patient in Trendelenburg to move the bowel out of the pelvis
- Place Veress needle through posterior cul-de-sac into retroperitoneal space similar to entry of a vaginal hysterectomy
- Can also place Veress needle through the uterine fundus into the abdomen
- Leave needle in place while obtaining transabdominal laparoscopic entry in confirm no colon injury

1/24/20
Laparoscopic entry gone awry...

**Bowel Injury:**
- Deep jolt
- At least two small and large bowel defects
- Deep jolt
- Repair with your friend's surgical colleagues
- Ok to continue the planned procedure
- Consider broad-spectrum antibiotic coverage for 24-48 hours

---

**Bladder Injury:**
- Greatly (you check that the Foley was still draining)
- As in any injury, a sign of bladder injury
- Tone up, urology consult and prophylactic Rx
- Antibiotics, Foley catheter, and urethral catheter
- Consider shock chamber if necessary
- Consider antibiotic prophylaxis
- Consider antibiotic prophylaxis

---

**Vascular Injury:**
- Change wound press
- Call for urology/vascular consult
- Utilize skin grafting to fill any gaps that are visible
- Consider shock chamber if necessary
- No more than 2-3 days
- Consult with vascular surgeon
- Consult with vascular surgeon

---
Operating on the challenging patient:
Robotic surgery and other tricks

Adhesiolysis
- Difficult entry is often associated with intraabdominal adhesions.
- Patients with previous surgery, endometriosis, history of infection or PID.

“The Curtain of Doom”
- You place your initial laparoscopic port and find yourself beneath the essential “curtain of doom.”
- Do not despair and no need to open.
- Find a clear spot to place another useful port.
- Work in the clear planes between the abdominal wall and the omentum and you will usually be able to clear the omentum.

Bowel adhesions
- This is a more difficult problem.
- Don’t be hesitant to call a surgical colleague (although gynecologists are often the most accustomed to dissection bowel adhesions with laparoscopy).
- Use sharp dissection with cold scissors.
- Have a plan for if an injury occurs (open, laparoscopic or robotic suturing, diversion).
- No data that bowel prep decreases the risk of bowel injury but may make surgical visualization better.

Operating on the challenging patient:
Robotic surgery and other tricks

Bowel Adhesiolysis

Finding the ureters
- Be familiar with dissection of the retroperitoneum
- Practice retroperitoneal dissection on the easy case
- Consider material aims or lighted scopes
- Robotic firefly technology can be helpful here

Finding the ureters (low tech)
- Start in a safe place
  - LATERAL is unusual this way
- In the case of fluid 
  - Open retroperitoneum widely
- Grasp IP ligament and suitably mobilise
- Spread graspers to dissect down to ureter

University of Pittsburgh, SAGES
Operating on the challenging patient:
Robotic surgery and other tricks

Finding the ureters (high tech)

Robotic firefly technology:
Instill the bladder cavity with 5 cc of indocyanine green (ICG) and activate Firefly technology.

Lighted ureteral stents:
Place the stents via cystoscopy before the procedure.

The difficult bladder flap

- BACKFILL the bladder
  - inject, etc. muscle blue
- Start the dissection laterally AFTER you have secured the ureteric vessels
- Aim for the colpoony cystoplane
  - BELOW the eversion plane
- Routine cystoscopy?

Routine cystoscopy


Operating on the challenging patient: Robotic surgery and other tricks

What happens if you have a urologic injury?
- Have a brisk (no need to tell) telling your favorite urologist
- Know who to call when you arrive and what to expect
- Laparoscopic or robotically
- Leave tisue catheter in for 1-2 weeks
- Consider oral antibiotics
- By-op adj. get the bladder, remove all tissue to confirm bladder repair is intact

Endometriosis
- Unexpected endometriosis is often one of the most difficult surgical pitfalls since it can turn your 30 minute diagnostic laparoscopy into an all day affair.
- Decide at the onset what is your plan:
  - Make the diagnosis
  - Manage or of the endometriosis
  - Consider laparoscopically or open

Endometriosis – make the diagnosis
- Avoid the “quick and dirty”
- Always do a biopsy by the specialist, no hesitation
- Do biopsies on the left and right ovary to look for a true diagnosis
- Many of the medical management
  - Virchow’s lymph node
  - Adnexal mass
  - Pelvic pain
- Ok to albeit some of the lesions as long as you BUSTY at least one for diagnosis
Operating on the challenging patient:
Robotic surgery and other tricks

Endometriosis – excise all of the lesions
- Obtain pathology samples as excised
- Send for a study (ex: immunohistochemistry)
- Excision of endometriosis can be time-consuming and may be helpful, here for ease of dissection and avoids morbidities.
- Even a good endometriosis reaction should be followed with medical management for persistent symptoms.
- If you have an endometrioma you should consider following endometriosis surgery.

Endometriosis – convert to open?
- Not a crime to convert to laparotomy
- May be indicated in cases of bowel resection, detorsion of the sac, or if you cannot do a laparoscopic procedure
- Can do a needle biopsy and send frozen
- Consider the need for the pathology such as Gyn Onc, Urology or general surgery

Unexpected cancer diagnosis
- Consider when unable to complete the normal staging surgery
- Obtain an MRI, US, and CT
- Can you make the diagnosis without laparoscopic enucleation?
- Laparoscopic enucleation without frozen
- Laparoscopic partial biopsy
- FECOL – a common secondary diagnosis
- If you have a cancer that is felt to be metastatic, cancer is performed by a Gyn Oncologist
Operating on the Obese Patient

- Trendelenburg limitations
- Ventilation issues
- Dealing with the patella
- Port placement and length
- Surgeon fatigue
- Postop complications
  - Infection
  - Thrombosis

Operating on the Obese Patient

- Large and soft tissues
- Lighted retractors
- Robotic-style retractor (up to 450 lb)
- Altus type retractor in the vagina
- Confirm the weight limit on OR table (typically 450 lbs, barstic type may be needed)
- Allen string (up to 500 lbs), barstic string (50 lbs, up to 300 lbs)

Operating on the Obese Patient

- Positioning
  - Non-slip padding
  - Tape over
  - Sacrum on bed, buttafe off
  - Arm bands
  - Tape up or down the stoma to access the umbilicus and upper abdomen for port placement
Operating on the Obese patient

- Consider placing ports above the umbilicus down towards the pubic symphysis
- Use longer ports
- Use balloon ports
- Consider continuous circulating Amo

Operating on the challenging patient: Robotic surgery and other tricks

Given all of these potential pitfalls, when to consider robotic surgery?

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic Surgery</th>
<th>Robotic Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss</td>
<td>Less than laparotomy</td>
<td>Less than laparotomy</td>
</tr>
<tr>
<td>Length of stay</td>
<td>1-2 days</td>
<td>&lt;1 day</td>
</tr>
<tr>
<td>Opioid use</td>
<td>Less than laparotomy</td>
<td>Less than laparotomy</td>
</tr>
<tr>
<td>Return to work</td>
<td>1-2 weeks</td>
<td>1-2 weeks</td>
</tr>
<tr>
<td>Surgeon fatigue</td>
<td>Worse</td>
<td>Better</td>
</tr>
<tr>
<td>Port sites</td>
<td>Fewer, no 10-mm ports</td>
<td>Usually 4-5</td>
</tr>
<tr>
<td>Cost</td>
<td>Cheaper</td>
<td>More expensive</td>
</tr>
<tr>
<td>Complication</td>
<td>Equal, fewer ports</td>
<td>Equal</td>
</tr>
<tr>
<td>Infection</td>
<td>Less than laparotomy</td>
<td>Less than laparotomy</td>
</tr>
<tr>
<td>Thromboembolic risk</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Time in OR</td>
<td>Shorter</td>
<td>Longer</td>
</tr>
<tr>
<td>Conversion to laparotomy</td>
<td>Higher</td>
<td>Lower</td>
</tr>
</tbody>
</table>

OR tips and associated cost

- Min Thalamotomy ($132)
- 30 degree scope (yes, already have 0)
- Positioning leg rests ($10)
- Picc port ($175)
- 1-way ($15)
- Additional diagnostic ($15-$25)
- Air vent ($175)
- Shaded fixation ($35)
- ICU ($360 per/night)
- Lighted tonsil scope ($5195)
- Dye-spray dye kit (85 mg, $25/each)
- Thank you!
Disclosures

- Advisory board
  - Iovance
  - Clovis
  - AstraZeneca
- Data monitoring committee
  - Genentech

Objectives

- Review features of common hereditary gynecologic cancer syndromes
  - BRCA
  - Lynch syndrome
- Describe approaches to hereditary cancer risk assessment and genetic testing
- Understand current and evolving landscape of genetic testing in gynecologic cancer susceptibility syndromes
BRCA and Genetics in Gynecologic Malignancies

Sporadic
- Later age at onset (60s or 70s)
- Little or no family history of cancer
- Single or unilateral tumors

Inherited
- Early age at onset (<50)
- Multiple generations with cancer
- Clustering of certain cancers (i.e. breast/ovarian)

Autosomal dominant inheritance
- Carrier Parent
- Non-carrier Parent

Hereditary susceptibility to gynecologic cancers
- Hereditary Breast-Ovarian Cancer (BRCA1/BRCA2)
  - Ovarian cancer
- Lynch syndrome (MLH1/MSH2/MSH6/PMS2/EPCAM)
  - Endometrial cancer, ovarian cancer
- Cowden syndrome (PTEN)
  - Endometrial cancer
- DICER1 syndrome (DICER1)
  - Sertoli-Leydig cell tumors of the ovary
- SMARCA4 mutations
  - Ovarian small cell carcinoma, hypercalcemic type
- Peutz-Jeghers syndrome (STK11)
  - Ovarian sex cord tumors, cervical adenoma malignum
BRCA and Genetics in Gynecologic Malignancies

Suspect hereditary cancers when:
- Cancer in 2 or more relatives (on same side of the family)
- Early age of cancer diagnosis
- Multiple primary tumors
- Constellation of tumors consistent with cancer syndrome
  - Example: breast and ovarian cancers
- Family history is key!

Verify family history

Verbally reported pedigree

After review of pathology reports

Family histories are dynamic

Initial History

2 years later

- Colon Ca, 50
- Bone Ca
- Prostate problems
- Breast Ca, dx 45, d. 59
- Prostate Ca, dx 54
- Ovarian Ca, dx 43, d. 49
- Colon Ca, 50
- Endometrial Ca, 44
- Colon polyps, 48
BRCA and Genetics in Gynecologic Malignancies

Hereditary breast and ovarian cancer

<table>
<thead>
<tr>
<th>Breast Cancer</th>
<th>Ovarian Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>15%-20% Sporadic</td>
<td>18-24% Ovarian Cancer</td>
</tr>
<tr>
<td>5-10% Family clusters</td>
<td></td>
</tr>
<tr>
<td>10% Hereditary</td>
<td></td>
</tr>
</tbody>
</table>

Genetic predisposition of ovarian cancer

2018 Estimated New Ovarian Cancer cases: 22,240

- BRCA1: ~45%
- BRCA2: ~27%
- Other single genes: ~27%
- Lynch syndrome: ~1%

Hereditary breast and ovarian cancer syndrome

BRCA2 BRCA1
BRCA and Genetics in Gynecologic Malignancies

BRCA gene
- BRCA genes are tumor suppressor genes
  - Function in the DNA repair process
    - Single/double strand breaks, homologous recombination
  - General population: 1 in 300 to 800 carry the mutation
  - BRCA mutation may be discovered in new incident case
    - In ovarian cancer, 40% have no prior family history
  - Majority of mutations are deleterious
    - Protein is non-functional
  - Over 2000 separate mutations have been identified

BRCA associated cancers
- Breast cancer
  - ~5% of all breast cancers (20% of hereditary cases)
- Ovarian cancer
  - 9-24% of all epithelial ovarian cancer cases
  - Risk begins to rise at age 40 and sharply rises after age 50
- Pancreatic cancer
  - BRCA 2 carriers have a 3x increased risk and 7% lifetime risk of pancreatic cancer
- Others: Prostate cancer, melanoma
  - Questionable association with serous uterine cancer

BRCA1
- Tumor suppressor gene on chromosome 17
- Autosomal dominant transmission
- Protein has role in genomic stability
- >600 different mutations reported

---

**BRCA1 associated cancers**

- Breast cancer 50-85% (often early age at onset)
- Second primary breast cancer 40%-60%
- Ovarian cancer 15-45%
- Possible increased risk of other cancers (eg, prostate)

**BRCA2**

- Tumor suppressor gene on chromosome 13
- Autosomal dominant transmission
- Protein has role in genomic stability
- ~450 different mutations reported

**BRCA2 associated cancers**

- Increased risk of prostate, laryngeal, and pancreatic cancers (magnitude unknown)
BRCA and Genetics in Gynecologic Malignancies

Guidelines for BRCA testing

- Women diagnosed with the following:
  - Epithelial ovarian, tubal, or peritoneal cancer (EOC)
  - Breast cancer
    - Diagnosed at age 45 years or less
    - Diagnosed at age 50 years or less with limited family history
    - And close relative diagnosed (<50 years) or EOC any age
    - And two or more close relatives with breast cancer
    - Two breast cancer primaries (first diagnosis before age 50)
    - Triple negative breast cancer at age 60 or less
    - Ashkenazi Jewish ethnicity
- Women unaffected with cancer with the following:
  - First degree or close relatives that meet the above criteria
  - Relative with a known BRCA mutation
  - Close relative with male breast cancer

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Guidelines for BRCA testing

- Most informative to test an affected person
  - If a harmful BRCA mutation is found → genetic counseling and cascade testing should be performed
  - If this person is not available or declines → testing is appropriate with a suggestive family history
- Professional societies do not recommend testing for children (even if known mutation in family)
  - Lack of risk-reduction strategies and should be deferred to adulthood
  - Risks a BRCA associated cancer are extremely low

NCCN Clinical Practice Guidelines in Oncology. 2017

20

BRCA genetic testing

- Multiple panel options
  - **Will discuss specific later**
- BRCA test: Classification of results
  - Positive
  - Negative
  - Variant of uncertain significance (VUS) or ambiguous

21
Interpreting the results: Positive

- Enhanced screening/surveillance
- Chemoprevention
- Prophylactic (risk reducing) surgery
- Cascade testing of family members

BRCA: Surveillance and risk reduction

- Breast cancer early detection/risk reduction
  - Breast awareness age 18
  - Clinical breast exam every 6-12 months starting age 25
  - MRI age 25-29y
  - MRI and mammography 30-75y
  - Individual management after age 75
  - Consider prophylactic mastectomy
    - Reduces breast cancer risk by ~90-95%
    - Consider chemoprevention (tamoxifen)
  - Possible screening for pancreatic cancer and melanoma

BRCA: Surveillance and risk reduction

- Ovarian cancer risk reduction
  - Bilateral salpingo-oophorectomy by age 35-40y
    - May delay to 45 with BRCA2
    - Pathology protocol with washings and serial sectioning
    - Residual risk of peritoneal cancer is ~1-6%
    - May reduce risk of breast cancer
  - Surveillance with annual transvaginal ultrasound with concurrent serum CA-125 (if decline/delay surgery)
    - No data to support reduction in mortality
  - Consider oral contraceptives
    - Reduce risk of ovarian cancer by ~50%
**BRCA associated ovarian cancers**

- BRCA1 tend to have better prognosis/outcomes
- Germline or somatic BRCA mutations: PARP inhibitor maintenance therapy after frontline chemotherapy
- Treatment strategies
  - Recurrence
  - Maintenance

**Surveillance recommendations**

**Males**

- Breast cancer early detection
  - Breast self examination age 35
  - Clinical breast exam every 12 months starting age 35
- Prostate cancer early detection
  - PSA and digital rectal exam starting 45
  - Stronger recommendation for BRCA2 than for BRCA1 mutation carriers
- Possible screening for pancreatic cancer and melanoma

**Interpreting the results: Negative**

- If a close relative has tested positive, a negative result means the person does not carry that harmful mutation and cannot pass it on; general population risk
- If tested person has a suggestive family history, but tests negative, it may be a result of an as-yet unknown harmful mutation that has not been identified. There is a low likelihood of missing a known harmful mutation
- May be the result of a mutation in a non BRCA gene
Interpreting the results: VUS

- A change in BRCA1 or BRCA2 that has not been previously associated with cancer
- May occur in ~10% of women undergoing BRCA testing
  - Unclear prevalence in population
  - Unclear impact on protein function
  - Unclear association with disease
- Increased testing rates will help reclassify these results
  - Important to keep records

Lynch Syndrome

MSP2
MSH6
MLH1

Hereditary susceptibility to colorectal cancer

- Sporadic (65%-85%)
- Rare CRC syndromes (<0.1%)
- Familial adenomatous polyposis (FAP) (1%)
- Familial (10%-30%)
- Lynch syndrome (3%)

Adapted from Burt RW et al. Prevention and Early Detection of CRC, 1996
Genetic features of Lynch Syndrome

- Genes: DNA mismatch repair (MMR) family
  - Mutations lead to microsatellite instability (MSI)
  - MMR proteins are missing (IHC useful), normally present
  - If protein is absent, gene is not being expressed
    - Mutation or methylation
  - Majority due to MLH1

Lynch syndrome
- Excluded if methylation
- Germline DNA testing is required if MLH is absent and no methylation
- Abnormal IHC (absent), considered MSI high
  - 90% of Lynch syndrome tumors are MSI
  - Better prognosis
  - Therapeutic target
    - Immunotherapy

Clinical features of Lynch Syndrome
- Age of diagnosis of colorectal cancer is ~45 years
- Tumor site in proximal colon predominates
- Extracolonic cancers
  - Endometrial
  - Ovarian
  - GI tract (stomach, pancreas)
  - Urinary tract (renal, ureter)
Brca and Genetics in Gynecologic Malignancies

Lynch syndrome risks (up to age 70)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Lynch syndrome</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon cancer (women)</td>
<td>18-61%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>16-61%</td>
<td>1-2%</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>5-10%</td>
<td>1%</td>
</tr>
<tr>
<td>Other LS cancers</td>
<td>5-10%</td>
<td>1%</td>
</tr>
</tbody>
</table>


Family history is key

Guidelines for Lynch syndrome testing

- Personal history of endometrial or colon cancer
- Universal tumor testing with IHC
- Tumor testing on at-risk patients
  - Modified Bethesda guidelines
    - Colon or endometrial cancer less than 50 years old
    - Synchronous Lynch syndrome associated cancers
    - Colon cancer with MSI high and less than 60 years
    - Colon cancer in two or more first or second degree relatives
  - Tumor testing on tumors diagnosed prior to age 60
  - Lower costs

Guidelines for Lynch syndrome testing
- 1st degree relative with endometrial or colorectal cancer <60 years or at risk from systematic clinical screen
  - Pitfalls: Paucity of female family members, few individuals reaching advanced age, or family members who had hysterectomy/BSO
- Pattern of repeated generations of Lynch syndrome associated cancers
  - Especially those diagnosed <60 years
- From families with a known Lynch syndrome gene mutation
  - Regardless of degree of relation

Approach to Lynch syndrome testing
- All proteins present
  - MLH1/PMS2 absent
    - Any other proteins absent
    - Pos family hx
      - No family hx
        - MLH1 promoter methylation
          - Pos
            - Unlikely to be LS
            - Germline testing
          - Neg
            - Lynch
            - Unlikely to be LS – consider tumor seq
      - Germline testing
        - Pos
          - Neg
            - Lynch
            - Unlikely to be LS – consider tumor seq

Lynch syndrome: Surveillance/risk reduction
- Colon cancer
  - Colonoscopy every 1-2 years beginning at age 20-25
    - Or 2 to 5 years before earliest cancer diagnosis in family
- Genitourinary tract cancers
  - Urinalysis with cytology every 1-2 years beginning at age 25-35
- No screening but also at risk for the following tumors:
  - Pancreas, biliary tract, brain, small bowel, etc.
BRCA and Genetics in Gynecologic Malignancies

Lynch syndrome: Surveillance/risk reduction
- Endometrial and ovarian cancer
  - Endometrial biopsy every 1-2 years
  - Transvaginal ultrasound every year beginning at age 30
- Chemoprevention
  - Oral hormonal therapy (OCPs, progestin therapy)
  - Levonorgestrel intrauterine device
- Prophylactic hysterectomy and bilateral salpingo-oophorectomy after completion of childbearing
  - Post-operative primary peritoneal carcinoma has been observed but magnitude of risk is unknown


Cowden Syndrome
- Incidence: 1 in 200,000 (likely underestimated)
- Autosomal dominant inheritance
- PTEN Gene on chromosome 10q23
- Pathognomonic muco-cutaneous lesions
- Associated cancers:
  - Breast
  - Endometrial
  - Follicular thyroid
- Cancer risk management strategies

NCCN guidelines Genetic/Familial High Risk Assessment: Breast and Ovarian v.1.2017
Pilarski et al. JNCI; 2013;105:1607-1616

Evolution of genetic testing

MANY labs offer cancer genetics panels – variability in cost and number of included genes

Targeted therapies "hit to the bull’s eye"
Multigene panel testing
- Genes other than BRCA1/BRCA2
- Current NCCN recommend multigene panel
  - When more than one syndrome suspected
  - When a person is negative for BRCA gene mutations but personal/family history is still highly suggestive
  - Consider referral/consultation with genetic experts in the context of pre and post test counseling

Genetic testing
- Next generation sequencing: multi-gene panel testing
  - More labs and more options
  - Prices range from $249 - $4,500
  - Number of genes included ranges from 2-90**
  - Turn-around time ranges from 3-12 weeks
- Advantages:
  - Multiple genes tested
  - Lower costs that older techniques
  - Options to customize
- Disadvantages:
  - Finding of unknown gene mutations
  - Higher chance of ambiguous results
  - More genes≠better

Multigene panel testing
- Approximately 6-10% of patients who test negative for BRCA may have another known gene mutation
  - RAD51C
  - RAD51D
  - BRI1
  - BARD1
  - PALB2
  - May or may not have evidence to support increased risk for hereditary cancer
  - Controversy with multi-gene panel testing versus BRCA specific testing
Non BRCA related ovarian cancer risks

<table>
<thead>
<tr>
<th>Gene</th>
<th>Relative Risk</th>
<th>Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRIP1</td>
<td>8-11</td>
<td>10-15%</td>
</tr>
<tr>
<td>RAD51D</td>
<td>6-12</td>
<td>8-15%</td>
</tr>
<tr>
<td>RAD51C</td>
<td>4-8</td>
<td>5-10%</td>
</tr>
<tr>
<td>PALB2</td>
<td>3-8</td>
<td>5-10%</td>
</tr>
<tr>
<td>Lynch Syndrome genes</td>
<td>Varies greatly by gene</td>
<td>5-10%</td>
</tr>
</tbody>
</table>

Knowledge continues to evolve – prospective follow up needed

Norquist et al. 2015; Rafnar et al. 2011; Ramus et al. 2015; Loveday et al. 2011; Peltari et al. 2011; Song et al. 2015; Loveday et al. 2012

Multigene panel mutations

- Breast MRI
- Discuss risk reducing mastectomy
- Recommend or consider risk reducing BSO

NCCN guidelines Genetic/Familial High Risk Assessment: Breast and Ovarian v.2.2016

Germline versus somatic mutations

- Germline genetic testing looks for inherited mutations
  - Usually a blood or saliva test
- Somatic genetic testing looks for mutations that occurred in the cancer cells
  - Tumor tissue tests/"Liquid biopsies"
  - No impact on family members
  - No known risk of other primary cancers
- Both may be important for therapeutic options
  - Germline or somatic BRCA mutations and PARP inhibitors
  - MSI high tumors and immunotherapy

Konstantinopoulos et al. Cancer Discov 2015;5:1137-1154
BRCA and Genetics in Gynecologic Malignancies

Genetic Information Non Discrimination Act (GINA) 2008

- Prevents health insurers from denying coverage, adjusting premiums, or otherwise discriminating on the basis of genetic information.
- Group and self-insured policies
- Insurers may not request that an individual undergo a genetic test
- Employers cannot use genetic information to make hiring, firing, compensation, or promotion decisions
- Sharply limits a health insurer’s or employer’s right to request, require, or purchase someone’s genetic information

Conclusions and potential future directions

- Accurate family history is critical: Verify and update
- Genetic testing
  - Surveillance
  - Chemoprevention or risk reducing surgery
  - Cascade testing
- Identify targeted therapeutics based on mutation status
  - Better outcomes/less toxicities
  - All cancer is genetic but may not be inherited
- Benefit of testing all women for BRCA mutations?
  - May prevent breast/ovarian cancer cases
    - Challenges: Penetrance differences, new genes/tests, invasive actions to reduce risk
- A CANCER-FREE WORLD BEGINS HERE

50
Follow-Up of Women after Treatment for Gynecologic Malignancies

Ritu Salani, MD
Associate Professor
Gynecologic Oncology

Disclosures

• Advisory board/Consultant
  ‒ Genentech
  ‒ Clovis
  ‒ AstraZeneca

Objectives

• Review cancer survivorship care and guidelines for patients with ovarian cancer
• Discuss the rationale for current examination practices and surveillance testing
• Provide an overview of symptom management for common issues in the survivorship period
Follow-Up of Women after Treatment for Gynecologic Malignancies

Cancer cases in 2019

- New cases: 891,480
- Gynecologic cancers 97,140

Breast 268,600
Colorectal 67,100
Uterus 61,880
Ovary 22,530
Cervix 13,170
Other gyn cancers 11,420

Cancer survivorship

- Survivorship begins at the time of cancer diagnosis
  - Maybe even when symptoms develop
- Over 8 million women living with or a history of cancer
  - Over 1.2 million are gynecologic cancer survivors!
- Estimated to increase by ~25% over the next ten years

Siegel, R. Cancer Statistics, 2019
Follow-Up of Women after Treatment for Gynecologic Malignancies

Cancer survivorship

- Over 8 million women who are cancer survivors
- ~1.2 million are gynecologic cancer survivors
- Continued growth expected


Cancer care overview

Essential components of survivorship care

DETECTION / SURVEILLANCE of recurrent cancers, new cancers, and late effects of cancer and its treatment

INTERVENTION for the long-term and late effects of cancer and its treatment

PREVENTION of recurrent and new cancers and other late effects

COORDINATION among providers to ensure that all survivor's health needs are met
Follow-Up of Women after Treatment for Gynecologic Malignancies

Cancer surveillance

Cancer surveillance visits

- Assessment of late and long term effects
- Genetic risk assessment
- Promotion of healthy lifestyle
- Screening for secondary malignancies
- Evaluation for early detection of recurrence

Gynecologic cancer surveillance

- No standard practice
  - Significant variation
  - Optimal interval unknown
  - Unclear impact on survival or detection of recurrence
  - Low value care
Follow-Up of Women after Treatment for Gynecologic Malignancies

History of surveillance

- Survey of gynecologic oncologist
- Surveillance practice in 1992
  - All stages and cancer types

Surveillance

- Most common methods of detection
  - Patient symptoms
  - Physical examination
  - Imaging

Surveillance: Physical examinations

**Current Recommendations**

- Review of symptoms and physical examination
- Bimanual pelvic and rectovaginal
- 20%-50% of recurrences occur within the pelvis

**Gaps and Limitations**

- Reproducibility is low and may not detect other common sites of recurrence
  - Such as retroperitoneal lymph nodes, upper abdominal organs, or lungs
- Physical examination alone may not be sufficient in certain patients
Follow-Up of Women after Treatment for Gynecologic Malignancies

Surveillance goals

- Impact Survival Outcomes: Both monitoring for disease recurrence and treatment should translate to decreased mortality.
- Balance Benefits and Pitfalls for Patients: Disease monitoring may result in negative psychological impact on patients.
- Remain Cost-Effective: Effective surveillance plans should aim to reduce excessive costs and unnecessary use of resources for conducting surveillance testing.
- Ensure Clinical Effectiveness: Adherence to recommended guidelines should minimize unnecessary testing while providing optimal surveillance.

Surveillance: Guidelines

- Increase Clinical Detection: Routine clinical examination and diagnostic testing can play a key role in detecting recurrence.
- Decrease Morbidity: Continual monitoring for disease recurrence and follow-up treatment can decrease morbidity.
- Use Cost-Effective Practices: Cost-effective practices and follow-up plans are essential for effective detection of recurrence.
- Improve Survival Outcomes: Thorough examination and educating survivors is the most effective method for detection of recurrence.

Cervix cancer

- 13,170 new cases
- 4,250 deaths
  - ~50% in stage I
  - Incidence decreasing
- Recurrences often occur within 3 years
  - Advanced disease with earlier and higher recurrence rates
Cervix cancer recurrence

- Symptoms (74%)
  - Vaginal bleeding/discharge
  - Abdominopelvic pain
  - Lymphedema or leg pain/sciatica
  - Systemic symptoms
- Physical exam 29-75%
  - Speculum and bimanual pelvic exam

Cervix cancer: Cytology

- Abnormal cervical/vaginal cytology (0-17%)
  - Cancer on cytology is rarely an isolated finding
  - Most often low grade changes
    - Series of 61 women, 5.6% abnormal Pap rate
    - 1 case required intervention (VAIN II)
    - Led to unnecessary interventions
  - Abnormal cytology with prior radiation therapy (up to 34%)
    - Benign or mild changes in absence of other findings

Cervix cancer: Cytology recommendations

- Limit use to no more than once/year
  - Reserve colposcopy for high grade changes
- Consider elimination in certain groups
  - After radiation therapy
  - Unclear role after trachelectomy
- Continue to evaluate for lower genital tract disease
  - Visual inspection
- Significance of HPV clearance?
Follow-Up of Women after Treatment for Gynecologic Malignancies

Cervix cancer: Imaging

- Chest x-rays and CT scans: Low rates of detection
  - No benefit for survival outcomes
- PET CT scans: Sensitivity 86% and specificity 87%
  - Prognostic significance
    - Post treatment in high risk patients
    - Additional studies are warranted
  - Role in asymptomatic patients is unclear
  - Best use when recurrence suspected


Cervix cancer: Recommendations


Endometrial cancer

- Estimated new cases 61,880
- Estimated deaths 12,160
  - Incidence increasing
    - ~70% in early stage
  - 95% recur within 3 years
    - Higher risk with advanced stage and type II histology

SEER.cancer.gov
Follow-Up of Women after Treatment for Gynecologic Malignancies

Endometrial cancer recurrence

- Approximately 90% of recurrences detected by...
- Symptoms
  - Vaginal bleeding
  - Pelvic pain
- Physical examination
  - Speculum exam
  - Bimanual exam

Endometrial cancer: Cytology

<table>
<thead>
<tr>
<th>Author</th>
<th>Study size</th>
<th>Recurrence rate (%)</th>
<th>Cytology alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berchuck 1995</td>
<td>354</td>
<td>44 (12%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Agboola 1997</td>
<td>4280</td>
<td>496 (11.6%)</td>
<td>2 (0.04%)</td>
</tr>
<tr>
<td>Gadducci 2000</td>
<td>131</td>
<td>24 (18%)</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>Monroe 2001</td>
<td>390</td>
<td>27 (6.9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Bristow 2006</td>
<td>717</td>
<td>36 (5.0%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Salani 2011</td>
<td>154</td>
<td>4 (2.6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Novetsky 2013</td>
<td>433</td>
<td>51 (11.8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Lee 2016</td>
<td>389</td>
<td>14 (3.6%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

References available upon request

Endometrial cancer: Imaging

- Evaluations of different modalities
  - Ultrasound, CT scans, MRI, PET/CT scans
- Recurrence rates:
  - Early stage: 3% low risk and 14% in high risk
  - Advanced stage: ~50%
- Detection of asymptomatic recurrence is low
- Recommend avoiding routine imaging
Impact on practice
- Database evaluation of surveillance exams
  - 17,638 stage I and II endometrial cancer patients
- Cytology rates consistent: 2011 performed in 66.9% of cases
- CT scans (abd/pelvis): 11.7% in 1992 to 24.8% in 2011

Endometrial cancer: Wasted costs
- Mean cost per patient
  - Cytology $63
  - CT scan $750

Endometrial cancer: Recommendations
Ovarian cancer

- Estimated new cases 22,530
- Estimated deaths 13,980
  - Incidence and death rate are decreasing
- ~75% are diagnosed in advanced stages
- Recurrence is common
  - Early and advanced stages

Ovarian cancer recurrence

- Symptoms (49%)
  - Abdominal bloating
  - Abdominopelvic pain
  - Nausea/vomiting
  - Satiety
  - Bowel issues
  - Urinary symptoms
- Physical exam (30-50%)
  - Pelvic disease in 25-50%
  - Abdominal distension
  - Limitations
  - Nodal assessment
  - Upper abdominal disease

Ovarian cancer: CA 125 levels

- Glycoprotein discovered in 1981
- Potential applications
  - Assess adnexal mass risk for ovarian cancer
  - Monitoring response to therapy*
  - Detection for recurrent disease
  - Levels rise months before clinical relapse
- Pitfall: May be elevated in other conditions
Ovarian cancer: CA 125 levels

- European study of 529 ovarian cancer patients
  - Randomized to treatment based on rising CA 125 level versus delayed treatment until symptoms
  - No difference in survival (25.7 vs 27.1 months)
  - Study findings question the role of CA 125
- European Society recommendation
  - Obtain CA 125 at time of relapse or if requested


Surveillance: CA 125 levels

Current Recommendations
- SGO: Measurement of CA-125 is optional
- NCCN: After biochemical relapse, recommended options include enrollment in a clinical trial, delaying treatment until symptoms arise, or best supportive care

Gaps and Limitations
- Elevated CA-125 may also be found in other cancers, and monitoring has been associated with significant distress and anxiety
- Early treatment of recurrence may not lead to an improved OS

Ovarian cancer: Imaging

- 412 women
  - 80% recurrence rate
  - Detection method
    - Exam 15%
    - Imaging 27%
    - CA 125 23%
    - CA 125 and imaging 35%
  - Did not report symptoms
  - No survival difference

- 218 recurrent ovarian cancer patients
  - Concordant CA 125 and imaging in 43% only
  - Did not report detection by exam or symptoms
  - No survival difference

Follow-Up of Women after Treatment for Gynecologic Malignancies

Ovarian cancer: Imaging

- CT Scans
- MRI Scans
- Ultrasound
- PET/CT Scans

<table>
<thead>
<tr>
<th>Limitation</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal anatomy not visible</td>
<td>60%-93%</td>
<td>98%-100%</td>
</tr>
<tr>
<td>Functional assessment may improve accuracy</td>
<td>82%-91%</td>
<td>66%-100%</td>
</tr>
<tr>
<td>PET scans may improve accuracy</td>
<td>40%-85%</td>
<td>40%-96%</td>
</tr>
</tbody>
</table>

Best reserved for evaluation of suspected recurrence

Salani R. Gynecol Oncol 2017;146:3; slide from GEMSTONE Oncology.

Recommendations

- Ensure patients know what to expect at each visit
  - Signs/physical findings of recurrence
  - Symptoms of recurrence
  - Review of signs/symptoms of cancer recurrence
  - A physical exam
  - If indicated, a review test results (tumor markers, imaging, etc).
- Ensure patients know what tests are not needed too
- Point of access care
  - Plan if symptoms/signs develop problems between visits

Surveillance

- Ensure patients know what to expect at each visit
  - Signs/physical findings of recurrence
  - Symptoms of recurrence
  - Review of signs/symptoms of cancer recurrence
  - A physical exam
  - If indicated, a review test results (tumor markers, imaging, etc).
- Ensure patients know what tests are not needed too
- Point of access care
  - Plan if symptoms/signs develop problems between visits
Coordination of care

- The following tools can be used in conjunction with information provided by physicians and the patient's cancer care team

- **Treatment Summary**
- **Survivorship Care Plan & Self-Care Plan**
- **Information Cards**
- **Survivorship Calendar**

Survivorship care plans

- Provide a summary of treatment and follow up schedule
- Improved coordination of care
  - Primary care physicians reported higher adherence to appropriate screening tests
  - Can help identify the responsible providers for each aspect of care
- Patient and caregiver empowerment
  - Reduces unnecessary anxiety

Long and late term effects
Follow-Up of Women after Treatment for Gynecologic Malignancies

Overview of late and long term effects

Existential/Spiritual
- Sense of purpose/meaning
- Appreciation of life
- Disillusionment
- Loss of faith

Social
- Changes in relationships
- Disruption to family dynamics
- Social isolation
- Altered intimacy

Psychological
- Depression
- Anxiety
- Uncertainty
- Fear of recurrence
- Cognitive complaints
- Altered body image

Physical/Medical
- Second cancer or recurrence
- Cardiac dysfunction
- Comorbid conditions (diabetes, osteoporosis, etc.)
- Physical symptoms

Financial
- Financial strain
- Job loss
- Restrictions to care
- Restrictions on insurance

Side effects of treatment versus recurrence

<table>
<thead>
<tr>
<th>Side effects of treatment</th>
<th>Signs of recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Pain</td>
<td>Persistent pain</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>Bloating/bowel changes</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>Vaginal bleeding</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>Unexplained weight loss</td>
</tr>
<tr>
<td>Scarring</td>
<td>New masses</td>
</tr>
</tbody>
</table>

Physical effects
- All patients have some degree of side effects
- Quality of life
  - Declines during active cancer treatment
  - Remains low for a short period afterwards
  - After 1 year, quality of life tends to be comparable to non cancer counterparts
### Physical effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Definition</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Persistent physical or emotional exhaustion</td>
<td>Rule out other causes; moderate exercise; psychosocial intervention</td>
</tr>
<tr>
<td>Incontinence</td>
<td>Difficulty falling or staying asleep</td>
<td>Cognitive behavioral therapy; sleep hygiene; medications</td>
</tr>
<tr>
<td>Pain</td>
<td>Post-operative, musculoskeletal, visceral, neuropathic*</td>
<td>Narcotic/NSAIDs; physical therapy; palliative surgery</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Nerve damage (often occurring in the hands and feet)</td>
<td>Anti-seizure medication; amino acid complex; acupuncture/biofeedback</td>
</tr>
<tr>
<td>Cognitive deficits</td>
<td>Loss of intellectual function; short-term memory deficits</td>
<td>Stress management; occupational therapy; neuropsych evaluation; psychostimulants</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Decreased bone density</td>
<td>Monitor bone health; calcium/vitamin D; bisphosphonates; estrogen therapy</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>Difficulty with sexual response or desire</td>
<td>Surgical preservation; fertility options; cognitive/sexual therapy; supportive care</td>
</tr>
<tr>
<td>Menopausal symptoms</td>
<td>Decrease in estrogen, hot flashes</td>
<td>Estrogen therapy; anti-depressants; relaxation/behavioral therapy; herbal supplements</td>
</tr>
<tr>
<td>Lymphedema</td>
<td>Blockage in lymphatic drainage</td>
<td>Compression stockings; physical therapy; surgical options</td>
</tr>
</tbody>
</table>

### Resources to manage distress

- **Cancer Education**
  - Learning about cancer and its treatment may reduce distress
  - Patient navigator programs are a useful resource

- **Social Work & Counseling**
  - Practical problems: illness, food, money, work, school, language, and caregiving
  - Psychosocial problems: wide range

- **Mental Health Services**
  - Psychoeducation
  - Medicine
  - Psychotherapy
  - Substance abuse treatment
  - Complementary and integrative therapies
  - Exercise

- **Chaplaincy Care**
  - Spirituality and religion are related to better mental health
  - Chaplains provide help for grief, guilt, and helplessness
Management of stress and distress

- Survivors may be referred to the following specialists, depending on their needs:
  - Nurses: the first to detect and screen for distress
  - Social Workers: provide help for practical and psychosocial problems
  - Psychologists: provide in-depth mental health and neurocognitive assessments
  - Psychiatrists: assess the physical and mental aspects of mental health
  - Chaplains: certified to care for issues like grief, guilt, loss of faith, and spiritual concerns

Financial effects

- Increased expenses
  - From cancer care
  - From indirect needs
- Decreased income
  - Days off work
  - Work discrimination
- Risk of bankruptcy
  - 2.6 fold higher in cancer survivors
- Resources
  - Financial counselors
  - Community support groups
  - Religious groups
  - Cancer awareness programs
  - Caregiver support

Advance directives

- Used to maintain patient autonomy
  - Do-not-resuscitate orders
  - Healthcare power of attorney
  - Living will
  - Life-sustaining treatment
- <1/3 of cancer survivors have advance directives
  - Though a majority of patients desire a discussion
- Benefits
  - Appropriate assignment of a health care decision maker
  - Patient preferences for care being honored
  - Improved patient and family satisfaction
Follow-Up of Women after Treatment for Gynecologic Malignancies

Transition to wellness

Healthy living
- After diagnosis, efforts should be directed to improving general health behaviors
- Opportunity for teachable moments
  - Patients and families are willing
  - Better cancer outcomes and quality of life
- Educational opportunities

Exercise
- Regular physical activity
  - Hasten recovery from treatment
  - May improve progression free and overall survival
  - Improves fatigue, depression and quality of life
- The American Cancer Society recommends
  - 150 minutes of moderate activity/week
  - Limit sedentary behavior
  - Ensure safety when starting new exercises
  - Know limitations
Follow-Up of Women after Treatment for Gynecologic Malignancies

Nutrition and weight

- Two-thirds of the population are overweight
  - Cancer risks increase with weight
- The American Cancer Society guidelines
  - Limit processed meats and red meat
  - Eat 2.5 cups of vegetables and fruit each day
  - Choose whole grains when possible
  - Monitor portion sizes
  - Limit alcohol intake

Routine cancer screening

- Survivors are at risk for secondary malignancies
  - Continue recommended screening
  - Treatment doesn’t protect from developing other cancers and actually might increase the risk!
- Reduce possible risk factors
- Advocate healthy behaviors

<table>
<thead>
<tr>
<th>Cancer screening</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>Mammograms every 1-2 years beginning at age 40-50</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>Annual fecal hemoccult/ColoGuard</td>
</tr>
<tr>
<td></td>
<td>Colonoscopy every 10 years beginning at age 45</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>Every 3-5 years (if indicated)</td>
</tr>
</tbody>
</table>

Management of medical co-morbidities

- A majority of survivors have at ≥ 1 medical condition
  - During treatment, patients tend to receive less care for other medical issues
  - Survivors report a lack of education of management
- Cancer and medical co-morbidities have a negative impact on one another
- Coordinating care and health promotion of other medical problems is essential
- Make sure patients have a primary care physician and keep appointments
Follow-Up of Women after Treatment for Gynecologic Malignancies

Tobacco cessation

- Associated with multiple cancers and serious health problems
  - Higher risk of complications from therapy
  - Increased risk of recurrence and second malignancies
  - Negative effect on survival
- Over 10% of cancer survivors continue to smoke
  - ~30% of gynecologic cancer survivors continue to smoke

- Patient education
- Counseling
- Supportive measures

Genetic predisposition

- Contributes to ~10% of gynecologic malignancies
  - BRCA1/BRCA2
  - Lynch syndrome
- Know your family history
  - Types of cancers
  - Age of diagnosis
- Identification of high risk patients
  - Prevention
  - Early detection of secondary malignancies
  - Education
  - Testing for family members

The future
Conclusions

- Survivorship is an essential component of cancer care
- Multifaceted surveillance strategies are required to ensure early detection of recurrent disease
  - Ensure patients know what to expect
- Many patients experience late and long term effects of cancer or cancer treatment
  - Identify management strategies
- Promotion of wellness can improve overall health outcomes

Thank You!
Ritu.Salani@osumc.edu
Friday
Management of HIV on Labor and Delivery

Joyce Sung, MD
University of Colorado
46th Annual Vail Ob/Gyn Conference
February 21, 2020

Disclosures

• I have no disclosures or conflicts of interest.

Learning Objectives

• Identify high-risk women who should be screened again for HIV in the third trimester.
• Counsel pregnant patients with HIV on optimal mode of delivery.
• Utilize available resources for clinical advice.
Management of HIV on Labor and Delivery

Outline

• Perinatal Transmission: Background
• Preventing Perinatal Transmission
  • Testing
  • Antepartum Treatment
  • Intrapartum Treatment
• Mode of Delivery
• Breastfeeding
• Neonatal Treatment
• Resources for clinical advice

Perinatal transmission: Background

1981
270 reported cases, 121 died

1982
1983
1984
1985
1986
1987
1990
1996

Dr. Ho
HAART


CDC: occupational exposure precautions for healthcare workers; identifies routes of transmission (blood-borne, sexual), and rules out other routes (casual, food, water, air, surfaces)

CDC reports AIDS in infant after blood transfusion

US Public Health Services: First recommendations for preventing perinatal transmission

HAART standard of care
Perinatal Transmission

1982: first reported pediatrics AIDS cases:
1. Transfusion
2. Perinatal transmission
3. 2 cases: Parents unknown status
4. Mother with risk factors

CDC MMWR December 10, 1982.
CDC MMWR December 17, 1982.

U.S. Pediatric HIV and AIDS Diagnoses

CDC Data
Question

Which intervention decreases perinatal HIV transmission rates the most?

A. Antiretroviral therapy
B. Scheduled cesarean delivery
C. Avoidance of breastfeeding
D. Treatment of infant

Perinatal HIV Transmission

- Transmission rates
  - pre-ART: 25% (~40% with breastfeeding)
  - With ZDV: 5-8%
  - With ZDV and scheduled CD: 2%
  - VL <1000/ml, <2% risk, even without CD

Timing of MTCT in the HAART era

- 1990-92: 18.1%
  - Antepartum (27%)
  - Intrapartum (73%)
- 1999-2000: 1.6%
  - Antepartum (80%)
  - Intrapartum (20%)
Management of HIV on Labor and Delivery

Outline

• Perinatal Transmission: Background
  • Preventing Perinatal Transmission
    • Testing
    • Antepartum Treatment
    • Intrapartum Treatment
    • Mode of Delivery
    • Breastfeeding
    • Neonatal Treatment
  • Resources for clinical advice

HIV Testing in pregnancy

HIV Testing Recommendations

• ACOG Recommendations (CO#752, Sept 2018)
  • Screen all pregnant women as early as possible
    • Opt-out approach permitted everywhere in U.S.
  • Repeat testing in third trimester, preferably <36 weeks, in at-risk women
  • If unknown status, rapid screening should be done on L&D
  • Results should be available 24h/6, within 1h
HIV Testing Algorithms

- Traditional: Ab screening test (ELISA) with confirmatory Western blot

- Updated guidelines:
  - HIV-1/2 Ag/Ab combination immunoassay (“4th Generation Immunoassay”)
  - If positive, differentiate between HIV-1 and HIV-2
  - If indeterminate/negative, HIV NAT (RNA)

CDC 2014: Lab testing for diagnosis of HIV; updated guidelines

Repeat third trimester testing

- Risk factors: (specified in ACOG update 2018)
  - IVDU or sex partner with IVDU
  - Exchange sex for money or drugs
  - Sex partner is HIV infected
  - New or ≥1 sex partner in pregnancy
  - Concerning signs/symptoms
  - Incarcerated
  - Health facility with screen positive incidence of >1/1000 pregnant women
  - Geographical
Repeat third trimester testing
• Geographical area with high incidence (CDC 2004)

Rapid HIV Testing on L&D
• Unknown HIV status
• Results in <1 hour
• Available 24 hours a day
• Start ART immediately while waiting for confirmatory testing
• The HIV 1/2 antigen-antibody screen can be done in some hospitals within 1 hour
• Other rapid tests are for HIV-1 antibodies only – may require confirmatory testing

Outline
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Antepartum Treatment

Zidovudine treatment (antepartum + intrapartum + neonatal x 6 weeks) → 67% reduction in perinatal transmission from 25.5% to 8.3%

Management of HIV on Labor and Delivery

Maternal Plasma HIV RNA Level (viral load) at delivery is associated with Perinatal Transmission

Transmission Rate (%) vs. Plasma HIV RNA load at Delivery (copies/ml)

Cooper E et al. JAIDS 2002;29:484-94

ART: the earlier the better for MTCT

% Perinatal Transmission vs. Time when ART initiated

Mandelbrot et al. CID 2015

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  - Neonatal Treatment
- Resources for clinical advice
Intrapartum management

Topics

• Another plug for Rapid HIV testing!
• Intrapartum treatment
• Mode of delivery
• Unanswered Questions:
  • Mode of delivery with low viral load when on HAART
  • Term PROM
  • PPROM

Intrapartum ARV

• Continue ART through labor/up until CD
• IV ZDV
  • Yes: HIV RNA > 1000 /ml, or unknown
  • No: HIV RNA < 50 / ml (≤1% MTCT)
  • Maybe: HIV RNA 50-999/ml (1-2% MTCT)
• Start IV ZDV 3 h before scheduled CD
• CHIP: Only NO if undetectable VL x last 12 weeks, AND good adherence to ART throughout pregnancy
  • Also give a single dose of PO Nevirapine
Management of HIV on Labor and Delivery

Question

In which scenario is cesarean delivery definitely recommended?

A. Patient has undetectable viral load
B. Patient has viral load of 500 copies/ml and is not in labor
C. Patient has viral load of 1500 copies/ml and is not in labor
D. Patient has viral load of 1500 copies/ml and is in active labor
E. Both (C) and (D)

Mode of delivery - guidelines

- Scheduled CD at 38 w if HIV RNA > 1000/ml
- If spontaneous labor or ROM, unclear
- If HIV RNA ≤ 1000/ml:
  - If needs CD for other reason, do at normal time
  - Duration of ROM does not increase risk of transmission → VD still ok

USDHHS, Nov 2017
ACOG, 2018

Early studies

- European Mode of Delivery Collaboration
  - RCT of elective CD at 38w vs planned VD
  - 1.8% transmission rate vs. 10.5% (significant)
  - By actual mode of delivery:

<table>
<thead>
<tr>
<th>Actual mode</th>
<th>MTCT rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective CD</td>
<td>2.4%</td>
</tr>
<tr>
<td>CD after labor or ROM</td>
<td>8.8%</td>
</tr>
<tr>
<td>VD</td>
<td>10.2%</td>
</tr>
</tbody>
</table>

> NS

Early studies

- International Perinatal HIV Group 2
  - Meta-analysis of 15 studies

<table>
<thead>
<tr>
<th>Delivery Mode</th>
<th>Overall</th>
<th>No ARV</th>
<th>ARV ante/intra/post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective CD</td>
<td>8.4 %</td>
<td>10.4 %</td>
<td>2 %</td>
</tr>
<tr>
<td>All others</td>
<td>16.7 %</td>
<td>19 %</td>
<td>7.3 %</td>
</tr>
</tbody>
</table>


Unanswered Questions

- Is scheduled CD beneficial in cases of low viral load when on HAART?
- How does duration of ROM affect decision for CD?
- When to deliver in cases of PPROM?

Delivery Mode in era of ART

- 1983 mother-child pairs in HAART era (1/97-5/04)
- Transmission
  - 6.5% NSVD vs 2.5% emergent c/s vs 1.6% elective c/s
  - Undetectable viral load (n=560)
    - Elective c/section (univariate) OR 0.07 (0.02-0.31)
    - Bivariate analysis (adjusted for none vs. any ARV’s) OR 0.52 (0.14-2.03)
  - Women on HAART (n=759)
    - Elective c/section OR 0.64 (0.08-5.37)

European Collaboration Study CID 2005
### Delivery Mode in Era of ART

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Mother-to-child HIV transmission in women receiving cART, 2000–2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>(1) Vaginal delivery</td>
</tr>
<tr>
<td>Overall</td>
<td>B</td>
</tr>
<tr>
<td>&lt;50 copies/mL</td>
<td>11,100</td>
</tr>
<tr>
<td>50–400 copies/mL</td>
<td>11,120</td>
</tr>
<tr>
<td>400–1000 copies/mL</td>
<td>11,160</td>
</tr>
<tr>
<td>1000–10,000 copies/mL</td>
<td>11,160</td>
</tr>
<tr>
<td>&gt;10,000 copies/mL</td>
<td>11,160</td>
</tr>
<tr>
<td>Total</td>
<td>55,000</td>
</tr>
</tbody>
</table>

*VL categories: <50 copies/mL, 50–400 copies/mL, 400–1000 copies/mL, 1000–10,000 copies/mL, >10,000 copies/mL.*

### Delivery Mode in era of ART

- Townsend et al 2014

### Risk of Cesarean Delivery for HIV+ Woman

- Maternal complications
  - Fever
  - Infections: wound, UTI, endometritis
  - VTE
  - Need for transfusion
  - Decreasing trends over time, but still higher than HIV-)
- Early term deliveries: transient tachypnea of the newborn
- Future delivery options compromised
Info from Kourtis et al.

- CS rate = 58.3% for HIV(+) women vs 33% HIV(-)
- Kourtis et al, 2014: In 2010-2011, increased risks in HIV(+) CS of:
  - Infection (aOR 1.70)
  - Surgical trauma (aOR 2.71)
  - Extended hospitalizations (aOR 1.96)
  - Death (aOR 8.74)

Unanswered Questions

- Is scheduled CD beneficial in cases of low viral load when on HAART?
- How does duration of ROM affect decision for CD?
- When to deliver in cases of PPROM?

ROM Duration

- Minkoff et al, AJOG 1995
  - 1986-1991
  - ≤5% used ZDV at any time in pregnancy
  - 207 HIV(+) moms, 191 infants with data: MTCT 25%
  - Low CD4+ levels: ROM > 4h increased MTCT with RR 4.53.
  - If higher CD4+ levels, no such association (RR 1.11)
Management of HIV on Labor and Delivery

ROM Duration

- Int’l Perinatal HIV Group, NEJM 1999
  - Elective CS: MTCT 8.4%
  - VD with ROM < 1h: 11.7%
  - VD with ROM < 4h: 13.5%

  - 2007-2012, singleton live births in UK/Ireland
  - Had to be on cART (3+ meds), and have data on VL, ROM duration, VD
  - 2398 pregnancies in 1814 women
  - No differences in MTCT with ROM <4h, 4-24h, and >24h

Table 2. Mother-to-child transmission rates by duration of ROM among 2032 term deliveries (I/2 weeks).

<table>
<thead>
<tr>
<th>Duration of ROM</th>
<th>All infants delivered at term</th>
<th>Infants delivered at term with available viral load</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 h (&lt;4 h)</td>
<td>0.00% (0/55)</td>
<td>0.00% (0/55)</td>
</tr>
<tr>
<td>4 h – 4.9 h</td>
<td>0.00% (0/55)</td>
<td>0.00% (0/55)</td>
</tr>
<tr>
<td>Total</td>
<td>0.00% (0/55)</td>
<td>0.00% (0/55)</td>
</tr>
</tbody>
</table>

*Viral load

Table 3. Cases of mother-to-child transmission in women delivering between 2007 and 2012, with duration of rupture of membranes reported among 1678 term deliveries (Table 2).

<table>
<thead>
<tr>
<th>Term deliveries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of ROM</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>0 h (&lt;4 h)</td>
</tr>
<tr>
<td>4 h – 4.9 h</td>
</tr>
</tbody>
</table>

Conclusion: Duration of membrane rupture not a risk factor for MTCT if VL <1000 and on cART.

ROM duration

- Cotter et al, 2012

<table>
<thead>
<tr>
<th>VL</th>
<th>Meds?</th>
<th>ROM Duration</th>
<th>MTCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL &lt;1000</td>
<td>cART</td>
<td>&lt;4h (144/493)</td>
<td>0</td>
</tr>
<tr>
<td>VL &lt;1000</td>
<td>cART</td>
<td>≥4h</td>
<td>3.8% (146 presented in labor, 55 had CD)</td>
</tr>
<tr>
<td>ZDV</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Duration of membrane rupture not a risk factor for MTCT if VL <1000 and on cART.
ROM Duration - Summary

• ROM > 4h was felt to be a risk factor for MTCT in studies done before viral load data was reported.
• With low viral load, ROM duration is not a risk factor for MTCT.

Unanswered Questions

• Is scheduled CD beneficial in cases of low viral load when on HAART?
• How does duration of ROM affect decision for CD?
• When to deliver in cases of PPROM?

PPROM

• Cotter et al, 2012
• PPROM = 12, no MTCT
Management of HIV on Labor and Delivery

PPROM

- Aagaard-Tillery et al, 2006
  - 7 patients with HIV and PPROM
    - IV AZT up to 48 h following PPROM, and then again just before delivery
    - Expectantly managed per obstetric management
    - 2/6 rate of MTCT (33%)
      - One mom without ART (was on placebo arm of PACTG 076)
      - Second mom only had AZT and VL not used to guide MOD
      - Others all had HAART, and CD if VL > 1000

  - 19 HIV(+) with PPROM
    - 1 excluded (delivered at 24 weeks and had NND)
    - 2/18 surviving neonates were HIV+ at 6 months of age
    - All were expectantly managed
    - All had cesarean delivery
    - 0/10 HIV+ neonates if mom had antepartum HAART and intrapartum ZDV
    - 2/8 HIV+ neonates in moms without prenatal care: PO nevirapine + IV ZDV, CS
PPROM - summary

• Need more data, but expectant management seems reasonable, especially if mom has been getting antepartum ART.

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Breastfeeding considerations

CHIP Breastfeeding Protocol

• BF NOT recommended in resource-rich settings
• Counseling with 2 CHIP team members
  • Consider maternal reasons for desiring BF
  • Consider maternal feelings if infant does contract HIV
  • Risk of up to 1%

CHIP BF Protocol

• Infants ≥ 36 weeks
• Start weaning at 6 months
• Mastitis increases risk
• Monthly visits:
  • Maternal: HIV VL on colostrum/BM and serum
  • Infant:
    • HIV NAT at birth, 2w, 4w, monthly, and then after weaning: 1, 3, 6 months (revising?)
    • Check for loss of antibodies at 12-18 months
    • Monitor for adverse effects of ART: CBC diff, LFTs
  • Standard ARV prophylaxis (6 weeks) and extended
• Stop BF if positive HIV VL at any time, and infant will receive full post-exposure prophylaxis (3 drug regimen)
Outline

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Take-home points

• Repeat third trimester testing in high-risk patients
• Rapid HIV testing on L&D if unknown HIV status
• Antepartum treatment is important!!
• Intrapartum treatment
  • Continue antenatal ART
  • Add IV ZDV if viral load > 1000
    • CHiP also does if any detectable VL in last 12 weeks, or if poor adherence in pregnancy
• Elective CD at 38 weeks if VL > 1000
• Breastfeeding not recommended

Neonatal treatment
Neonatal Treatment

- Antiretroviral prophylaxis (>1 ARV)
  - E.g. Mom on ART with viral suppression → 4 weeks of ZDV
  - If risk factors, multi-drug ARV
    - No antepartum/intrapartum ARV
    - Only IP ARV
    - AP ARV but no viral suppression
    - Primary/acute HIV in pregnancy/BF
- Empiric HIV therapy
  - High-risk infant, combination 3-drug ARV
  - If risk factors above, can also do this
- HIV Therapy
  - 3-drug ARV treatment doses (ART)
  - Risk Factors (multi-drug ARV ppx OR empiric HIV therapy)

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Resources

- Children's Hospital Immunodeficiency Program (CHIP) Clinic
  - 24 hour Perinatal HIV Consult Line 303-281-9695
- National Perinatal HIV Hotline
  - 888-448-8765
  - http://nccc.ucsf.edu
- U.S. Department of Health and Human Services (USDHHS)
  - www.aidsinfo.nih.gov
Management of HIV on Labor and Delivery

Expanding the effort to decrease MTCT

- HIV positive woman
  - Preventing unintended pregnancy
  - Preconception care
  - Testing in pregnancy + retesting 3rd tri and postpartum
  - Preventing seroconversion: PrEP, condoms

- HIV negative woman
  - Antepartum: ARV to decrease VL
  - Intrapartum: C/S and ARV pm
  - Neonatal ARV
  - Avoid breastfeeding

Seroconversion in pregnancy

- Perinatal transmission rates higher if HIV acquired in pregnancy vs. pre-pregnancy
  - 22% vs 1.8% (2002-2005, NY)
  - 12.9% vs 1.6% (2005-2010, U.S.)

USCHHS Guidelines 2018

HIV Transmission to Women in Pregnancy and Postpartum

- Thomson KA et al., JID 2018
Management of HIV on Labor and Delivery

Conception

- Consultation with Reproductive Endocrinology/Infertility
- Discordant couples (male +)
  - Treatment to reduce viral load
  - Donor sperm
  - IUI with washed sperm
  - IVF/ICSI with washed sperm
  - PrEP for female partner
- Discordant couples (female +)
  - IUI, or “home” insemination
- Natural conception:
  - Screen/treat both partners for other STIs
  - Treatment of HIV+ partner
  - PrEP for HIV(-) partner
  - Timed intercourse (ovulation predictor kits)

Selected References

- U.S. DHHS: www.aidsinfo.nih.gov
- CDC MMWR December 10, 1982.
- CDC MMWR December 17, 1982.
Extra slides
(Not for this talk)

AIDS-defining illnesses

- Infections
  - Bacterial
  - Fungal
  - Viral
- Malignancies
  - Kaposi Sarcoma
  - Lymphoma
  - Invasive cervical cancer
- Wasting syndrome
- Encephalopathy

https://www.cdc.gov/hiv/policies/law/states/

- Pregnancy provider is obligated to test for syphilis and HIV early in pregnancy. Patient may decline, and should document in chart.
  - If HIV unknown in hospital, opt-out testing; document if declines.
  - Birth/stillbirth certificates must state whether HIV and syphilis testing done (but not the result).
Antepartum Care (CHIP)

- Routine prenatal labs
  - Pap
  - TB, HCV Ab (if >12 months)
  - Hep A Ab
  - CMV IgG and IgM
  - Varicella status, HSV status
- Immunizations
  - Influenza, PCV 13, HBV, HAV, Tdap

Antepartum Care (CHIP)

Appendix A: CHIP Lab Evaluation Schedule for OB Client Management

<table>
<thead>
<tr>
<th>Test-Year</th>
<th>First Visit</th>
<th>After start or change of ARV</th>
<th>Q Month 1st TR</th>
<th>Q Month 2nd TR</th>
<th>Clinical Indication</th>
<th>Repeat prior to transition</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV ag/ab</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>HIV quant</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X (14 Mo. if part)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>HCV a/b</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>CMV IgG</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>CMV IgM</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Lipase</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Phosphorous</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Non-fasting lipid profile</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quantiferon TB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMV IgG,IgM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxo IgG, IgM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPR</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>VZV</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>HSV</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

1 Unless prior results/source documentation are readily available
2 May have been performed at OB - obtain records, abstract to DB or EPIC depending on data source
3 If symptomatic or at risk
4 Defer if prior serology positive
5 Repeat Q pregnancy if prior seronegative and >12 months since last test
6 If uncertain hx of wild type disease or vaccine
7 Perform if screening serology positive for suspected disease
8 Until TND documented
9 Perform once after client is stable on ARV
10 If untreated, unsuppressed; HIV DNA genotype if HIV VL <1,000 cp/ml
11 For returning clients, rescreen if prior seronegative and travel to endemic region
12 If on TDF or TAF; recheck Q 6 months
13 Rescreen Q pregnancy if prior seronegative
14 If mother toxo IgG positive, desirable to send postpartum within 1 month of newborn toxoplasma testing for titer comparison

Antepartum ARV

- Backbone of 2 NRTI (nucleotide reverse transcriptase inhibitor)
  - Abacavir/lamivudine
  - Tenofovir/emtricitabine
  - Tenofovir + lamivudine
- Plus:
  - Protease inhibitor, or
    - Atazanir + ritonavir
    - Darunavir + ritonavir
  - Integrase inhibitor
    - Dolutegravir (after 1st tri)
    - Raltegravir

USDAHHS Guidelines 12/2018; aidinfo.nih.gov
Antiretrovirals in Pregnancy – risks?

• Antiretroviral Pregnancy Registry
  • 1-800-258-4263
  • www.APRegistry.com

Antiretrovirals in Pregnancy: Maternal concerns

• Mitochondrial toxicity → lactic acidosis
  • Avoid didanosine and stavudine if possible
  • 3 maternal deaths reported due to lactic acidosis (2 fetal deaths)
  • Nevirapine: skin rash, hepatotoxicity

Antiretrovirals in Pregnancy: Maternal concerns

• Protease inhibitors: glucose intolerance
  • Probably no increase in GDM rate
  • Routine screening vs early screening

• Dosing adjustments
  • TDF and atazanavir may decrease, esp in 3rd tri
  • Lopinavir-ritonavir, QD → BID in 2nd and 3rd tri
  • Not recommended due to PK changes in pregnancy*

  • Atazanavir/cobicistat
  • Darunavir/cobicistat
  • Elvitegravir/cobicistat

* Not recommended due to PK changes in pregnancy.
Antiretrovirals in Pregnancy: Fetal concerns

- Growth restriction / SGA: ?? Conflicting results
  - Growth ultrasound vs follow fundal height
- Increased PTB, esp protease inhibitors: mild
  - OR 1.35 [1.08-1.70]
- Very PTB/NND
  - Tenofovir disoproxil fumarate + lopinavir-ritonavir
  - TDF alone still one of the preferred medications

Antiretrovirals in pregnancy: Fetal concerns - teratogenicity

- Antiretroviral Pregnancy Registry
  - Overall rate of 2.7% (1st tri), 2.8% (2nd/3rd tri)
  - (baseline risk of 2.7%)
  - **Dolutegravir**:
    - Recommended to avoid in 1st trimester (preconception and conception) due to increased risk of neural tube defects
    - Can use after first trimester
    - UPT prior to initiation
    - Don't use if not on effective contraception
- Efavirenz: use not restricted

Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

Disclosures

- Advisory board/Consultant
  - Clovis
  - AstraZeneca
  - Iovance
- Data monitoring committee
  - Genentech

Objectives

- Review management of endometrial hyperplasia (EH)
- Discuss factors that influence management
- Describe challenges/controversies
  - Classifications
  - Lymph node assessment
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

**Definition**
- Proliferation of endometrial glands
  - Gland-to-stroma ratio >50 percent and crowded appearance
  - Varying shapes/sizes and presence of cytologic atypia
- Results from chronic estrogen stimulation

**Incidence**
- Estimated 133 cases/100,000 woman years
  - More common in postmenopausal ages
  - Difficult to determine/capture true rates
  - Treatment modalities vary
  - Terminology changes

**Risk factors**
- Increasing age
- Unopposed estrogen therapy
- Obesity
- Early menarche/late menopause (>55 years)
- Nulliparity
- Polycystic ovary syndrome
- Lynch syndrome
- Diabetes
- Estrogen secreting tumor
- Cowden syndrome/family history

*Likely mirrors endometrial cancer rates*
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

Presentation
- Abnormal/postmenopausal uterine bleeding
- Detection on cervical cytology
  - AGUS
    Endometrial cells present
- Incidental finding of thickened imaging
  - High risk patient

Diagnosis
- Endometrial sampling is the gold standard
- Office biopsy is acceptable
  - D&C is not necessary
  - May increase detection of unexpected cancer
    - 33% vs 47% rate
- Repeat/additional sampling
  - Insufficient cells
  - High clinical suspicion
  - Persistent or recurrent bleeding within 3-6 months

Terminology
- 1994 WHO classification
  - Hyperplasia with or without atypia
- Simple hyperplasia
- Complex hyperplasia
  - Simple hyperplasia with atypia
  - Complex hyperplasia with atypia
Terminology

- Concerns about inter-observer variability
  - 269 specimens of complex atypical hyperplasia underwent blinded review
    - 25% were downgraded to less severe histology
    - 29% were upgraded to cancer

- Only 67% sensitivity for precancerous lesions
  - Goal to identify true pre-malignant conditions that require therapeutic intervention

Terminology

- International Endometrial Collaboration Group
- Computerized morphometric analysis: D-score
  - Prognostic value assigned based on 3 features
    - Architectural complexity
    - Nuclear abnormalities
    - Glandular volume

<table>
<thead>
<tr>
<th>Feature</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Architectural complexity</td>
<td>Evaluates degree of nuclear overlap</td>
</tr>
<tr>
<td>Nuclear abnormalities</td>
<td>Baseline nuclear features, classification, etc.</td>
</tr>
<tr>
<td>Glandular volume</td>
<td>Estimates glandular proliferation</td>
</tr>
</tbody>
</table>

Benign D<1 and endometrial intraepithelial neoplasia D>1

Terminology: 2014 WHO classification

- Hyperplasia without atypia (non-neoplastic, benign)
  - Changes typically observed with anovulation or other etiology of prolonged exposure to estrogen
  - E.g. Proliferative endometrium or "simple hyperplasia"
- Atypical hyperplasia/Endometrial intraepithelial neoplasia (EIN)
  - Precancerous changes and epithelial crowding displaces stroma

| Diagnostic Criteria for Endometrial Intraepithelial Neoplasia (EIN) |
|---------------------------|------------------------|----------------------|
| Architecture | Hyperplasia | Benign endometrial hyperplasia |
| neighbour | Architectural complexity | Endometrial intraepithelial neoplasia |
| Nuclear abnormalities | Exfoliation | Endometrial adenocarcinoma |
| Glandular volume | Endometrial intraepithelial neoplasia | Benign endometrial hyperplasia |

References:
- Emons G. Geburtshilfe Frauenheilkd. 2015.
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

Diagnosis Considerations

Risk of progression versus co-existing cancer

Risk of Progression: Rates

1994 WHO classification

<table>
<thead>
<tr>
<th>Hyperplasia</th>
<th>Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>1%</td>
</tr>
<tr>
<td>Complex</td>
<td>3%</td>
</tr>
<tr>
<td>Simple with atypia</td>
<td>8%</td>
</tr>
<tr>
<td>Complex with atypia</td>
<td>23%</td>
</tr>
</tbody>
</table>

Kurman 1985

Risk of Progression: Rates

- Retrospective cohort of 1443 women with complex or atypical hyperplasia
  - No hysterectomy for at least 8 weeks; followed up to 21 years
  - Rate of progression was 14.9%
  - Three to five fold higher in women not treated with a progestin
- Case control study of 7947 women with hyperplasia
  - Odds of progression (cumulative risk)

Lacey, 2010

<table>
<thead>
<tr>
<th>Hyperplasia</th>
<th>Year 4</th>
<th>Year 9</th>
<th>Year 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonatypical</td>
<td>1.2%</td>
<td>1.9%</td>
<td>4.6%</td>
</tr>
<tr>
<td>Atypical</td>
<td>8.2%</td>
<td>12.4%</td>
<td>27.5%</td>
</tr>
</tbody>
</table>

Risk of carcinoma remained elevated for five years or greater[40].

[32] 1/24/20
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

**Risk of Progression: Time**
- Population-based study 1
  - Median time to progression 2.5 years (1.01 to 7.9 years) for atypical hyperplasia
  - 5.1 years (1.1 to 11.6 years) among women with complex hyperplasia
  - Excluded cases diagnosed within one year (concomitant carcinoma)
- Population based study 2
  - Median time to progression ~6 years (all hyperplasia)
- Non-population-based study
  - Mean time to progression 4 years (maximum 10 years)
  - Maximum 18 years of follow-up

---

**Coexisting Endometrial Cancer**
- 289 hysterectomy specimens for atypical hyperplasia
  - Hysterectomy within 12 weeks
  - 43% with co-existing cancer
  - 18% with less than atypical hyperplasia on biopsy
  - 35% with high risk features
  - 11% had >50% myoinvasion (Stage IB)

---

**Coexisting Endometrial Cancer**

---
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

Coexisting Endometrial Cancer

- Review of 2572 patients
  - 37% had endometrial carcinoma on subsequent biopsy or hysterectomy
- 127 women with endometrial intraepithelial neoplasia
  - 23% cancer incidence
- 150 women with complex atypical hyperplasia
  - 37% with cancer on hysterectomy specimen
  - 44% with endometrial biopsy
  - 28% with D&C
  - 25% had high risk features warranting a lymph node dissection

Coexisting Endometrial Cancer

- 48% rate of concurrent cancer
- 2 fold risk if stripe thickness ≥ 2 cm

Coexisting Endometrial Cancer

<table>
<thead>
<tr>
<th>Clinical factor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 60</td>
<td>6.86 (1.75-25.3)</td>
</tr>
<tr>
<td>BMI ≥ 35 kg/m²</td>
<td>2.32 (1.09-4.93)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.51 (1.16-5.39)</td>
</tr>
<tr>
<td>Hyperplasia type</td>
<td>3.91 (1.09-14.6)</td>
</tr>
</tbody>
</table>
Updates in the Management of Complex Atypical Hyperplasia  
(Endometrial Intraepithelial Neoplasia)

Coexisting Endometrial Cancer: Risk factors

- Presence of nuclear atypia
- Normal weight versus morbidly obese  
  - Rate of cancer: 45% versus 26%
- Low risk if confined to a polyp  
  - Pooled estimate risk of 5.6%  
  - In absence of EIN, negative predictive value 100%

Management Options

- Removal of source of unopposed estrogen
- Main management options
  - Surveillance  
    - Limited to use in low risk patients  
    - E.g. Patient with anovulation, now corrected  
    - Resample as indicated
- Progestin therapy
- Surgery

Progestin therapy

- Candidates:  
  - Fertility preservation  
  - Medically unfit for surgery
- Goals of therapy  
  - Clearance of disease  
  - Normalization of endometrium  
  - Prevention of cancer
- Contraindications  
  - History of VTE/stroke  
  - Severe liver dysfunction  
  - Progesterone receptor positive breast cancer
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

Progestin therapy

- Megestrol acetate
- Medroxyprogesterone
- Norethindrone acetate
- Levonorgestrel intrauterine device
  - Minimal systemic absorption
  - Considered 1st line

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose (mg)</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megestrol acetate</td>
<td>10-20 mg</td>
<td>PO</td>
<td>1-3 times per month</td>
</tr>
<tr>
<td>Medroxyprogesterone</td>
<td>5-20 mg</td>
<td>PO</td>
<td>1-3 times per month</td>
</tr>
<tr>
<td>Norethindrone acetate</td>
<td>0.5-2 mg</td>
<td>PO</td>
<td>1-3 times per month</td>
</tr>
<tr>
<td>Levonorgestrel intrauterine</td>
<td>12-20 mg</td>
<td>IO</td>
<td>12-14 days per month</td>
</tr>
<tr>
<td>Levonorgestrel intrauterine</td>
<td>12-20 mg</td>
<td>IO</td>
<td>12-14 days per month</td>
</tr>
</tbody>
</table>

Progestin Therapy: Limited data

- Oral contraceptives (estrogen-progestin)
  - Limited studies
- Progestin injections
  - Some data on Depot MPA
  - Typically second line
- Progestin implants
  - Not well studied

Progestin therapy: Response rates

- Meta-analysis of 391 patients with hyperplasia/early stage cancer
  - Variety of progestin therapies
- 78% response rate
- 53% complete response (median 39 months follow up)
  - Higher rates in hyperplasia
- Median time to response: 6 months
- Recurrence rates of 23-35%
- Persistent disease in up to 25%
Maintenance therapy

- After regression, progestin maintenance therapy is often appropriate
  - Regimen depends on the following
  - Patient preference
  - Costs
  - Adherence
  - Convenience
  - Side effects
- Options: Levonorgestrel releasing IUD, oral progestin, OCP
- Sources of excess estrogen exposure should be corrected
- Repeat sampling as indicated

Progestin Therapy: Unanswered Issues

- Optimal dose and duration
  - Estimate 12 months
- Appropriate length of follow up after treatment
- Appropriate measures of the clinical and histologic response
- Post-hormonal treatment surveillance
  - May include serial endometrial sampling every 3-6 months

Non standard management options

- Pharmaceutical options
  - Gonadotropin-releasing hormone (GnRH) agonists
  - Aromatase inhibitors
  - Ovulation induction (e.g. clomiphene or aromatase inhibitors)
  - Metformin
  - Danazol
Fertility preservation

- Meta-analysis of pregnancy after progestin therapy
  - 30% (111/370) achieved one or more pregnancies
- Another study reported pregnancy rates
  - 35% in women with cancer
  - 41% in women with hyperplasia

Pregnancies
- 41% (hyperplasia), 35% (cancer)

Total Hysterectomy

- Postmenopausal women
- Do not desire future fertility
- High risk of concomitant endometrial cancer
  - Previously discussed risk factors

Surgical management

- Hysterectomy
  - All surgical routes are acceptable
  - Supra-cervical hysterectomy is inappropriate
  - Morcellation is unacceptable
- Retention of ovaries may be an option
- Endometrial ablation is not acceptable
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

Lymph node assessment
- Mayo criteria: Intraoperative evaluation
  - Grade 1-2 endometrioid histology
  - Inner 50% invasion
  - Tumor < 2 cm

- Staging
  - Prognostic information
  - Informs adjuvant therapy
- Lymph node assessment
  - Palpation
    - 72% sensitivity
    - Limited to open approach
  - Pre-operative imaging
    - False negative rate
    - Cost-prohibitive

Sentinel Lymph Nodes


Non standard management options
- Alternative surgical treatments
  - Hysteroscopic resection
  - Bariatric surgery
Updates in the Management of Complex Atypical Hyperplasia (Endometrial Intraepithelial Neoplasia)

Sentinel Lymph Node Assessment

- Disadvantages
  - Information does not often change management
  - Unnecessary surgery/overtreatment
  - Risk of complications

- Advantages
  - Eliminate need for second surgery if malignancy on final pathology
  - Alternative to all or none approach
  - Used in DCIS
  - Minimal risks

Sentinel Lymph Node Assessment

- Inadequate surgery versus unnecessary procedure
- Consider stratifying approach based on risk assessment

Best approach is a shared decision-making approach

Conclusions

- CAH/EIN is a premalignant lesion
  - Coexisting cancer rates of 40%
  - Cancer progression 27%
- Management options
  - Medical management
  - Hysterectomy +/- lymph node assessment
- Correct the underlying source of unopposed of estrogen
Important Hernia Concepts for the OB/GYN Patient

February 21, 2020

Paul Montero, MD
Associate Professor
Surgery

DISCLOSURES

• None

AGENDA

• Abdominal wall hernias in pregnant patients
• Chronic pelvic pain and groin hernia
• Rectus diastasis in the post-partum patient
• Femoral hernia management
QUESTION 1
A 25 y/o G1P1 patient has a mildly symptomatic umbilical hernia and desires more children. Regarding the hernia, which of the following is the most appropriate:
A. Wait for repair; recurrence risk is markedly higher with subsequent pregnancy after hernia repair
B. Repair the hernia to prevent significant risk of future hernia complications
C. Repair the hernia but without mesh due to the risk of uterine adhesions in future pregnancy
D. Wait and repair at the same time as c-section with the next child

DISCLOSURE: HERNIA DATA ARE HARD TO COME BY
- Many variables
  - Surgeon/Technique
  - Materials/Mesh
  - Patient factors
    - BMI, DM, Smoking, Prior Repairs, Immunosuppression, Activity
- Challenging endpoints
  - Recurrence (how long to wait?)
  - Mesh infection
  - Pain
WHAT ARE THE RISKS OF HERNIA REPAIR WITH SUBSEQUENT PREGNANCY?

- Recurrence
- Pain
- Mesh complications (infection, adhesion)
- Obstruction

- 11,020 US women who underwent hernia repair
- 840 had subsequent pregnancy
- Recurrence defined as re-operation for same hernia
- Overall recurrence rate of 8.3%
- 13.1% recurrence rate in those with subsequent pregnancy
- After risk adjustment of confounding factors (BMI, smoking, wound complications), 1.73 risk of recurrence with subsequent pregnancy

Risk likely under-reported in this retrospective study

Conclusion: “risk of recurrence and subsequent reoperation must be balanced against the risk of incarceration and emergent surgery during pregnancy”
Important Hernia Concepts for the OB/GYN Patient

**RISK OF INCARCERATION AND EMERGENT SURGERY DURING PREGNANCY**

- "Ventral hernias in pregnancy are rare, with most occurring in the second trimester, and account for less than 5% of bowel obstruction cases during pregnancy"

  - Oma et al. Hernia 2017
  - Jensen et al. Hernia 2019

---

**5 studies; 14,638 hernia repair females (1144 pregnant)**

- 12% recurrence (subsequent pregnancy) versus 9% recurrence (no subsequent pregnancy)

- "Female patients of childbearing age with asymptomatic or minimally symptomatic ventral hernias that do not pose a significant strain on the patients' quality of life could be provided with the option of watchful waiting..."

  - Hernia 2018

- One study cited "no adverse impact on the course of pregnancy or delivery" from watchful waiting (n = 12)

  - Nouh et al, Hernia 2018
Important Hernia Concepts for the OB/GYN Patient

MESH COMPLICATIONS?
• Is suture repair better?
• Does it matter where the mesh goes?

OPEN REPAIR MESH POSITIONS
• Onlay
• Inlay (Bridge)
• Underlay (Sublay)
  • Retrorectus
  • Pre-peritoneal
  • Intraperitoneal (aka IPOM)

Dutch study (contained system)
• n = 8, included incisional hernias from port site, c-section
• Retrospective evaluations
• 5 patients had “tearing” or “pulling” pain during pregnancy, with one patient being admitted twice for oral analgesics. All pain “disappeared” after delivery.
• No other pregnancy-related or delivery-related complications
• One recurrence which was asymptomatic
Important Hernia Concepts for the OB/GYN Patient

- Pregnancy causes 1.6-fold increased risk of recurrence
- Pregnancy causes 73% increased risk of reoperation for recurrence
- Emergent UH repair during pregnancy carries minimal 30-day morbidity to the mother
- Several studies show no difference in recurrence with suture only versus mesh repair
  - In general, suture only repair carries a substantially higher risk of recurrence (up to 64%)

Am J Surg 2019

- Few (29%) primary ventral hernias that occur during pregnancy require repair afterwards due to lack of symptoms
- Concomitant VH repair with C-section is safe
  - No increased risk of post-operative complications, with or without mesh (level 4 evidence based on retrospective analysis of case-control series)

Am J Surg 2019

VENTRAL HERNIAS IN FEMALES

- NSQIP 2005-2015
- Females had greater LOS, OR time, wound infection, organ space SSI, UTI, and bleeding requiring transfusion (statistically significant)
- Females have greater morbidity compared to males with same BMI

Data presented at AHS Hernia Congress 2018
HERNIAS IN PREGNANCY

- Watchful waiting is reasonable for minimally symptomatic hernias in pregnant patients or patients of child-bearing age
- Complications from hernia during pregnancy are rare
- Complications are more common in women than men overall for ventral hernia repair

QUESTION 2

A 42 y/o G2P2 female with chronic pelvic pain had a pelvic US suggesting a left-sided indirect, fat-containing inguinal hernia with an 8 mm neck. Symptoms include diffuse, non-cyclical pelvic pain, constipation, intermittent dysuria, and dyspareunia. The hernia is not palpable on exam.

Which of the following would be most appropriate in management?

A. Open inguinal hernia repair with mesh
B. Open inguinal hernia repair with suture only
C. Laparoscopic inguinal hernia repair without mesh
D. Dynamic CT imaging
QUESTION 2

42 G2P2 chronic pain with pelvic US suggesting 8mm left indirect fat-containing hernia.

Which of the following would be most appropriate in management?

A. Open inguinal hernia repair with mesh
B. Open inguinal hernia repair with suture only
C. Laparoscopic inguinal hernia repair without mesh
D. Dynamic CT imaging

ONCE AGAIN, DATA ARE LIMITED

Things I learned while preparing for this talk:

- Chronic pelvic pain is common
- Accounts for 10% of all GYN consults
- International Pelvic Pain Society
- Often multi-factorial

Conundrum for the general surgeon:

- Adhesions?
- Non-palpable, US+ inguinal hernia

THE NON-PALPABLE, RADIOGRAPHICALLY PRESENT INGUINAL HERNIA

- "Never operate on a non-palpable inguinal hernia for pain- it only results in more pain (for the patient and the surgeon)"
- Mesh is designed to scar into place and is not easily removed
- Once a mesh is in place, further workup for persistent pain is much muddier
- Laparoscopic evaluation could be done concomitantly during repair
Hernia is part of a broad differential diagnosis list
- Found in 1.6 to 6% of women with chronic pelvic pain
- CT considered of little value in initial workup
- US considered useful, especially for hernia and abdominal wall endometriosis

Anecdotally (with shared opinion of senior colleagues and mentors), US is not to be 100% trusted in IH diagnosis
- Inguinal hernias are often over-called
  - Limitations: habitus, user, interpretation for surgeon
US VERSUS CT

**US**
- No radiation
- No IV
- Dynamic: with Valsalva, coughing, upright, etc
- User-dependent
- Habitus-limiting
- Accuracy?
- Surgeon interpretation limited

**CT**
- IV, radiation
- Static, supine
- Can be done with Valsalva
- May observe other etiologies of pain
- Surgeons can interpret

---

Discusses laparoscopic inguinal exploration and empiric mesh placement, with 35% showing improvement (retrospective) and an additional 42% showing improvement with later recurrence of pain.

Also discusses conscious laparoscopic pain mapping, involving diagnostic laparoscopy under mild sedation.

None of the above are recommended; further studies needed.
Laparoscopic inguinal hernia repair requires mesh.
Dynamic CT and/or MRI can supplement hernia detection if clinical picture unclear.

CHRONIC PELVIC PAIN AND GROIN HERNIA
Hernia is a rare cause of chronic pelvic pain but can be diagnosed preferably by exam, but also with imaging (US, dynamic CT if not palpable).

QUESTION 3
A 34 y/o G3P3 patient is 10 weeks post-partum and complains of a large upper abdominal wall bulge. There is no pain but it is unsightly, particularly when exerting herself. Which of the following is the most likely diagnosis?

A. Primary epigastric hernia
B. Omphalocele
C. Soft tissue tumor
D. Rectus diastasis
QUESTION 3
A 34 y/o G3P3 patient is 10 weeks post-partum and complains of a large upper abdominal wall bulge. There is no pain but it is unsightly, particularly when exerting herself. Which of the following is the most likely diagnosis?

A. Primary epigastric hernia
B. Omphalocele
C. Soft tissue tumor
D. Rectus diastasis

The general surgeon's perspective of rectus diastasis. A systematic review of treatment options

- Definition: inter-rectus distance (IRD) of 22 mm, measured 3 cm above the umbilicus
- Multiple repair techniques, with no data to compare efficacy: open, endoscopic, laparoscopic, robotic; plication or modified ventral hernia repair with mesh
- Regresses spontaneously in most women after childbirth
  - Persists in up to 33% at one year
- No physiotherapy program was effective at diminishing the IRD in the relaxed state
RECTUS DIASTASIS: THIS GENERAL SURGEON’S PERSPECTIVE

- Cosmetic; not typically covered by insurance, mostly repaired by plastics
- PT at UCH has an effective program for post-partum patients
- ~ Dozen referrals per year from PCPs, NPs, and PAs for asymptomatic, “massive” ventral hernias in the upper abdomen without prior surgery
- In the setting of prior incision, CT scan reports often describe a “diastasis” that is actually a hernia on exam

Pain is rare; concomitant epigastric hernias can be sought with imaging (US or dynamic CT) if not apparent on exam
- Robotic repair is feasible (with mesh reinforcement)
- Excellent opportunity to diagnosis with physical exam alone
- Rectus Diastasis is a risk factor for recurrence in suture repair of hernia (mesh repair and/or diastasis repair should be pursued)

PHYSICAL EXAM: RECTUS DIASTASIS

- Upright and supine, the abdominal wall is flat since the rectus abdominus muscles are relaxed
- When actively leaning back, the patient invariably grabs my wrist and points at the bulge occurs (and disappears as soon as they are supine)
- Nearly always between the umbilicus and xiphoid
QUESTION 4
A 24 y/o G4P4 patient has a minimally symptomatic right groin bulge and seeks management options. Which of the following is most appropriate?

A. Watchful waiting, with education of possible risks of incarceration/strangulation
B. Open repair without mesh
C. Open repair with mesh
D. Laparoscopic repair

Groin hernias are 8-10 times more common in men
Femoral hernias are 4 times more common in women
Femoral hernia incarceration is more common than inguinal hernia incarceration
17% of females with groin hernias require emergent repair
5% of men with groin hernias require emergent repair
23% of emergent femoral hernia repairs require bowel resection; 5% of emergent inguinal hernias require bowel resection
Open groin hernia repair in women has a higher re-operative rate
In 40% of re-operations, femoral hernias are found

International guidelines suggest all female groin hernias undergo laparoscopic repair when available due to lower risks of chronic pain and ability to detect/repair femoral hernias

CASE EXAMPLE: MIS REPAIR OF BILATERAL INGUINAL HERNIAS IN A FEMALE

Healthy, 45 yo G3P4 patient with mildly symptomatic, bilateral inguinal hernias.
US: spontaneously reducible, fat-containing, direct and indirect bilateral inguinal hernias
HERNIAS IN OBGYN PATIENTS

- Watchful waiting is okay in pregnant patients
- Hernias may be a component of chronic groin pain; diagnosis and patient education are key
- Rectus diastasis does not carry the complication risks of ventral hernias but can be repaired in similar manners
- Watchful waiting is not okay in non-pregnant patients with groin hernias
- Hernia diagnosis is not always straightforward!

THANK YOU

- PAUL.MONTERO@CUANSCHUTZ.EDU