The Department of Medicine
Division of General Internal Medicine
University of California, San Francisco School of Medicine
presents

Controversies in Women’s Health

December 6-7, 2012
Hotel Nikko
San Francisco, California

Course Chair
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Professor of Medicine;
Associate Dean for Graduate and Continuing Medical Education;
Vice Chief, Division of General Internal Medicine

Course Co-Chairs
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University of California, San Francisco

University of California, San Francisco School of Medicine
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  S. Andrew Josephson, MD
Every Patient is an Athlete
  Carlin Senter, MD

Participant List
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U.S. Food and Drug Administration/Office of Women’s Health
Controversies in Women’s Health

OVERVIEW
Increasing appreciation of the unique needs of women patients and women health care providers has created a need for innovative educational programs on women’s health. This program will provide a practical update on a full range of common but controversial issues in women’s health. Emphasis will be placed on new developments in preventive care for women, issues in reproductive health, and clinical strategies in the diagnosis and treatment of common gynecologic and medical disorders of women. An audience response system will be used, and ample time will be provided for questions and discussion. This course is presented by the Division of General Internal Medicine, Department of Medicine, in close collaboration with the Department of Obstetrics, Gynecology, and Reproductive Sciences and is sponsored by the University of California, San Francisco.

EDUCATIONAL OBJECTIVES
The purpose of this course is to increase competence and improve clinician practice in primary care and women’s health. We specifically anticipate improvements in skills and strategies:

- to discuss and implement new guidelines in office-based preventive medicine for women for prevention and early detection of cancer with clinical exam, pap tests, diagnostic imaging, and the HPV and influenza vaccines;

- to diagnose and treat common problems in women’s health including osteoporosis, menopause, breast masses and breast cancer, allergies, sports injuries, incontinence, anxiety and depression;

- to counsel patients about treatment options in contraception and therapeutic abortion;

- to diagnose and treat common skin problems in women and to discuss options in cosmetic dermatology;

- to assess and treat common sports injuries and musculoskeletal complaints in women;

- to better care for older patients presenting with osteoporosis, cerebrovascular disease, and chronic medical illnesses;

- to participate in public policy, advocacy and re-design for women’s health.
ACCREDITATION

The University of California, San Francisco School of Medicine (UCSF) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

UCSF designates this educational activity for a maximum of **13.50 AMA PRA Category 1 Credits™**.

*Physicians should only claim credit commensurate with the extent of their participation in the activity.*

This CME activity meets the requirements under California Assembly Bill 1195, continuing education and cultural and linguistic competency.

**Nurses:**
For the purpose of recertification, the American Nurses Credentialing Center accepts **AMA PRA Category 1 Credits™** issued by organizations accredited by the ACCME.

**Physician Assistants:**
AAPA accepts category 1 credit from AOACCME, Prescribed credit from AAFP, and **AMA PRA category 1 credits™** from organizations accredited by the ACCME.

**Pharmacy:**
The California Board of Pharmacy accepts as continuing professional education those courses that meet the standard of relevance to pharmacy practice and have been approved for **AMA PRA Category 1 Credits™**.

**Family Physicians:**
This activity, Controversies in Women’s Health, with a beginning date of December 6, 2012, has been reviewed and is acceptable for up to **13.25** Prescribed credits by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

**Obstetricians and Gynecologists:**
The American College of Obstetricians and Gynecologists has assigned **14** cognate credits to this program.

**Geriatric Medicine:**
The approved credits shown above include **6.50** credits toward meeting the requirement under California Assembly Bill 1820, Geriatric Medicine.

**Licensed Clinical Social Workers and Marriage & Family Therapists:**
This course meets the qualifications on an hour-for-hour basis of continuing education credit for MFT’s and/or LCSW’s as required by the California Board of Behavioral Sciences. Approval No. PCE 1272.
General Information

Attendance Verification / CME Certificates
Please remember to sign-out on the sign-in sheet on your last day by attesting to the number of hours you attended. You only have to sign-in once for the course, when you first check in, and sign-out by recording the number of credits/hours that you earned. For your convenience, an hour by hour credit calculation is available at the registration desk.

CME Certificates will be mailed to participants approximately 3-4 weeks post course. You must attest to the number of hours you earned in order to receive a CME certificate. If you need to leave the course before it concludes you may sign-out early at the UCSF Registration Desk.

Evaluation
Your opinion is important to us – we do listen! Please complete and return the course evaluation as it is important to future course planning. The evaluation is the yellow hand-out that you received inside the cover of your course syllabus. Please turn in the evaluation prior to leaving the course.

Security
We urge caution with regard to your personal belongings and syllabus books. We are unable to replace these in the event of loss. Please do not leave any personal belongings unattended in the meeting room during lunch or breaks or overnight.

Exhibits
Exhibits are located outside the general session room during breakfasts and coffee breaks.

Final Presentations
PowerPoint presentations will be available on our website: www.cme.ucsf.edu approximately 2-4 weeks post event. We will only post presentations for those authorized by the presenters.
Federal and State Law
Regarding Linguistic Access and Services for Limited English Proficient Persons

I. Purpose.
This document is intended to satisfy the requirements set forth in California Business and Professions code 2190.1. California law requires physicians to obtain training in cultural and linguistic competency as part of their continuing medical education programs. This document and the attachments are intended to provide physicians with an overview of federal and state laws regarding linguistic access and services for limited English proficient (“LEP”) persons. Other federal and state laws not reviewed below also may govern the manner in which physicians and healthcare providers render services for disabled, hearing impaired or other protected categories.

The Federal Civil Rights Act of 1964, as amended, and HHS regulations require recipients of federal financial assistance (“Recipients”) to take reasonable steps to ensure that LEP persons have meaningful access to federally funded programs and services. Failure to provide LEP individuals with access to federally funded programs and services may constitute national origin discrimination, which may be remedied by federal agency enforcement action. Recipients may include physicians, hospitals, universities and academic medical centers who receive grants, training, equipment, surplus property and other assistance from the federal government.

HHS recently issued revised guidance documents for Recipients to ensure that they understand their obligations to provide language assistance services to LEP persons. A copy of HHS’s summary document entitled “Guidance for Federal Financial Assistance Recipients Regarding Title VI and the Prohibition Against National Origin Discrimination Affecting Limited English Proficient Persons – Summary” is available at HHS’s website at: http://www.hhs.gov/ocr/lep/.

As noted above, Recipients generally must provide meaningful access to their programs and services for LEP persons. The rule, however, is a flexible one and HHS recognizes that “reasonable steps” may differ depending on the Recipient’s size and scope of services. HHS advised that Recipients, in designing an LEP program, should conduct an individualized assessment balancing four factors, including: (i) the number or proportion of LEP persons eligible to be served or likely to be encountered by the Recipient; (ii) the frequency with which LEP individuals come into contact with the Recipient’s program; (iii) the nature and importance of the program, activity or service provided by the Recipient to its beneficiaries; and (iv) the resources available to the Recipient and the costs of interpreting and translation services.

Based on the Recipient’s analysis, the Recipient should then design an LEP plan based on five recommended steps, including: (i) identifying LEP individuals who may need assistance; (ii) identifying language assistance measures; (iii) training staff; (iv) providing notice to LEP persons; and (v) monitoring and updating the LEP plan.

A Recipient’s LEP plan likely will include translating vital documents and providing either on-site interpreters or telephone interpreter services, or using shared interpreting services with other Recipients. Recipients may take other reasonable steps depending
on the emergent or non-emergent needs of the LEP individual, such as hiring bilingual staff who are competent in the skills required for medical translation, hiring staff interpreters, or contracting with outside public or private agencies that provide interpreter services.

HHS’s guidance provides detailed examples of the mix of services that a Recipient should consider and implement. HHS’s guidance also establishes a “safe harbor” that Recipients may elect to follow when determining whether vital documents must be translated into other languages. Compliance with the safe harbor will be strong evidence that the Recipient has satisfied its written translation obligations.

In addition to reviewing HHS guidance documents, Recipients may contact HHS’s Office for Civil Rights for technical assistance in establishing a reasonable LEP plan.

The California legislature enacted the California’s Dymally-Alatorre Bilingual Services Act (Govt. Code 7290 et seq.) in order to ensure that California residents would appropriately receive services from public agencies regardless of the person’s English language skills. California Government Code section 7291 recites this legislative intent as follows:

“The Legislature hereby finds and declares that the effective maintenance and development of a free and democratic society depends on the right and ability of its citizens and residents to communicate with their government and the right and ability of the government to communicate with them.

The Legislature further finds and declares that substantial numbers of persons who live, work and pay taxes in this state are unable, either because they do not speak or write English at all, or because their primary language is other than English, effectively to communicate with their government. The Legislature further finds and declares that state and local agency employees frequently are unable to communicate with persons requiring their services because of this language barrier. As a consequence, substantial numbers of persons presently are being denied rights and benefits to which they would otherwise be entitled.

It is the intention of the Legislature in enacting this chapter to provide for effective communication between all levels of government in this state and the people of this state who are precluded from utilizing public services because of language barriers.”

The Act generally requires state and local public agencies to provide interpreter and written document translation services in a manner that will ensure that LEP individuals have access to important government services. Agencies may employ bilingual staff, and translate documents into additional languages representing the clientele served by the agency. Public agencies also must conduct a needs assessment survey every two years documenting the items listed in Government Code section 7299.4, and develop an implementation plan every year that documents compliance with the Act. You may access a copy of this law at the following url:

http://www.spb.ca.gov/bilingual/dymallyact.htm
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Disclosures  
The following faculty speakers, moderators and planning committee members have disclosed NO financial interest/arrangement or affiliation with any commercial companies who have provided products or services relating to their presentation(s) or commercial support for this continuing medical education activity:  

Robert B. Baron, MD  
Lindy P. Fox, MD  
Katherine E. Gundling, MD  
Ellen Haller, MD  
Rebecca Jackson, MD  
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The following faculty speakers have disclosed a financial interest/arrangement or affiliation with a commercial company who has provided products or services relating to their presentation(s) or commercial support for this continuing medical education activity. All conflicts of interest have been resolved in accordance with the ACCME Standards for Commercial Support:  

Jeanette S. Brown, MD  
Grant/Research Support  
Pfizer  

This UCSF CME educational activity was planned and developed to: uphold academic standards to ensure balance, independence, objectivity, and scientific rigor; adhere to requirements to protect health information under the Health Insurance Portability and Accountability Act of 1996 (HIPAA); and, include a mechanism to inform learners when unapproved or unlabeled uses of therapeutic products or agents are discussed or referenced.  

This activity has been reviewed and approved by members of the UCSF CME Governing Board in accordance with UCSF CME accreditation policies. Office of CME staff, planners, reviewers, and all others in control of content have disclosed no relevant financial relationships.
COURSE PROGRAM

Thursday, December 6, 2012

7:30 am  Course Registration and Continental Breakfast

8:20  Welcome  Robert B. Baron, MD, MS

KEYNOTE ADDRESS
8:30  The Impact of the Accountable Care Act on Women’s Health Care  Michael S. Policar, MD, MPH

PREVENTIVE MEDICINE FOR WOMEN
Moderator: Robert B. Baron, MD, MS

9:10  Q and A
9:20 (G)  Cancer Screening: New Recommendations, New Controversies  Judith M. E. Walsh, MD, MPH
10:00  Q and A
10:10  Break

10:30 (G)  Cervical Cancer Prevention Update: 2012 and Beyond  George F. Sawaya, MD
11:10  Q and A
11:20 (G)  Vaccinations for Adult and Adolescent Women  Katherine A. Julian, MD
12:00 pm  Q and A
12:10  Lunch on Your Own

CLINICAL STRATEGIES IN WOMEN’S HEALTH I
Moderator: Katherine A. Julian, MD

1:30  Mental Health and Women’s Health  Ellen Haller, MD
2:10  Q and A
2:20  Incontinence: As Easy as 1, 2, 3  Jeanette S. Brown, MD
3:00  Q and A
3:10  Break

3:30 (G)  New Oral Anticoagulants: Impact for Primary Care Practice  Tracy Minichiello, MD
4:10  Q and A
4:20 (G)  Hot Topics in Allergy and Immunology  Katherine E. Gundling, MD
5:00  Q and A
5:10 pm  Adjourn
Friday, December 7, 2012

8:00 am  Continental Breakfast

CLINICAL STRATEGIES IN WOMEN’S HEALTH II
Moderator: Robert B. Baron, MD, MS

8:30  Breast Cancer: Key Issues for the Non-Oncologist  Leah Karliner, MD, MAS
9:10  Q and A
9:20  Best Practices in Contraception: Preventing the Unintended  Carolyn Sufrin, MD, MA
10:00  Q and A

10:10  Break

10:30  New Guidelines for Menopause Management  Michael S. Policar, MD, MPH
11:10  Q and A
11:20  Lumps, Bumps and Pain: Management of Common Breast Disorders  Rebecca Jackson, MD
12:00 pm  Q and A

12:10  Lunch (On Own)

CLINICAL STRATEGIES IN WOMEN’S HEALTH III
Moderator: Nancy Milliken, MD

1:30  Common Dermatologic Disorders: Tips for Diagnosis and Management  Lindy P. Fox, MD
2:10  Q and A
2:20  New and Emerging Therapies for Osteoporosis  Anne Schafer, MD
3:00  Q and A

3:10  Break

3:30  Advances in Prevention and Treatment of Stroke: What Every Clinician Needs to Know  S. Andrew Josephson, MD
4:10  Q and A
4:20  Every Patient is an Athlete  Carlin Senter, MD
5:00  Q and A

5:10 pm  Adjourn/Evaluations/Attendance Verification

G - Geriatric Credit
The Impact of the ACA on Women’s Health Care in California

Michael S. Policar, MD, MPH
Clinical Professor of Ob,Gyn, & RS
UCSF School of Medicine
policarm@obgyn.ucsf.edu

I have no commercial disclosures for this lecture
**Health Care Reform...Always a Tough Road**

**Health Policy versus Health Politics**

- **Health Policy**: Which policies, structures, and financing lead to optimal clinical and economic health outcomes?
  - The Clinton Health Security Act
- **Health Politics**: What is possible...who wins and loses?
  - Patient Protection and Affordable Care Act
“Patient Protection and Affordable Care Act” (ACA)  
March 23, 2010

- First step: Expand access to health insurance
  - Everyone has coverage
  - Fairer insurance practices
  - Expand coverage to 32 million by 2019

- Second step: Improve quality of care
  - Focused on prevention and primary care

- Third step: Stabilize cost of health care
  - Change incentives: shared risk, P4P
  - Reduce waste and fraud

The ACA is just the beginning of health reform
**ACA Step 1: Expanding Access**  
**A Three Part Formula**

1. **Insurers must offer coverage to everyone**, regardless of pre-existing conditions
2. **Federal subsidies** will help people to afford coverage  
   - Direct payment of a share of insurance premiums  
   - Tax credits for co-payments, deductibles
3. **Everyone must have health insurance**  
   - Risk pool must include healthy people...makes premiums more affordable  
   - Only way to cover those with pre-existing conditions

---

**The Individual Mandate**

- All citizens, legal immigrants must have coverage
- Tax penalty if no coverage (by 2016)...*higher of*  
  - $695/person; up to 3 times for a family, or  
  - 2.5% of household income
- Exemptions granted for  
  - Undocumented persons  
  - No coverage for less than 3 months  
  - Lowest cost plan > 8% personal income  
  - Financial hardship  
  - Religious objection
US Supreme Court
Ruling on ACA
June 21, 2012

• Can the court rule on a tax matter before the tax starts?
  – Yes
• Did the individual mandate exceed constitutional authority?
  – No, based upon their power to levy and regulate taxation
• Are other parts of the ACA severable?
  – Yes
• Does the ACA impose an unconstitutional burden on states?
  – Yes…feds can’t require a “take-it-or-leave-it” decision
  – States can continue Medicaid programs without expansion

Little or no change

| Military Veterans Admin | Insured through employer | Undocumented individuals |

Minor changes

| Medicare         | Medicaid |

Major changes

| Uninsured | Self employed | Small business |
Minor changes

**Medicare**

*The good*
- Close Part D (drug coverage) “doughnut hole” by 2020
- No copayments for preventive care (2011)

*The bad*
- Increase Part A, B premiums for high earners

*The ugly*
- Reduce payments to Medicare Advantage plans → reduced benefits

---

Minor changes

**Medicaid**

- Expand Medicaid eligibility to 138% of fed’l poverty level
  - $14,400 individual; $30,657 family of 4
- Federal government pays 100% of new costs till 2017
- Cover the same “essential benefits” that are required in State Health Insurance Exchanges
- Maintain CHIP until at least 2019
Major Changes

- Uninsured
- Self employed
- SB <50 employees
- Small business (50-100)

50%

40%

100%

State Health Insurance Exchanges

- CA Health Benefit Exchange
  “Covered California”
- Small Business Health Options Program

50%

100%

Employer based

What Are Health Insurance Exchanges (HIX)?

- State regulated “insurance marketplaces”
  - “Travelocity” of health insurance plans
  - Consumers will compare plans by quality and cost
  - All will offer the same “essential health benefits”
  - Optional participation by health insurance plans

- Subsidies for families 133-400% FPL (federal poverty level)
  - Premium credit (toward purchase of insurance), and
  - Cost-sharing tax credit (rebate on OOP costs)

- If a state does not develop a HIX, default to the federal HIX
Insurance Status of Non-elderly Women in CA

Insurance Status
- Individual
- Public
- Uninsured
- Employer based

Uninsured by Income*
- <=133%
- 134-399%
- 400% and above

Total: ~2.6 M

*Income Data 2007

credit: www.yalibair.com

Women ages 18-64
Kaiser Family Foundation
Insurance Data 2008-2009
**Transition to the ACA in California**

**CA “Bridge to Reform” 1115 waiver**

- LIHPs (limited income health program) in early 2013
  - Early enrollment for upcoming Medi-Cal expansion
  - Will not cover family planning services, but dual eligibility for Family PACT is acceptable

- Preparation of clinics and private practices as “portals of entry” into either Medi-Cal expansion or HIX

- Covered California opens for enrollment in October 2013

**ACA Step 2: Initiatives to Improve Quality of Care**

- Electronic health records (EHR) incentives
- PCORI: Patient Centered Outcomes Research Institute
  - Comparative Effectiveness Research
- PQRI: Physician Quality Reporting Initiative
  - Medicare payments increased (up to 2%)
  - Data used for “Physician Compare” website (2013)
  - Medicare Value Based Payment Modifier (2015)
    - Adjustment to rates based on quality & cost performance
ACA Step 3: Cost Savings

- **Prevention**: remove barriers, improve access
- **Primary care**: ideally in patient centered medical home
- **ACOs**: Medicare Accountable Care Organizations
  - Similar to PHOs (physician-hospital orgs); capitated
  - Move away from case-based reimbursement
- **Independent Payment Advisory Board (IPAB) 2015**
  - To recommend payment adjustments, but not benefits
- **Tort reform**: $50 million over 5 years to evaluate reform

The Impact of the ACA on Ob-Gyns

- **Direct access to Ob-Gyns**
  - No referrals or pre-authorizations permitted
  - No restriction on number of visits or types of services
- **Patient centered medical home**
  - IM, FM, pediatricians...and OBGYNs
- **Increased support for**
  - CNMs: Medicare payment equivalent to physicians
  - Free standing birth centers (Medicaid)
  - Tobacco cessation in pregnancy (Medicaid)
  - Maternal Infant Home Visiting Program
The Impact of the ACA on Women’s Health Care

- Preventive services
- Family planning services
- Abortion services

Promoting Prevention through the Affordable Care Act

- Specified preventive services must be covered with no cost-sharing (no out-of-pocket costs)
- Applies to private and public programs
  - (New) Private insurance policies 2010
  - Medicare, Medicaid 2011
  - State insurance exchanges 2014
- Improves coverage for preventive services in many individual and small group plans
Preventive services include all services
- USPSTF grade [A] or [B] recommendations
- AAP Bright Futures recommendations for adolescents
- CDC ACIP vaccination recommendations

IOM recommended to HRSA additional women’s prevention benefits not addressed by USPSTF...intended to “close the gaps”

Institute of Medicine
- Committee on Preventive Services for Women
- “Closing the Gaps” released July 20, 2011
- 16 member panel
- 8 additional preventive services recommended
IOM: Women’s Preventive Services

• **Wow**: important advances
  – Contraceptive counseling and methods
  – IPV screening and counseling
  – Breastfeeding support
• **Helpful**: facilitates improved provision of care
  – Well woman visit

IOM: Women’s Preventive Services

• **Yawn**: no change from what we are doing already
  – GDM screening
  – Counseling for STIs
• **Be cautious**: if over-utilized, may make things worse
  – Annual counseling and screening for HIV
  – Cervical cytology + HPV testing every three years for women 30 and older
Reproductive Health | Cancer | Healthy Behaviors | Pregnancy related | Immunizations | Chronic conditions
---|---|---|---|---|---
STI and HIV counseling (adults at HR; all sexually active F) | Breast Cancer Mammography | Alcohol S&C | Alcohol S&C | Tdap, Td booster, MMR, varicella | CV: HTN, lipids
Ct, GC, Syphilis screening | Genetic S&C Tobacco C&I | Tobacco C&I | Influenza | T2DM screen
HIV screening (adults at HR; all sexually active F) | Preventive medication counseling | Diet counseling if CVD risk | Folic acid supplement | Hepatitis A, B Meningococcal | Depression screen
Contraception (women w/repro capacity) | Cervix: Cytology HPV + cytology | Interpersonal and DV S&C | GDM screen Rh screen Anemia screen | HPV (women 19-26) | Osteoporosis screen
Colorectal: FOBT, Colonoscopy, Sigmoid | Well-woman visits | STI screen Bacteruria screen | Pneumococcal Zoster | Obesity screen; C&I if obese
| Lactation Supports

S&C screening and counseling C&I counseling and interventions

**Closing the Gaps...Opportunities**

- Improved access to important benefits, especially contraceptive services and breastfeeding support
- Greater visibility for some under-performed services
  - Sexual history (STI and HIV counseling)
  - Reproductive life plan (contraceptive services)
  - Preconception care (well women visits)
  - IPV and DV screening and counseling
- Reduced barriers for well woman visits, prenatal care, lactation support by elimination of cost sharing
**Closing the Gaps...Cautions**

- These are benefits, *not clinical practice guidelines*
  - Just because the patient has annual coverage for a service, doesn’t mean she needs it annually
- Promote correct use, especially those prone to overutilization
  - Repetitive HIV screening in average risk women
  - Annual HPV + cytology on women who have recently screened negative for each

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**Women’s Preventive Services**

<table>
<thead>
<tr>
<th>Service</th>
<th>HHS Guideline for Insurance Coverage</th>
<th>Frequency</th>
<th>USPSTF</th>
</tr>
</thead>
</table>
| Well-woman visits        | Well-woman visits annually to obtain services that are age and developmentally appropriate, including preconception and prenatal care | • Annual  
  • Several visits may be needed to obtain all recommended services, depending on health status, health needs, and other risk factors | Not addressed     |
Women's Preventive Services

<table>
<thead>
<tr>
<th>HHS Guideline for Insurance Coverage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>All FDA approved contraceptive methods, sterilization procedures, and patient education &amp; counseling</td>
<td>As prescribed</td>
</tr>
<tr>
<td>for women with reproductive capacity</td>
<td></td>
</tr>
</tbody>
</table>

- All methods must be covered, but not all products
- Limited exclusion for religious institutions (e.g., churches) from providing contraceptive coverage for insured employees

When Does the “Contraception As Prevention” Benefit Start?

<table>
<thead>
<tr>
<th>Plan Creation Date</th>
<th>Definition</th>
<th>Cost-sharing?</th>
<th>When is cost-sharing prohibited?</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Plan</td>
<td>Created after 8/1/2012</td>
<td>None</td>
<td>Now</td>
</tr>
<tr>
<td>Non-grandfathered plan</td>
<td>Created 3/23/10-8/1/12</td>
<td>Yes*</td>
<td>Next “new plan year”; mostly by 1/1/2013</td>
</tr>
<tr>
<td>Grandfathered plan</td>
<td>Created before 3/23/2012</td>
<td>Yes*</td>
<td>Once plan changes; mostly in 2014</td>
</tr>
</tbody>
</table>

* Unless plan agrees to remove cost sharing earlier than deadline
Contraception as a Preventive Service... as of November 2012

- **Exempt employers** (mainly churches)
  - Exists for the purpose of Inculcating religious values
  - Primarily employs & serves persons who share religious tenets
  - Meets certain provisions of the tax code
- **Accommodation (mainly hospitals, universities)**
  - Religiously-affiliated employers who do not meet exemption but who have a religious objection
  - Insurer offers rates that excludes contraceptives, but health plan covers contraceptive benefit
  - One year safe-harbor from enforcement

Many Questions...Not Many Answers

- If I can’t collect a co-payment, will the Plan pay it?
  - In the short term...yes
  - In the long term, the “cost-sharing” model will change
- Is there cost-sharing for global OB care?
  - No cost-sharing for routine prenatal, post-partum visits
  - Cost-sharing applies to the delivery itself
- If I manage other conditions at a well woman visit, should a co-pay be collected?
  - Yes, if separate office visit is billed with -25 modifier
Federal Medicaid Funding of Abortion

- **Hyde Amendment**: no federal funding for abortion, unless the pregnancy is the result of “rape or incest” or “would, as certified by a physician, place the woman in danger of death unless an abortion is performed”
- **Currently**
  - 17 states cover all or most medically necessary abortions under Medicaid
  - 33 states provide no or minimal Medicaid coverage of abortion beyond federal requirements

The ACA and Elective Abortion

- **The Stupak-Obama Compromise**
  - Presidential Executive Order (3/24/10) enforcing Hyde
  - Applies to exchanges, Medicaid, PCIPs, Community Health Center Fund
- **No federal subsidies may be used to purchase coverage for abortion beyond Hyde**
- **In state health insurance exchanges (starting in 2014)**
  - No plans can be required to offer abortion coverage
  - State laws may ban abortion coverage in exchange
### The ACA and Elective Abortion

- Plans in exchange that cover abortion
  - Must notify enrollees of abortion benefit
  - Must pay with “separate check” for abortion coverage
  - Abortion premiums and pay-outs are kept in separate account, apart from taxpayer money
- No plan can discriminate against a provider or facility because of unwillingness to provide abortion services
- Does not apply to health plan products that have no members with federal support

### Health Care Reform: Who Won? Who Lost?

#### The Winners
- Most of the uninsured
- Women insured by indiv and small group plans
- Women’s health services
- Children under 26 yrs old
- Primary care providers
- CNMs, NPs, PAs
- Insurance companies
- Pharma companies

#### The Losers
- Undocumented persons
- Women needing abortions
- Most specialists
- Medicare recipients
Concluding Thoughts

- Health reform will be a major issue in our lifetimes
  - Tension between demand for care and ability to pay for it
- Challenges in 2013-2014
  - “Everyone has a plane ticket, but not a seat assignment”
    - Determination eligibility for Medicaid or the state HIX
    - Choosing a health plan and enrolling in it
    - Assignment to an open PCP practice
  - Absorption of private practices into integrated delivery systems ...and new ways of being paid

Concluding Thoughts

- Be open in your thinking......
  - Based on the reality of health politics, covering >93% of Americans is a good first step
  - Correctly puts prevention and primary care at the center of the American health care universe
  - If quality and cost containment is successful, the ACA will revolutionize U.S. health delivery
  - The first signed legislation since 1965 to evolve from a health care market to a health care system
2014 is tomorrow

The Window of Opportunity is Open
Additional Resources

- **National Women’s Law Center**
  - Excellent advice re: accessing preventive services
  - nwlc.org

- **Kaiser Family Foundation**
  - Analysis of the effect of ACA on consumers, providers
  - kff.org

- **National Family Planning and Reproductive Health Assn**
  - Advice for delivery of family planning services
  - nfprha.org
Cancer Screening

New Recommendations,
New Controversies

Judith M.E. Walsh, MD, MH
Division of General Internal Medicine
Women’s Health Center of Excellence
University of California, San Francisco

Disclosure

• I have nothing to disclose
Selected Controversies

• Breast Cancer Screening
  – Who should be screened?
  – Digital Mammography
  – MRI

• Ovarian Cancer
  – Should we screen?

• Cervical Cancer
  – What are the new screening guidelines?

Selected Controversies

• Lung Cancer
  – Does screening work?
  – What about CT screening?

• Colorectal Cancer
  – What test and how often?
  – Are there new screening options?
Breast Cancer Screening

• Maggie Graham is a 50 year old woman with no family history of breast cancer. She has been reading news articles about the “increased accuracy” of screening ultrasound or MRI in women with dense breasts.

• You perform a clinical breast examination, which is normal.

Breast Cancer Screening

• What do you recommend to Maggie?
  – Add ultrasound
  – Add breast MRI
  – Mammogram alone
  – Add ultrasound and MRI
The Debate Continues…

The Debate Continues…

June 28, 2011

"ACR urges USPSTF to withdraw mammography screening guidelines"

Breast Cancer Screening

- Breast cancer is the most common cancer in women and the second leading cause of cancer death
- Screening mammography reduces mortality from breast cancer
- Younger women have lower breast cancer risk
- Increased density of pre-menopausal breast tissue leads to decreased sensitivity
Harms Of Screening

- **False positives**
  - Anxiety
  - Additional tests including biopsies
  - One-third of total screening cost

- **Over-diagnosis**
  - Cancers diagnosed that never would cause symptoms: patients receive all the costs and harms of treatment
  - Estimates: 10% to 26% of invasive breast cancers and 34% of all breast cancers

- **Radiation exposure**
  - One breast cancer for 3000 women screened annually for 10 years

Jorgensen, BMJ, 2009

USPSTF New Guidelines

**Mammography**
- Age 50-74: screening mammography every 2 years
- Age 40-49: individualize decision to begin biennial screening according to patient’s context and values
- Age ≥75: no recommendation (insufficient evidence)

**Breast Exam**
- Clinical breast examination alone – insufficient evidence
- Recommend against teaching women to perform routine breast self-examination
  - No mortality benefit
  - Higher rates of benign breast biopsies

USPSTF, 2009
Age and Mammography


**Table 1.** Pooled RR for Breast Cancer Mortality From Mammography Screening Trials for All Ages

<table>
<thead>
<tr>
<th>Age</th>
<th>Trials Included, n</th>
<th>RR for Breast Cancer Mortality (95% CI)</th>
<th>NNI to Prevent 1 Breast Cancer Death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>39-49 y</td>
<td>8*</td>
<td>0.85 (0.75-0.96)</td>
<td>1904 (929-6378)</td>
</tr>
<tr>
<td>50-59 y</td>
<td>6†</td>
<td>0.86 (0.75-0.99)</td>
<td>1339 (322-7455)</td>
</tr>
<tr>
<td>60-69 y</td>
<td>2‡</td>
<td>0.68 (0.54-0.87)</td>
<td>377 (230-1050)</td>
</tr>
<tr>
<td>70-74 y</td>
<td>1§</td>
<td>1.12 (0.73-1.72)</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Mammography and Age

“Mammography screening at any age is a tradeoff of a continuum of benefits and harms. The ages at which this tradeoff becomes acceptable to individuals and society are not clearly resolved by the available evidence.”

USPSTF
Frequency of Mammography

• Similar reduction in mortality with screening every one or two years
• Every two years (compared to annually) maximizes benefits of screening & minimizing harms

Mandelblatt, *Annals IM, 2009*

Probability of False Positives

• Cohort study of 169,456 women who underwent first screening at age 40-59 and 4,492 women with incident invasive breast cancer
• After 10 years, over half of women will have at least one false positive recall and 7-9% will have false positive biopsy recommendation
  – Biennial screening decreases cumulative probability of false positives but may be associated with a small absolute increase in probability of late stage cancer diagnosis

  Hubbard, *Annals Int Med, 2011*
ACS Recommendations: Average Risk Women

- Begin mammography at age 40
- Clinical breast exam
  - At least every three years for women in their 20s and 30s
  - Annually for women age 40 and over
- Women should be informed about the benefits and limitations of breast self examination (BSE)
  - Prompt reporting of any breast symptoms
  - Technique may reviewed, but it is acceptable not to do it
- Women should become informed about benefits, limitations and potential harms of routine screening

The Debate Continues….

June 28, 2011: 133,000 women followed for 29 years.
Age 40-49 years: mammography every two years; 50-74 years: every three.
27% decrease in BC mortality. Total mortality not reported.
Newer Technologies

- Digital Mammography
- Breast MRI
- Ultrasound and Mammography

Digital mammography

- Higher sensitivity, same specificity in women < 50 years old
  - Sensitivity 82% versus 76% film
  - Specificity 88%
- Cancer detection rates overall similar between film and digital mammography
- Test characteristics better for women aged 40-49, dense breasts and estrogen receptor negative tumors

» Kerlikowske, Ann Intern Med, 2011
MRI Screening

- Does MRI have a role for screening in high risk women?
  - MRI is a very sensitive method of breast imaging and has been used as a diagnostic tool in women with breast cancer
  - Not influenced by breast density
  - Specificity is variable
  - Expensive

Sensitivity And Specificity Of Breast Cancer Screening Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>77%</td>
<td>95%</td>
</tr>
<tr>
<td>Mammography</td>
<td>36%</td>
<td>99.8%</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>33%</td>
<td>96%</td>
</tr>
<tr>
<td>Clinical Breast Exam</td>
<td>9%</td>
<td>99%</td>
</tr>
</tbody>
</table>
Mammography plus Ultrasound

- Screening ultrasound may detect small cancers not seen on mammography
- 2809 high risk women underwent mammography and ultrasound
- Mammography alone compared to mammography plus ultrasound
- Adding an ultrasound will find 1.1 to 7.2 more cancers per 1,000 but with a significant increase in false positives
  - Berg et al JAMA 2008

Mammography plus Annual Ultrasound or Single MRI

- 2,809 high risk women with dense breasts
  - Annual ultrasound and mammography for 3 years
  - 612 of 703 women who had MRI had complete data
- Adding MRI will find 14.7 more cancers per 1,000 but with many false positives
- Number of screens to detect one cancer
  - Mammography 127
  - Supplemental U/S 234
  - Adding MRI* 68
  - *After mammogram and ultrasound negative
  - Berg, JAMA 2011
Impact For Clinical Practice

- MRI may be useful in screening high risk women
- The effect of MRI screening on mortality is not known
- MRI is not currently recommended for screening average risk women
- Ultrasound adds little to mammography

Bottom line

- 40-49 informed consent
- 50-74 screen every 2 years
- 75+ informed consent - don’t if life expectancy less than 10 years
- Don’t promote SBE
- Digital mammography for women < 50
- BRCA equivalent: MRI
Ms. O. is a 52 year old woman whose best friend was recently diagnosed with ovarian cancer. She is concerned about ovarian cancer and wants “whatever test you can give her” for it. What do you recommend?
Ovarian Cancer: What Test?

- CA-125
- Transvaginal ultrasound
- CA-125 and transvaginal ultrasound
- None of these tests

Ovarian Cancer: Should We Screen?

- Lifetime risk of ovarian cancer
  - No affected relatives 1%
  - One affected relative 5%
  - 2 affected relatives 7%
  - Hereditary syndrome 40%

- Ovarian cancer limited to the ovaries is associated with a much higher survival rate
Ovarian Cancer: Screening Techniques

- Serum CA-125 assay
- Trans-vaginal ultrasound
- Serum CA-125 plus ultrasound

Prostate, Lung, Colorectal and Ovarian (PLCO) Trial 2011

- AIM: To determine whether annual screening with CA-125 and transvaginal sonography can reduce ovarian cancer mortality

PLCO

• 78,216 women aged 55-74 randomized to screening or usual care
• Annual CA 125 plus ultrasound
  – CA 125 >35 or abnormal sono was positive
• Follow-up of positive screens by patients’ physicians
• 12.4 years follow-up

**PLCO Results**

<table>
<thead>
<tr>
<th>Group</th>
<th>Screen</th>
<th>Control</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>39,105</td>
<td>39,111</td>
<td>--</td>
</tr>
<tr>
<td>OC diagnosis</td>
<td>212 (5.7)</td>
<td>176 (4.7)</td>
<td>1.2 (1.0-1.5)</td>
</tr>
<tr>
<td>Deaths</td>
<td>118 (3.1)</td>
<td>100 (2.6)</td>
<td>1.2 (0.8-1.7)</td>
</tr>
</tbody>
</table>

Ovarian Cancer (rate/10,000)
PLCO Results

- 3285 women with false positive screens
  - 1080 surgical follow-up
  - 163 serious surgical complications

**Conclusion:** “Annual screening for ovarian cancer…with simultaneous CA-125 and transvaginal ultrasound does not reduce disease-specific mortality in women at average risk for ovarian cancer but does increase medical procedures and associated harms.”

Primary Prevention of Ovarian Cancer

- Oral contraceptives
  - 37% risk reduction
- Pregnancy
- Breast feeding
Lung Cancer Screening

Question?

• Mr. Nico Teen is a 69 year old man with a 50 pack-year history of smoking and COPD. You have previously been unsuccessful in encouraging him to quit smoking. He comes in for a check-up, is worried about developing lung cancer and wants to know what test you think he should have. What do you recommend?
  – Chest X ray
  – Sputum cytology
  – Spiral CT
  – None of these tests
Lung Cancer Screening: Systematic Review of Chest X-rays

- 7 trials of lung cancer screening
- Frequent screening with chest x-rays was associated with an increase in mortality
  - RR 1.11 (95% C.I. 1.00-1.23)
- No difference in chest X-ray plus cytology versus chest X-ray alone

Manser, Thorax, 2003

Low Dose Spiral Computed Tomography

- Scans lung in < 20 seconds (single breath)
- No IV contrast
- More radiation exposure than CXR but less than conventional CT
- Can detect much smaller lesions than chest X-ray
The National Lung Screening Trial (NLST):

53,454 participants randomized to CT or CXR
- Current or former heavy smokers: ≥ 30 pack-years
- Ages 55 to 74
- Annual CT scans x 3 years. 6.5 years follow-up

20% reduction in lung cancer death; 7% reduction in all deaths!

<table>
<thead>
<tr>
<th></th>
<th>LDCT</th>
<th>CXR</th>
<th>RR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer Deaths</td>
<td>247</td>
<td>309</td>
<td>.80 (0.73-0.93)</td>
</tr>
<tr>
<td>Any death</td>
<td>1877</td>
<td>2000</td>
<td>.93 (0.86-0.98)</td>
</tr>
</tbody>
</table>

20% reduction in lung cancer death; 7% reduction in all deaths!

Balanced by…

- 75,000 CT scans
- 18,146 positive tests
- 17,066 false positive tests
- 673 thoracotomy / mediastinoscopy
- 303 broncoscopies
- 99 needle biopsies
- To prevent 62 deaths from lung cancer
Health Policy in Transition

- ~ 94 million current or former smokers in the U.S.
- ~ 7 million meet NLST criteria
- The only cancer screening trial with a statistically significant decrease in total mortality
- Expensive… $ $ $ 

Health Policy

- California Technology Assessment Forum assessed LDCT for lung cancer screening
- Panel voted that LDCT met criteria for screening high risk individuals (like those in NLST) at specialized centers

» CTAF, October, 2011
Health Policy: ACCP and ASCO 2012

• For smokers and former smokers aged 55-75 who have smoked for 30 pack-years or more and either continue to smoke or have quit within the past 15 years, annual screening with LDCT should be offered
  – Only in settings that can deliver the comprehensive care provided to NLST participants

Health Policy: ACCP and ASCO 2012

• For those who have accumulated fewer than 30 pack years of smoking or are younger than 55 or older than 74 or who quit smoking more than 15 years ago or who have severe comorbidities that would preclude potentially curative treatment, CT screening should not be performed
The NLST Setting

- 76% of sites were NCI designated cancer centers
- 82% were large academic medical centers
- All likely to have specialized thoracic radiologists and board certified thoracic surgeons on site
- CT scanners extensive quality control
- Nodule management algorithm but not mandated

Other organizations

- Stay tuned
- New recommendations will be forthcoming
Primary Prevention Of Lung Cancer

- Smoking cessation
- Smoking cessation
- Smoking cessation
- Smoking cessation
- Smoking cessation
- Smoking cessation
- Smoking cessation

Colorectal Cancer
Question?

- What do you most commonly recommend for colorectal cancer screening?
  - Fecal occult blood test (FOBT)
  - Sigmoidoscopy
  - Colonoscopy
  - Air contrast barium enema
  - Virtual Colonoscopy
  - Fecal DNA
  - Fecal immunochemical Test (FIT)

Colorectal Cancer: Evidence For Screening

- U.S. Men and Women: 3rd most common cancer and cause of death from cancer
- Screening with fecal occult blood test (FOBT) or sigmoidoscopy is associated with a reduction in CRC mortality
- Case-control study showed that colonoscopy was associated with fewer CRC deaths
  - Left sided CRC

Baxter, Annals IM, 2009
Sigmoidoscopy: New Evidence

- PLCO Trial
- 154,900 men and women aged 55-74 assigned to screening with FS with repeat at 3-5 years vs usual care
- 11.9 year follow up
- Reduced incidence of both proximal and distal CRC
- Reduced mortality in distal CRC (RR 0.50 (0.38-0.64) but not proximal CRC
  - Schoen et al NEJM 2012

Joint Guideline: ACS, ACR,…

- FOBT annually
- Fecal immunochemical test annually
- Flexible sigmoidoscopy every 5 years
- DCBE every 5 years
- CT colonography every 5 years
- Colonoscopy every 10 years
- Stool DNA testing (interval uncertain)

Levin, Gastroenterology, 2008
Joint Guideline Recommendation

• Clinicians should make patients aware of the full range of screening options
• Offer patients a choice between a screening test that is effective at both early cancer detection and cancer prevention through the detection and removal of polyps and a test that is primarily effective at cancer detection
• CRC prevention should be the primary goal of screening

Joint Guideline Recommendation

• Providers and patients should understand the limitations and requirements of noninvasive tests
  – Less likely to prevent cancer than the invasive tests
  – Must be repeated at regular intervals to be effective
  – If test is abnormal, invasive test (colonoscopy) will be needed
USPSTF Recommendation

• Screen with FOBT, sigmoidoscopy or colonoscopy in individuals aged 50-75
  – Risks and benefits of each method vary
• No routine screening for individuals age 76-85
• Do not screen individuals aged 85 and over
• Evidence is insufficient for CT colonography or fecal DNA

Newer Tests

• Virtual Colonoscopy
• Stool-based molecular testing
  – Fecal DNA
• Fecal immunochemical tests
**Computed Tomographic Colonography (Virtual Colonoscopy)**

- Non-invasive radiological technique
  - Radiation dose similar to barium enema
- Bowel preparation similar to colonoscopy
  - Prep-less technique is being evaluated
- Does not require sedation
- Colon distended with carbon dioxide or air
- Breath holding for 20-50 seconds
- Colonoscopy to remove polyps

**Laxative-Free CT Colonography**

- Low fiber diet, orally ingested contrast material and specialized processing software “electronic cleansing”
- 605 adults underwent CTC and OC
- CTC was more accurate in detecting adenomas 10 mm or larger and less so for smaller lesions
  - 91% sensitivity vs 70% for adenoma 8 mm or larger
- Patients preferred it

Potential Harms

- Radiation Exposure
  - 1/1000 could develop solid cancer or leukemia
- Procedure related harms
  - Perforation rate low
- Extra-colonic findings

Extra-colonic Findings

- Extra-colonic findings common: 27 – 69%
- “High” clinical significance require surgical or medical treatment or intervention or further investigation
  - 5 - 11%
- 7-16% of individuals need additional evaluation for extra-colonic findings, but very few abnormalities ultimately required definitive treatment
Fecal DNA Testing

• PCR test for DNA mutations in the stool

• Potential advantages
  – Non-invasive
  – No preparation
  – Detection along entire length of the colon

Fecal DNA Testing

• Screening test in multi-center study
• Fecal DNA test (23 mutations), FOBT, and colonoscopy
• 4482 average risk adults
• Fecal DNA detects more neoplasms than FOBT, but with more false positive results
• Expensive: $400 to $800 versus $3 to $40 for FOBT

Ahlquist, 2008
**Fecal Immunochemical Testing (FIT)**

- Uses labeled antibodies that attach to antigens of any human globin present in the stool
- Globin does not survive passage of the upper GI tract
- No dietary restrictions (easier than FOBT)

**Fecal Immunochemical Testing**

- FIT is more sensitive in detecting CRC and large adenomas (>1 cm) than FOBT
- FIT is a little less specific than FOBT
How Are We Doing?

- National Health Interview Survey
  - 62.9% of adults aged 50-75 up to date based on USPSTF recommendations
- Rates are increasing but very slowly

Colorectal Cancer Screening: Conclusions

- Any screening is better than no screening for reducing colorectal cancer mortality
- Increase awareness of the importance of colorectal cancer screening
- Virtual colonoscopy and fecal DNA testing are included as options in the new joint guidelines but not in USPSTF guidelines
Summary Of Recommendations

- Women aged 50 to 74 should undergo mammography every 2 years
- Screening decisions for women in their forties and for women and for women aged 75 and older should be individualized
- MRI screening for breast cancer may be useful in high risk women
- All men and women aged 50 -75 should be screened for colorectal cancer
  - Any screening is better than no screening

Summary Of Recommendations

- Screening for ovarian cancer is harmful
  - No reduction in ovarian cancer mortality
  - False positives with surgery and complications
- Screening for lung cancer with low-dose CT reduces mortality
  - Policy recommendations are still pending
Thank you!

Questions?
Cervical Cancer Prevention Update: 2013 and Beyond

George F. Sawaya, MD
Professor
Department of Obstetrics, Gynecology and Reproductive Sciences
Department of Epidemiology and Biostatistics
University of California, San Francisco
Director, Cervical Dysplasia Clinic, San Francisco General Hospital

I have no financial interests in any product I will discuss today.
Objectives

• To understand the latest cervical cancer screening guidelines (updated in 2012)
• To understand areas of existing controversy
• To understand the current role of the bimanual pelvic examination in the context of less-than-annual screening

Background

• ~12,000 cervical cancer cases and 4,200 deaths per year in the US (ACS, 2010)
• ~50-60% of cases occur in never- and poorly-screened women
• ~80 million women at risk in the US
• Most effective approach: screen unscreened and poorly-screened women

*Obstet Gynecol 94:307-10

Incidence Rates by Race

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>8.1 per 100,000 women</td>
</tr>
<tr>
<td>White</td>
<td>7.9 per 100,000 women</td>
</tr>
<tr>
<td>Black</td>
<td>10.1 per 100,000 women</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>7.5 per 100,000 women</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>7.7 per 100,000 women</td>
</tr>
<tr>
<td>Hispanic</td>
<td>12.0 per 100,000 women</td>
</tr>
</tbody>
</table>


From virus to cancer

Schiffman and Wright *NEJM* 2003;348(6):489-490
Cytology Primer

- ASC-US: atypical squamous cells of undetermined significance
- LSIL: low-grade squamous intraepithelial lesion
- HSIL: high-grade squamous intraepithelial lesion
- AGC: atypical glandular cells of undetermined significance (AGUS)

Histology Primer

Cervical intraepithelial neoplasia (CIN)
Graded based on proportion of epithelium involved

- CIN 1: indicates active HPV infection; treatment discouraged since spontaneous resolution is high
- CIN 2: most are treated, but about 40% resolve over a 6-month period; treatment may be deferred in young women
- CIN 3: proximal cancer precursor
US recommendations: the big 3


Guidelines do not apply to immunocompromised women (HIV+), those with in utero DES exposure and those with prior CIN 2 or 3 or cancer.

Evidence Review

Evidence Synthesis
Number 86

Screening for Cervical Cancer: A Systematic Evidence Review for the U.S. Preventive Services Task Force

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Guither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. HHS-290-2007-10057-I, Task Order No. 3

Prepared by:
Oregon Evidence-based Practice Center
Portland, Oregon

Evidence Based Practice Center: Evidence Report, May 2011

- Liquid-based and conventional cytology do not differ.
- HPV testing finds more precancerous lesions but has unclear effects on cancer and on harms (e.g., additional colposcopies).
- HPV positivity incurs short-term adverse psychological effects.
- Women with negative HPV tests and normal cytology may be at particularly low risk.


Age to Begin Screening

- ACOG (2012): same as ACS/ASCCP/ASCP

- ACS/ASCCP/ASCP (2012): begin at age 21 (“no screening” under age 21)

- USPSTF (2012): begin at age 21 “regardless of sexual history”, “D” recommendation (don’t screen under age 21)

All agree: do not screen before age 21 years
Age to Begin Screening: Rationale

- Most dysplastic lesions low-grade and transient
- Long progression time of preinvasive lesions to invasive cancer
- Potential adverse effects of treatment (e.g., LEEP, cone biopsy) on pregnancy

Potential adverse effects of LEEP

- Preterm delivery: 70% increase
- Low birth weight: 82% increase
- Preterm premature: 169% increase
- ROM

*Lancet* 2006 367:489-98

Potential severe adverse effects of cone biopsy (not LEEP or cryotherapy)

- Perinatal mortality: 187% increase
- Severe preterm delivery: 178% increase
- Extreme low birthweight: 186% increase

*BMJ* 2008 Sep 18;337

No randomized trials; evidence inconsistent.
Screening frequency: ages 21-29

- **ACOG (2012):** same as ACS/ASCCP/ASCP
- **ACS/ASCCP/ASCP (2012):** cytology every 3 years
- **USPSTF (2012):** cytology every 3 years (“A”)

All agree: *no annual screening*
ACS/ASCCP/ASCP: “Women of any age should not be screened annually by any screening method.”

All agree: *no HPV testing for primary screening*
USPSTF: “D” recommendation women under 30

Screening frequency: ages 30-65

- **ACOG (2012):** same as ACS/ASCCP/ASCP
- **ACS/ASCCP/ASCP (2012):** screen every 3 years with cytology alone or every 5 years with cytology plus HPV testing (*preferred’ strategy, but a ‘weak’ recommendation*)
- **USPSTF (2012):** screen every 3 years with cytology alone or every 5 years with cytology plus HPV testing (*but only for ‘women who want to lengthen the screening interval’*)
Do you perform co-testing (HPV plus cytology) for screening women aged 30-65?

1. Yes
2. No

Which statements are true about co-testing (HPV plus cytology)?

1. Only should be performed in women over age 30 years.
2. If HPV+/cytology normal, may either repeat both tests in 12 months OR perform type-specific HPV testing (16/18).
3. It is the “preferred” screening strategy for women aged 30-65 years by ACS and ACOG, but not by the USPSTF.
4. All of the above
USPSTF Conclusion: Co-testing

“Although there is evidence of harms of strategies that incorporate HPV testing in women age 30 to 65 years, the USPSTF concludes that there is adequate evidence that the longer screening interval for HPV testing with cytology reduces the magnitude of these harms by decreasing the opportunity for false-positive test results.”

Modeling

<table>
<thead>
<tr>
<th></th>
<th>False positives</th>
<th>Colposcopies</th>
<th>CIN 2-3</th>
<th>Cancers</th>
<th>Cancer deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology q3 years, ages 21-65</td>
<td>350</td>
<td>758</td>
<td>80</td>
<td>8.5</td>
<td>1.55</td>
</tr>
<tr>
<td>Cytology q3 years until age 30 then co-testing q5 years</td>
<td>281</td>
<td>625</td>
<td>85</td>
<td>7.1</td>
<td>1.29</td>
</tr>
</tbody>
</table>

Per 1000 women screened over a lifetime.
NB: Women with normal cytology and persistent HPV+ were returned to routine screening if colposcopy was normal.

“Modeling studies support similar benefits of co-testing every 5 years and cytology every 3 years, demonstrating small differences in expected cancer cases and cancer deaths.”
Current controversy

Should co-testing (HPV plus cytology) be preferred over cytology alone?

Are cervical cancer screening strategies “preference-sensitive”?

HR HPV DNA testing

- **Hybrid Capture 2:** tests for one or more of 13 oncogenic HPV types; the low-risk probe has no clinical utility

- **Cervista:** tests for one or more of 14 oncogenic HPV types; type-specific testing available (16, 18)

- **Cobas HPV test:** tests for one or more of 14 oncogenic HPV types; type-specific testing available (16, 18)
**USPSTF: Co-testing caveat #1**

- “The percentage of U.S. women undergoing co-testing who will have a normal cytology test result and a positive HPV test result (and who will therefore require additional testing) ranges from 11% among women age 30 to 34 years to 2.6% among women age 60 to 65 years.”

**USPSTF: Co-testing caveat #2**

- “Women choosing co-testing … should be aware that positive screening results are more likely with HPV-based strategies… and that some women may require prolonged surveillance with additional frequent testing if they have persistently positive HPV results.”
What to do with women who are HPV positive but have normal cytology?

Recommendations by ACS/ASCCP/ASCP and ACOG (2012)

Option 1:
Repeat HPV testing and cytology at 12 months.
If still HPV+ or LSIL+, perform colposcopy.
If both are normal (or ASC-US/HPV-), repeat co-testing in 5 years.

Option 2:
Perform HPV 16/18 testing.
If positive, perform colposcopy.
If negative, repeat HPV testing and cytology at 12 months.

Note: the 12-month risk of CIN 3 in this group is ~2.5%

ACOG Practice Bulletin Number 131, November 2012
Managing ASC-US: a change

- If ASC-US/HPV positive, perform colposcopy (no change)
- If ASC-US/HPV negative, *return to routine screening*:
  - for women aged 21-29 years or those of any age screened with cytology alone, *rescreen in 3 years*
  - for women aged 30-65 years screened with both cytology and HPV, *rescreen in 5 years*

Age to End Screening

- **ACOG (2012):** same as ACS/ASCCP/ASCP
- **ACS/ASCCP/ASCP (2012):** end at age 65 in those with adequate negative prior screening (see next slide)
  Once ended, do not resume screening in women who have new partners.
- **USPSTF (2012):** end at age 65 in those with adequate negative prior screening
What is “adequate prior screening”?

3 consecutive negative cytology results
or
2 consecutive negative co-tests

within the 10 years before ceasing screening, with the most recent test occurring within the past 5 years

USPSTF: Co-testing caveat #3

• “Because HPV test results may be positive among women who would otherwise be advised to end screening at age 65 years on the basis of previously normal cytology results alone, the likelihood of continued testing may increase with HPV testing.”
Screening after total hysterectomy

• ACOG, ACS and USPSTF: all agree that screening following total hysterectomy with removal of the cervix for benign disease is not indicated. USPSTF: “D” recommendation

• ACOG (2012): If history of CIN 2+ in the past 20 years or cancer ever, continued routine screening (cytology alone every 3 years) for 20 years “seems reasonable” (Level B evidence).

ACOG: focus on other important issues in women’s health

  immunizations
  smoking cessation
  breast disease (CBE)
  depression screening
  violence screening
    STI screening
  family planning
  wellness

Chelmow et al Obstet Gynecol 2012;119:695-9
ACOG: bimanual pelvic examinations

• “No evidence supports the routine internal examination of the healthy, asymptomatic patient before age 21 years…”
• “No evidence supports or refutes the annual pelvic examination or speculum and bimanual examination for the asymptomatic, low-risk patient.” but
• “Annual pelvic examination of patients 21 years of age or older is recommended by the College.”
• Recommendation based on expert opinion

ACOG Committee Opinion No. 534 August 2012

Do you perform bimanual pelvic exams in asymptomatic women?

1. Yes
2. No
Routine exams

“The decision to perform an internal pelvic examination, breast examination, or both should be made by the physician and the patient after shared communication and decision making.”

“Concerns, such as individual risk factors, patient expectations, or medical–legal concerns may influence the decision to perform an internal pelvic examination or clinical breast examination.”

ACOG Committee Opinion No. 534 August 2012

After removal of the uterus and ovaries in asymptomatic, low-risk* women

“The decision to receive an internal examination can be left to the patient…”

“Annual examination of the external genitalia should continue.”

*no history of VIN, CIN 2+, immunocompromise and in utero DES exposure

ACOG Committee Opinion No. 534 August 2012
CDC- Advisory Committee on Immunization Practices (ACIP) Recommendations (May 2010): Females

- routine vaccination of females aged 11 or 12 with 3 doses of either HPV2 (Cervarix) or HPV4 (Gardasil)
- second dose administered 1 to 2 months after the first dose; third dose administered 6 months after the first dose
- vaccination recommended for females aged 13 through 26 years who have not been vaccinated previously
- ideally, vaccine should be administered before potential exposure to HPV through sexual contact
- avoid in pregnancy

Source: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5920a4.htm?s_cid=mm5920a4_e

HPV4 (Gardasil) phase 3 trial outcomes: CIN3+ among all women enrolled

Munoz et al JNCI 2010
Summary

• No cytology screening prior to age 21
• Annual cytology not recommended for most women
• Annual screening is recommended for high-risk women: immunocompromised (HIV+), in utero DES exposure and prior CIN grade 2 or 3 and cancer
• Annual screening recommended “for at least 20 years” in those with prior CIN grade 2 or 3 (ACOG, ASC)
• Co-testing (HPV plus cytology) every 5 years may be equivalent to cytology every 3 years for women aged 30-65 years

Summary

• CDC: HPV vaccine advised for females ages 11-26
• All agree: screen HPV vaccinated women same as others

• Women aged 30-65 who are resistant to screening every 5 years are poor candidates for co-testing (HPV plus cytology)

• Screening with (conventional) cytology alone (without HPV testing) every 3 years is still a great option (and perhaps the least complicated)
Which statements are true about co-testing (HPV plus cytology)?

1. Co-testing should only be performed in women over age 30 years.
2. If HPV+/cytology normal, may either repeat both tests in 12 months OR perform type-specific HPV testing (16 or 16/18).
3. Co-testing is the “preferred” screening strategy for women aged 30-65 years by ACS and ACOG, but not by the USPSTF.
4. All of the above
Vaccinations for Adult and Adolescent Women

Katherine Julian, MD
Professor of Clinical Medicine, UCSF
December 6, 2012

No Conflicts of Interest
Vaccines Generally Available in the U.S.

- Tetanus
- Diphtheria
- Pertussis
- Measles
- Mumps
- Rubella
- Varicella
- Meningococcus
- Pneumococcus
- Human Papillomavirus
- Influenza

- Hepatitis B
- Hepatitis A
- Haemophilus influenzae type B
- Rotovirus
- Inactivated polio
- Rabies
- Typhoid
- Yellow fever
- Japanese encephalitis
Vaccines for Special Populations

- Plague
- Tularemia
- Smallpox
- Anthrax
- Botulism
- Tuberculosis – BCG
- Adenovirus

Key Website

Centers for Disease Control and Prevention

http://www.cdc.gov/vaccines
Case I

- 45 yo woman here for regular visit. PMH: Healthy
- SH: smoker  Vaccine history: “all the regular vaccines as a child”, but last vaccine was given “as a teen”. What vaccines should be given now?

1) Td
2) Tdap
3) Pneumovax
4) #1 and #3
5) #2 and #3
Pertussis...Not Just for Kids

- Annual cases of pertussis have increased
  - 66-500 cases/100,000 persons each year
- Post-tussive emesis and inspiratory “whoop”= increased LR of pertussis
- Residual immunity from prior vaccination may modify the clinical presentation
  - Among adults, prolonged cough may be the only manifestation of pertussis
  - 13-32% of adolescents/adults with cough >6 days have serologic evidence of infection with pertussis

Hewlett EL et al. NEJM, 2005;35:12
Cornia PB, et al. JAMA, 2010;304(8)

- Adults may act as reservoirs of the disease to vulnerable populations
  - Since 2004, approx 20 deaths/year with majority in infants <2 months
  - Highly contagious to home contacts
- Immunity for pertussis wanes in adults after childhood vaccination

Hewlett EL et al. NEJM, 2005;35:12
Pertussis Vaccine

- In 1980’s, acellular vaccine created
  - Contains purified, detoxified pertussis antigens
- Childhood DTaP: diphtheria toxoid, tetanus toxoid, and acellular pertussis (full dose)
- Adult/adolescent Td and Tdap: tetanus toxoid (full dose) and reduced dose diphtheria toxoid +/- reduced dose acellular pertussis antigens
- Adacel: age 11-64
- Boostrix: ≥10 years

Pertussis Vaccine – How Effective?

- 2781 subjects aged 15-65 randomized to reduced dose of acellular pertussis vaccine or hepatitis A placebo
- Followed for 2.5 years
- Based on primary pertussis definition (cough and positive culture/PCR), vaccine 92% effective

Ward JL et al. NEJM, 2005;353(13)
Tdap Recommendations

• Adults ≥19 years: Tdap regardless of interval since last tetanus (if never had Tdap)
• Children 11-18 single Tdap if completion of primary series
• Contraindication: encephalopathy without a known cause < 7 days after previous pertussis vaccination, Guillain-Barré syndrome < 6 weeks after previous tetanus vaccine.

Tdap Recommendations

• Other
  • Recommended for all >65 yo
    • Does not depend on contact with young children
  • Both Adacel and Boostrix appear to be immunogenic
    • If a choice, give Boostrix for now
Tdap Recommendations

- If pregnant woman
  - Administer Tdap during pregnancy, preferably during the third or late second trimester (after 20 weeks’ gestation)
  - If not administered during pregnancy, Tdap should be administered immediately postpartum
  - Studies underway to look at timing of vaccination in pregnancy (2nd vs. 3rd trimester)

Tdap Recommendations

- Recommended for healthcare workers with patient contact
- No current recommendations for Tdap booster
  - Give once – then back to Td
  - Look for more on this soon...
Pneumococcus - Background

- Colonizes the upper respiratory tract
  - Gram + diplococcus, polysaccharide capsule
  - Over 90 serotypes
  - U.S. annual incidence of pneumococcal bacteremia is 15-30 cases/100,000
  - Causes 40,000 deaths annually in the U.S.
- Mainly transmitted by direct contact with respiratory secretions (ex: household)

Pneumococcus - Background

- Risk factors for invasive disease
  - Age >65 or <2 years
  - People with chronic illness, immunocompromised
  - Crowding, PPI’s
  - Antecedent respiratory infection and recent Abx
  - Smokers
Pneumovax – 2 Vaccine Types

- **Polysaccharide**
  - Purified capsular polysaccharide antigens of *S. pneumoniae*
  - Induce antibodies by T-cell independent mechanisms
    - T-cells=immunogenic memory
    - Shorter Ab duration
- **Conjugate**
  - Conjugates the bacterial capsular polysaccharide to a carrier protein
  - Involves T-cell immunity
  - Longer Ab duration

Pneumovax Polysaccharide

- Adult vaccine=23 purified capsular polysaccharide antigens of *S. pneumoniae* (PPSV23)
  - Represent at least 85-90% of the serotypes that cause invasive pneumococcal infections
  - Shorter Ab duration
- Good evidence it decreases pneumococcal bacteremia
  - Retrospective cohort 47K people >65 yrs; HR 0.56
  - Likely no effect on PNA

Pneumovax Conjugate Vaccine

- 13-valent vaccine pneumococcal conjugate vaccine (PCV13)
- 7-valent vaccine used in children 2000-2007
  - Decreased invasive pneumococcal disease (IPD) in children AND adults
  - Little change in IPD in pts with HIV
    - 2010: 50% of IPD in HIV pts were from serotypes in the PCV13 vaccine
- What about using PCV13 in immunocompromised adults (instead of PPSV23)?

ACIP. MMWR, 2012;61(40).

Pneumovax Polysaccharide vs. Conjugate vaccine

- FDA data comparing PPSV23 vs. PCV13
  - Ab titers for PCV13 equal or higher in adults 60-64 yrs
  - Adults 50-59yrs given PPSV23 first had lower antibody titers when given PCV13 booster compared to those given PCV13 for 2 doses
- Similar result for PPSV23 vs. PCV7 in HIV+ patients

ACIP. MMWR, 2012; 61(40).
Pneumovax Polysaccharide Vaccine- Recommendations

- Age >65
- Immunocompetent people ≥ 2 years old** with chronic illness
  - Chronic cardiovascular disease
  - Chronic pulmonary disease including ASTHMA
  - Chronic liver disease, ETOH
  - Diabetes
  - Smokers
- People aged 2-64 living in environments in which the risk for invasive pneumococcal disease is increased (no longer American Indians or Alaskan natives)

Pneumovax Conjugate Vaccine (PCV13)- Recommendations

- Give instead of polysaccharide vaccine
- Age >19 AND
  - Immunocompromising conditions
    - HIV, Chronic renal failure, nephrotic syndrome, malignancy, transplant
    - Functional or anatomic asplenia
    - CSF leaks
    - Cochlear implants
Pneumovax Boosters – More Complicated...

- No history of pneumovax
  - If indication for PCV13: give PCV13 first and then PPSV23 booster 8 weeks later
  - Then give PPSV23 booster 5 years later
- Previous vaccination with PPSV23 AND indication for PCV13:
  - Give PCV13 dose at least 1 year after previous pneumovax
- People >65 years with chronic illness should get PPSV23 booster 5 years after first vaccine dose (if first dose was given before they were 65).

Pneumovax...Future Changes?

- 13-valent conjugate vaccine in all adults?
  - **Prevnar 13 approved by the FDA Dec 2011** (for adults ≥50 years) but not yet recommended by ACIP aside from immunocompromised
  - Functional antibody responses higher than for polysaccharide vaccine
  - Need data on clinical efficacy against S. Pneumo PNA
  - May be more cost-effective depending on effectiveness

Smith KJ et al. JAMA, 2012;307(8)
Case I

- 45 yo woman here for regular visit. PMH: Healthy
- SH: smoker  Vaccine history: “all the regular vaccines as a child”, but last vaccine was given “as a teen”. What vaccines should be given now?
- 1) Td
- 2) Tdap
- 3) Pneumovax
- 4) #1 and #3
- 5) #2 and #3

Bonus Question to Case I

- What type of pneumovax should she have?
  1) Polysaccharide vaccine?
  2) Conjugate vaccine?
Case 2
63 yo woman
PMH: htn, DM
Meds: HCTZ, metformin
SH: Married, non-smoker

What vaccine(s) does she need?
1) Hepatitis B
2) Varicella (zoster)
3) Seasonal Influenza
4) #2 and #3
5) All of the above

Varicella - Background
• After primary VZV infection (chickenpox), latent infection is established in the sensory-nerve ganglion
  • Decline in cell-mediated immunity with age predisposes to zoster
• Zoster develops in 30% of people over a lifetime
• Post-herpetic neuralgia 13-40%; directly correlated with age

Zoster Vaccine

- Originally licensed as the “chickenpox vaccine”
  - Live attenuated virus vaccine
  - Older adults need higher titer of live attenuated virus to produce a durable increase in cell-mediated immunity
  - Zoster vaccine contains more plaque-forming units/dose than the chickenpox vaccine
  - Vaccine “boosts” older adults’ waning immunity to prevent reactivation of varicella

Varicella Zoster Vaccine...The Evidence

- Randomized, double-blind, placebo-controlled trial of 38,546 adults ≥ 60 yrs
  - Zoster vaccine vs. placebo
  - Primary endpoint: “burden of illness” due to zoster
    - Incidence, severity of pain, duration of pain
  - Secondary endpoint: incidence of post-herpetic neuralgia (pain >120 days)

Oxman MN et al. NEJM, 2005;352(22)
**Varicella Zoster Vaccine...The Evidence**

- **Results:** followed median 3.12 years
  - Incidence of zoster reduced by 51.3%
  - Incidence of post herpetic neuralgia decreased by 66.5%
  - Burden of illness due to zoster decreased by 61.1%
  - Higher efficacy ages 60-70
- **Newer study shows efficacious in 75K community dwellers 6.4/1000 person-years vs. 13/1000 (HR 0.45)**

Oxman MN et al. NEJM, 2005;352(22)
Tseng HF et al. JAMA, 2011;305(2)

**Varicella Zoster Vaccine**

- **Licensed in March 2011 for adults ≥ 50 years**
  - Study presented at IDSA meeting
    - 22K adults 50-59 years followed 1 year
    - Zostavax vs. placebo decreased risk of zoster by 69.8% (CI 54.1-80.6)
- **ACIP:** recommended for >60 years due to vaccine production shortages
- **No need to determine if immune to chickenpox**
Varicella Zoster Vaccine - Contraindications

- h/o anaphylaxis to gelatin, neomycin
- Immunodeficiency or immunosuppressive therapy
  - OK if healthy HIV patient with CD4>200
- Pregnant women (for varicella vaccine)
- Pts with active (untreated) TB

Varicella Zoster Vaccine

- Frozen for storage, administered immediately after reconstitution
- Cost of vaccine approx $150
- Not recommended to give pneumovax at the same time
- Cost per quality-adjusted life-year ranges from $14,877 to $34,852.
  - Vaccinate 17 people to prevent 1 case of zoster
    - Cost $3,330 for each case of zoster prevented
  - Vaccinate 31 to prevent 1 case of postherpetic neuralgia
    - Cost $6,405 for each case of postherpetic neuralgia

Kimberlin DW. NEJM, 2007;356
Varicella Zoster Vaccine

- Remaining questions
  - What happens in the future with childhood varicella vaccine?
  - What is the efficacy of the vaccine in people who have had zoster?
- New evidence Olmstead County of 1669 people with h/o zoster showing risk for recurrent zoster ~1/160


Seasonal Influenza Vaccine

- Types of vaccines
  - Trivalent inactivated influenza vaccine (TIV)
    - “Regular”
    - High-dose
    - Intradermal
  - Live attenuated influenza vaccine (LAIV) – FluMist
    - “Regular” trivalent
    - Quadrivalent approved 2/12
**Influenza Vaccine Strains for 2012-2013 Flu Season**

- Trivalent—2 A strains and 1 B strain
  - A/California/7/2009 (H1N1-like)
  - A/Victoria/361/2011 (H3N2-like)
  - B/Wisconsin/1/2010-like (Yamagata lineage)

**Seasonal Influenza Vaccine**

- Trivalent inactivated influenza vaccine (TIV)
  - Given IM
  - Approved for all ≥ 6 months
- Live attenuated influenza vaccine (LAIV) - FluMist
  - Same strains as TIV
  - Intra-nasal vaccine; cold-adapted, temp sensitive
  - Runny nose, congestion, HA, wheezing
  - Approved in the U.S. for healthy 2-49 year-olds
High Dose TIV Vaccine

- 12/09 FDA licensed Fluzone High-Dose for ≥65 yrs
  - Contains 60µg of hemagglutinin per strain virus vs. 15 µg in regular TIV
  - May enhance immune response compared to standard dose (phase 3 trials)
  - More local reactions
  - No trials yet of prevention of influenza...wait for later 2012...

Intradermal Influenza Vaccine

- Fluzone intradermal vaccine approved by FDA in May 2011
- Developed in hopes of conserving vaccine supply
- Needle is about one-tenth of standard length
- Contains 9 mcg hemagglutinin per strain versus standard 15 mcg
  - Dose is 0.1 mL versus standard 0.5 mL
- Approved ages 18 – 64 years
- Local reactions are more common
Seasonal Influenza Vaccine...  

The Evidence

- In children, several studies suggest better efficacy of LAIV compared to TIV
- In adults, studies suggest better efficacy of TIV
  - RCT of 1952 healthy adults age 18-49 during 2007-2008 flu season
  - Absolute efficacy of the inactivated vaccine to prevent influenza A was 73% (positive = culture)
  - Absolute efficacy of the live vaccine was 51%
    - Too few cases to determine efficacy of influenza B


Seasonal Influenza Vaccine

Indications

- All people older than 6 months
  - Unless there is a contraindication...
Who Should NOT Get the Live Attenuated Influenza Vaccine?

- Outside recommended age ranges (<2yrs or >49yrs)
- Chronic medical conditions including asthma
- Pregnant women
- History of Guillain-Barré
- Egg allergy (only hives): give TIV
- Anaphylaxis to eggs: refer to allergist
- Highly immunosuppressed
  - Contact with highly immunosuppressed

Coming Soon...

- LAIV Quadrivalent vaccine
  - Approved 2/12
- This year, trivalent vaccine:
  - A/California/7/2009 (H1N1-like)
  - A/Victoria/361/2011 (H3N2-like)
  - B/Wisconsin/1/2010-like (Yamagata lineage)
- Quadrivalent can include both B lineages
- Expected 2013-2014 season
- Inactivated quadrivalent vaccines in development
Hepatitis B Vaccine

• Since 1996, 29 outbreaks of HBV infection in long-term care facilities
  • 25 involved adults with DM receiving assisted blood glucose monitoring
  • Diabetics 23-59 yrs without hep B risk factors 2.1x odds of developing hep B compared to non-diabetics
• 10/11 ACIP recommended all unvaccinated adults 19-59 yrs with DM be vaccinated for hep B (rec category A)
• Unvaccinated adults >60 with DM may be vaccinated at discretion of treating clinician

Hepatitis B Vaccine

• 3 doses: 0, 1, 6 months
• Less protective immunogenic response with age
• Post-vaccination serologic testing recommended 1-2 months after last injection for:
  • Healthcare workers (at high exposure risk)
  • Patients on hemodialysis
  • HIV/immunocompromised
  • Others at high risk of exposure
  • If not immune...re-vaccinate

Estimated cost per QALY saved was $75,100 for persons aged 20-59 yrs but increases with age
Case 2

63 yo woman
PMH: htn, DM
Meds: HCTZ, metformin
SH: Married, non-smoker

What vaccine(s) does she need?
1) Hepatitis B
2) Varicella (zoster)
3) Seasonal Influenza
4) #2 and #3
5) All of the above

Case 3

17 yo young woman getting ready to go to college and is seeing you for a routine physical. She has not had a vaccine since age 9 (when she had a tetanus shot).
What (if any) vaccines does she need?

1) No vaccines are needed at this time
2) HPV vaccine
3) Meningococcal vaccine
4) Both 2 and 3
Human Papillomavirus (HPV)

Background
- 20 million people currently infected with HPV
- 6.2 million new cases each year
  - Most HPV infections self-limited
  - Lifetime cervical cancer risk 3.6%

Human Papillomavirus (HPV)

Vaccine
- Quadrivalent viral protein vaccine (Gardisil)
  - Contains major capsid protein L1 from types 6, 11 and 16, 18
- Bivalent vaccine (Cevanix) contains proteins from types 16 and 18
- Efficacy nearly 100% in preventing infection of the virus types included in the vaccine

Koutsky LA et al. NEJM, 2002;347(21)
HPV Vaccine Recommendations

- IM in a 3-dose schedule (0, 1-2, 6 months)
- Little effect on HPV infections present prior to vaccination
- Approved for girls as young as 9; focus on 11-12 yo
  - Catch-up vaccination for 13-26 yo if not previously vaccinated
  - h/o HPV NOT a contraindication to vaccination
- SE: low-grade fever, local reactions, fainting
  - Contraindicated in anyone with hypersensitivity to yeast or to the vaccine

HPV Vaccine in Boys/Men...

- HPV4 recommended for males 13-21 years who have not been vaccinated
- Males 22-26 may be vaccinated
- MSM recommended to be vaccinated through age 26 yrs
HPV Vaccine in Boys/Men

- HPV4 approved 2010 for prevention of anal cancer ages 9 – 26
  - 602 MSM
  - Gardasil was 50% effective (ITT) vs. 78% effective (per protocol) in preventing HPV 16 and 18 related anal intraepithelial neoplasia
- HPV4 decreases external anal/genital lesions
  - 4065 males aged 16-26 yrs RCT, f/u 2.9 yrs
  - ITT: 60.2% efficacious
  - Per-protocol (n=2805): efficacy 90.4%

NEJM, 2011;365
NEJM, 2011;364:401-411

HPV Vaccine Questions

- What about women> 26 yrs?
  - 3817 women aged 24-45 yrs, randomized, placebo-controlled, double-blind study
  - No h/o genital warts or cervical disease
  - Quadrivalent vaccine vs. placebo – 3 doses
    - Outcome=disease/infection related to HPV 6, 11, 16, 18
    - Per protocol efficacy 90.5%
    - ITT efficacy: 30.9%

HPV Vaccine Questions

- Will non-vaccine viral strains emerge?
- What is the durability of the immunity?

Meningococcus Background

- Approximately 10% of adults carry N meningitidis in the nasopharynx
- Rates of invasive disease 0.8-1.3 cases/100,000
- Case fatality rates range 3-10%
- 13 serogroups of meningococci
  - A: rare in U.S.
  - B, C, Y: each cause approx 30% of meningococcal disease in the U.S.
Meningococcal Vaccine

- Tetravalent polysaccharide vaccine (MPSV4) - Menomune
  - Contains polysaccharide antigens to capsular serogroups A, C, Y, W-135
  - Stimulate a B cell immune response
    - Antibody response is short-lived (1-5 yrs)
    - Not effective in age < 2; FDA approved for ages 2-10 and >55
  - Does NOT protect against serogroup B, which is the most prevalent in U.S.

Meningococcal Conjugate Vaccine

- Tetravalent polysaccharide conjugate vaccine (MCV4) – Menactra and Menveo
  - Conjugates the bacterial capsular polysaccharide to a carrier protein (diptheria toxoid)
    - Results in a T cell dependent immune response—longer Ab titers
  - Contains antigens to serogroups A, C, Y, W-135 (NOT B)
  - Menveo produced a statistically higher seroresponse than Menactra for serogroups A, W, and Y
    - Clinical relevance is unknown
  - **Now approved 9 months-55 years**
Meningococcal Vaccine Recommendations

- Give conjugate to 11 to 12 year-olds with booster at age 16 years (if given ages 13-15---booster age 16-18)
  - If vaccine at/after age 16, no booster needed
- Vaccinate those at increased risk
  - College freshman living in dorms
  - Military recruits
  - Travelers to areas with hyperendemic disease
  - Microbiologists
- Cost effectiveness better for 2-dose series

Meningococcal Vaccine Recommendations

- For those with asplenia or immunodeficiencies (>9 months old)
  - 2-dose primary series 2 months apart
  - Booster dose
  - 5 years after primary series if primary series given ≥ 7 years of age
Case 3

17 yo young woman getting ready to go to college and is seeing you for a routine physical. She has not had a vaccine since age 9 (when she had a tetanus shot). What (if any) vaccines does she need?

1) No vaccines are needed at this time
2) HPV vaccine
3) Meningococcal vaccine
4) Both 2 and 3

Take Home Points...

- Don’t forget Tdap boosters ages 11+
- Pneumococcus vaccine ≥ 65, people with asthma, chronic illness, and smokers
- Pneumococcus conjugate vaccine immunocompromised, asplenic, cochlear implants
- Zoster vaccine ages ≥60 (licensed for ≥50)
- Influenza vaccine everyone
- HPV vaccine ages boys/girls 9-26; continue pap smears
- Meningococcal conjugate vaccine ages 11-55
- http://www.cdc.gov/vaccines
Mental Health and Women’s Health

Ellen Haller, M.D.
UCSF Department of Psychiatry

Disclosure information

I have nothing to disclose.
Learning Objectives

- Know what to do when a pt c/o PMS/PMDD
- Gain knowledge about depression in women
- Be able to review risks/benefits of antidepressants during pregnancy
- Learn about post-partum mental health
**Premenstrual Syndrome**

Braverman 2007

- PMS described for centuries & across cultures; term first used in 1950s
- 30-80% of women have some PMS symptoms during some of their ~400 menstrual cycles
- More significant PMS symptoms in ~30%

**Premenstrual Dysphoric Disorder (PMDD)**

Bailey, Cohen 1999; Di Giulio, Reissing 2006

- 3-8% of women
- Starts in 20s; worsens over time
- Approx 40% of pts seeking PMDD tx actually have premenstrual exacerbation of underlying mood d/o
- PMDD DSM dx criteria in syllabus
  - Currently in DSM Appendix and coded as “Dep NOS”
  - DSM-V coming in May, 2013
  - PMDD will be separate dx in Mood d/o section
**Daily Symptom Diary**

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<th>2</th>
<th>3</th>
<th>4</th>
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**Days of period**

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</table>

**Days of period**

Month: April 2010

Grade each symptom daily:
- **None** = 0
- **Mild** = 1
- **Moderate** = 2
- **Severe** = 3

---

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<tr>
<th>Symptoms</th>
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**Days of period**

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</thead>
</table>

**Days of period**

Month: April 2010

Grade each symptom daily:
- **None** = 0
- **Mild** = 1
- **Moderate** = 2
- **Severe** = 3
**Etiology**
Di Giulio, Reissing 2006

- No abnormal levels of hormones
- No hormonal dysregulation
- Sensitivity to normal cyclical hormonal changes

---

**Which of the following interventions is proven to help reduce PMS/PMDD symptoms?**

1. Progesterone supplementation
2. The antidepressant, bupropion (Wellbutrin)
3. Calcium supplementation
4. Increasing salt intake
Which of the following interventions is proven to help reduce PMS/PMDD symptoms?

1. 
2. 
3. Calcium supplementation 
4. 

**PMS/PMDD Treatment**
Kroll, Rapkin, 2006

- Initial approach = basic wellness:
  - Healthy diet
  - Stop smoking
  - Exercise
  - Adequate sleep
  - Stress management
**PMS Treatment with Calcium**


- Multi-center, randomized, placebo controlled study, N=497
- 600 mg bid x 3 cycles
- **55%** had >50% improvement in global sxs
  - 36% with placebo
- **48%** reduction in total sxs scores
  - 30% with placebo
- Calcium relieved *both* emotional & physical sxs

**PMDD Treatment**

- Serotonergic antidepressants
  - *Continuous dosing*
  - *Luteal phase dosing*
    - AKA Intermittent dosing
Efficacy of SSRIs in PMS

Brown J et al, Cochran Library, 2009

OCPs for PMDD

Joffe, Cohen, Harlow 2003

- Not helpful: Progesterone alone & most combo OCPs
  - May make sx worse

- Helpful: Yaz
  - Drospirenone 3 mg + ethinyl estradiol 20 mcg
Yaz for PMDD
Yonkers et al, 2005

- Multi-site, DB, RCT
- N=450, all with PMDD, 18-40 yo
- Daily ratings
- 24 days on & 4 days off (with inert pill)

Yaz for PMDD
Yonkers et al, 2005

- Found signif. difference betw groups
- Total sx score:
  - 47% ↓ in active drug group over 3 tx cycles
  - 38% ↓ in PBO group
- Response (50% ↓ in scores)
  - 48% of active drug group
  - 36% of PBO group
- Drop-outs: 15% vs 4%
  - Most common SE = nausea & intermenstrual bleeding
How common is depression in women?
Kessler, 2003

- 20-25% of all women will experience at least 1 episode of depression in their lives
- Boys & girls have equal rates of depression
- Beginning with puberty, rates ↑ for girls
- Overall, twice as common in women
**Why is depression more common in women?**

- Changes in adolescence
  - roles and expectations change dramatically
- Hormonal factors
  - menstrual cycle, pregnancy, postpartum, perimenopause
- Medical illnesses such as thyroid disease
- Medications such as BC pills

**Psychosocial factors**

- Relationships
- Victimization
- Low self-esteem
- Multiple expectations
- Socialization
- Focus on weight, looks
“I feel miserable”

32 yo with 6 mo h/o depressed mood and:
- insomnia
- low energy
- poor concen.
- decr appetite
- less interest
- passive SI
-Fn at work impaired
-Sxs began after parents announced div.
-Had 1 prior episode depression

Treatment Plan for “I feel miserable”

• Course of Cognitive Behavioral Therapy (CBT)
• Rx with an SSRI
• Depression significantly improved
One year later...

- Depression in full remission
- Pt. married & planning to become pregnant
- “What’s the risk of taking antidepressant while pregnant?”

Depression and Pregnancy
Flynn, 2006

- Pregnancy NOT protective
- 10-20% of pregnant women dev MDD
- Risk factors for depression in preg:
  - Prior h/o dep
  - Poor social support
  - Psychosocial stresses
  - Ambiv about pregnancy
**Course of Depression in Pregnancy**  
Cohen et al, 2006

- N = 201
- All with past h/o MDD but in full remission
- Recurrence during pregnancy if stayed on meds = 26%
- Recurrence if d/c meds = 68%

**Depression During Pregnancy**  
Yonkers et al, 2009

- Poor prenatal care
- Smoking & substance abuse
- Suicide
- Preterm delivery
- Low birth weight
- Post-partum depression
Treatment of Depression During Pregnancy

• Psychotherapy proven effective
  – Interpersonal Psychotherapy (IPT)
  – Cognitive Behavioral Therapy (CBT)

• Antidep Rx--main areas of concern:
  – Congenital organ malformations
  – Adverse effects in newborn
  – Long-term behavioral problems

Which is the most true statement about antidepressant Rx in pregnancy?

1. SSRIs are completely safe
2. TCAs are contraindicated
3. Not enough data exists to help make an educated recommendation
4. An individualized risk-benefit assessment must guide decision-making
5. SSRIs are contraindicated
Which is the most true statement about antidepressant Rx in pregnancy?

1. 
2. 
3. 
4. An individualized risk-benefit assessment must guide decision-making
5. 

**TCAs During Pregnancy**

Yonkers et al, 2009

- No congenital malformations
- Nortriptyline & desipramine preferred
- Some potential for neonatal w/d sx & antichol. sx
  - Jitteriness, tachypnea, tachycardia, irritability, feeding difficulties, diaphoresis
  - Constipation, bladder distension
**SSRIs During Pregnancy**
Bakker, 2012; Diav-Citrin & Ornoy, 2012; El Marroun et al, 2012

- No incr rate of congenital malformations
- BUT, paroxetine is different
  - Incr risk cardiac malformations
  - Now Class D per FDA

**Other antidepressants during pregnancy**
Cole et al, 2007; Yonkers et al, 2009

- Bupropion: no evidence of congenital malformations
- Duloxetine, escitalopram, mirtazapine, nefazodone, venlafaxine, and duloxetine
  - Fewer reports; no evidence of congenital malformations
**Perinatal Effects of SSRIs**  
Levinson-Castiel, 2006

- Multiple sx reported in 30% of exposed neonates
  - Agitation, jitteriness, sleep disturbance
  - Tremor
  - Rigidity
  - Feeding problems
  - Excessive crying
- Typically resolve w/in 48 hrs w/o medical intervention
- Consider ↓ or d/c of antidep. prior to delivery

---

**Child Development After Fetal Exposure**  
Nulman et al, 2012

- Prospective study of kids of depressed women
  1. Venlafaxine (n=62)
  2. SSRIs (n=62)
  3. Untreated depression (n=54)
  4. Non-depressed Controls on no meds (n=62)
- Intelligence and behav outcomes measured betw ages of 3-6 yrs
- Grps 1, 2 & 3 had lower IQs and incr behav problems than grp 4
- Severity of maternal dep in preg & at testing predicted child behav
Deciding to Rx Antidep in Pregnancy
Yonkers et al, 2009; El Marroun et al, 2012; Diav-Citrin & Ornoy, 2012

- Need to perform individual risk:benefit analysis
- Assess severity of anxiety/depression & h/o response to treatment
- Document other exposures
  - alcohol, cigs, Rx & OTC drugs
- Document informed consent

Post-partum mental health
“I just feel so tired”

• 37 yo primip
• No prior h/o depression
• Now 7 wks postpartum
• Sxs:
  – depressed mood
  – fatigue
  – overwhelmed and ashamed
  – anxious about caring for baby; fears mistake
  – ↓ appetite
  – insomnia--even when baby asleep

Post-partum depression occurs in what percent of women?

1. 0-5%
2. 6-10%
3. 11-15%
4. 16-20%
5. 21-25%
Post-partum depression occurs in what percent of women?

1. 
2. 
3. 11-15%
4. 
5.

---

**Spectrum of Postpartum Mood Changes**

- **Postpartum Blues**
  - ↑ risk for MDD
  - 50% to 70%

- **Postpartum Depression**
  - 2/3 have onset by 6 wks postpartum
  - 10-15%

- **Postpartum Psychosis**
  - 70% are affective (bipolar, MDD)
  - 0.01%

---

**PPD Risk Factors**
Bloch et al, 2005

- Psychosocial stress
- h/o depression
- h/o PMDD
- Prior h/o PPD (50% risk)
- Depression during current pregnancy

---

**Therefore,**

- During *prenatal* care, screen for past h/o mood d/o
- At 6 wk *post-partum* check, screen for current sxs
**Edinburgh Postnatal Depression Scale**
Cox, 1987

- 10 item questionnaire
- Score of \( >12 \) indicates probable postpartum depression
- In syllabus

---

**PPD Management Recommendations**
Yonkers et al, 2011; Carter et al, 2010; Apter et al, 2011; Studd & Nappi, 2012

- Reassurance & support
- Postpartum Support International
  - [www.postpartum.net](http://www.postpartum.net)
- Psychotherapy
  - Interpersonal Psychotherapy (IPT)
  - Cognitive Behavioral Therapy (CBT)
- Medications
**Pharmacotherapy for PPD**
Yonkers et al, 2011; Apter et al, 2011; Studd & Nappi, 2012

- Relatively few studies have evaluated antidep specifically for PPD
- No study compares psychotx to pharmacotx

**BOTTOM LINE:** Assume Rx for PPD has same response as tx for other depression

---

**Psychotropic Drugs During Lactation**
Davanzo et al, 2011; Sharma & Sharma, 2012

- All are excreted in human breast milk
- As a class, have more data in breastfeeding than any other
- Sertraline, paroxetine, NTP & IMI are most evidence-based meds
Summary

- PMS/PMDD are real d/o
  - Prospective charting useful tool
  - Mgmt = basic wellness → calcium → SSRIs intermittently or Yaz → SSRIs continuously
- Depression is more common in women
- For pregnant pts, complete an individualized risk-benefit analysis
- 3 classes of postpartum mood disorders

Resources

Office of Women’s Health
www.4woman.gov/owh/

American Psychiatric Association patient info
www.healthyminds.org

Center for Women’s Mental Health at Mass Gen’l
www.womensmentalhealth.org

Info on meds in breastfeeding
Urinary Incontinence: 
Easy as 1, 2, 3…. 
What are we thinking? 

Jeanette S. Brown, MD 
Professor 
UCSF Obstetrics, Gynecology, & RS, 
Urology, & Epidemiology 

Disclosures 

Will discuss today: 
Pfizer: Contract for research 
Astellas: Contract for research 

Not in lecture: 
Allergen: Scientific Advisor
Urinary Incontinence

- Common
  - 25% reproductive age women
  - 40% postmenopausal women
- Chronic - social seclusion
  - Falls & Fractures (Brown JAGS 2000)
  - 3x Nursing home admits
- Costly
  - $26 billion annually
  - More than all cancer care for women

Evidence-Based Guidelines

1996 AHRQ Clinical Practice Guidelines:
  - Primary Care diagnosis & treatment
16 years later, where are we?

Barriers for Primary Care:
- Work up too time consuming & complex
- Recommended tests & exams not feasible in a busy practice
Diagnostic Aspects of Incontinence Study (DAISy)

3 Incontinence Questions (3 IQ) vs. Extended Evaluation
Multi-center (N=301):

• Loyola University
• University of Alabama at Birmingham
• University of California, San Francisco
• University of Iowa
• University of Texas Health Science Center, San Antonio

Brown Annals 2006

3 Incontinence Questions (3IQ)

1. During the last 3 months, have you leaked urine, even a small amount? **If yes:**
2. Stress UI: physical activity, coughing, sneezing, lifting, or exercise
   Urge UI: urge, feeling need to empty but could not get to the toilet fast enough
   Other: Don’t know

3. **Type of UI** **MOST OFTEN:** Stress, Urge, Mixed (=), Other
Primary Care UI Patients

**Inclusion criteria:**

_Incontinent women appropriate for Primary Care_
- Community dwelling, ambulatory, weekly UI
- Bothersome enough to seek treatment

**Exclusion criteria:**

_Complex UI: Incontinent women for referral_
- Failed surgery, failed UI treatment
- Fistula, CNS etiology: MS, spinal cord injury

---

**Accuracy of 3 IQ**

Compared to Extended Evaluation

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<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<th>LR+</th>
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<tr>
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<td>0.75</td>
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<td>0.79</td>
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<tr>
<td>Stress UI</td>
<td>0.86</td>
<td>0.60</td>
<td>0.74</td>
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</table>

> Similar to other diagnostic tests

Brown JS. Annals 2006
Summary

Primary Care Clinicians:
- 3 IQ Simple, feasible, reproducible (kappa 70%)
- Include urinalysis (UA)

DAISy Take Home Message:
3 IQ is a good test for type of UI, especially because the risk of missed Dx and Rx low

We can remove barriers to care for women with UI!

3 Incontinence Questions (3IQ)

1. During the last 3 months, have you leaked urine, even a small amount? If yes:
2. Stress UI: physical activity, coughing, sneezing, lifting, or exercise
   Urge UI: urge, feeling need to empty but could not get to the toilet fast enough
   Other: Don’t know
3. Type of UI MOST OFTEN: Stress, Urge, Mixed (=), Other
Ms. I. Gotta Go is a 60 yo teacher G0P0: I have a hard time waiting until the end a class to go to the bathroom and usually have to run to get there. Almost every day I leak on the way to the bathroom. When I have a severe cough, I may leak also but that occurs rarely.

And the diagnosis is?

1. Stress UI
2. Urge UI
3. Mixed UI
4. Other UI
5. Refer
3 IQ in Action

Ms. Stressed is a 54 yo Techie  G2P2:
Ever since my first birth, when I am physically active - I leak urine. Recently, almost every day I leak with a cough or when I lift something heavy. Sometimes when I wait too long, I leak on the way to the bathroom but that occurs rarely.

And the diagnosis is?

1. Stress UI
2. Urge UI
3. Mixed UI
4. Other UI
5. Refer
3 IQ in Action

Ms. Don’t Know is a 44 yo Techie G3P3:
I can’t really describe what happens, I just leak.

And the diagnosis is?

1. Stress UI
2. Urge UI
3. Mixed UI
4. Other UI
5. Refer
Ms. M. Problems is a 64 yo G3P2:
I leak all the time. I recently had pelvic radiation and a hysterectomy. I have tried many medications and nothing works.

And the diagnosis is?

1. Stress UI
2. Urge UI
3. Mixed UI
4. Other UI
5. Refer
BRing Simple Urgency Incontinence DiaGnosis & TrEatment to ProviderS (BRIDGES)

Study Design: Multi-center RCT (12 weeks) followed by 9 month open label N= 645

Participants: Women with urgency-predominant UI identified by 3IQ (Appropriate for PCC) Is the 3 IQ Safe & Effective?

Interventions:
- Fesoterodine (4 or 8 mg) vs placebo
- Pt directed dose adjustment

Primary outcome: Mean change from baseline of urgency UI frequency
Summary of Results BRIDGES

- Compared to prior phase III trials:
  - ↑ placebo effect
  - ↑ effect of fesoterodine on incontinence

- Result:
  
  Net difference in effect of fesoterodine vs placebo: similar to prior studies

3IQ + UA can be used by PCP, then treat

Huang Am J Ob Gyn 2012

BRIDGES 9 month Open Label Study

Summary: Confidential

- N= 498 started on 4 mg fesoterodine
- 91% completed

At 9 months: 93% satisfied with meds
  - 92% satisfied with improved UUI

No harm Pending publication
Initial Visit

- Clinical diagnosis - 3 IQ, UA
- Patient information
- Urinary diary
- Estrogens?
- Weight loss
- Consider Rx

National Association For Continence:

- Web site: [www.nafc.org](http://www.nafc.org)
- Phone: 1-800-BLADDER
- Disease state and treatment information
- FAQs
- Q&A forum
Patient Information

- 222 women with Urge UI: RCT
  - Biofeedback 63%
  - Verbal/vaginal instruct 69%
  - Self-help booklet 59%

*Not statistically different*

*Bottom line: Educate & Empower!*

Burgio JAMA 2002
Urinary Diary

- Excellent education & intervention

Estrogen Therapy for UI

- Receptors in urethra, bladder
- ↑ UI in observational studies
- Clinical therapy
- What a difference a day makes....
Estrogen Therapy for UI

- Receptors in urethra, bladder
- ↑ UI in observational studies
- Clinical therapy
- What a difference a day makes….

Hormone Therapy: Prevention & Treatment

- 7 RCTs N=15,593
  - HERS (Grady Ob Gyn 2001); WHI (Hendrix JAMA 2005)
  - Oral: CEE 0.625mg + 2.5mg MPA; CEE alone
- For Stress, Urge, & Mixed UI:
  - Worsens 40 - 50% at 4 months → 4 yrs
  - Incident UI at 1 yr: ↑15% to 2 X

Bottomline: HT not for prevention or Rx
- Vaginal or Patch?
Weight Reduction & UI

- In women about 200 lbs:
  - Weight loss: > 5% or 30 lbs
  - > 50% Incontinence reduction
- Effective therapy for UI
- Unique motivator for weight loss
- Public Health Implications

Subak NEJM 2009

Incontinence Treatment: Behavioral

- Initial Rx similar for stress & urge
- Behavioral Management
  - Fluids modification
  - Pelvic Floor Exercises (Coughing up)
  - Bladder training
**Bladder Training**

- Re-establishing voluntary control
- Schedule voids q 30-60 minutes
- Diary, relaxation, urge suppression
- RCT demonstrated:
  \( \geq 50\% \) improvement in 75% of participants
- Stress and Urge UI  (Fantyl 1991)

**Behavioral vs. Meds**

- 197 women with Urge UI; RCT
  \( \downarrow \text{UI} \)
- Biofeedback/behavioral  81%
- Medication  69%
- Placebo  40%

*Greater satisfaction in behavioral group*

*Bottom line: Educate & Empower*

*Burgio 1998*
Is Less More?

- 222 women with Urge UI: BCT
  
  - Biofeedback: 63%
  - Verbal/vaginal instruct: 69%
  - Self-help booklet: 59%

  Not statistically different

  Bottom line: Educate & Empower!
  
  Burgio 2002

Additional Rx

- Stress UI
  - Timed voids to prevent full bladder
- Urge UI: Urge suppression
  - Quick pelvic contractions
  - Urge distraction
OAB Medications: Patient-Directed Balance

- Relax the bladder
- Symptom relief
- Balance

Side effects:
- dry mouth
- constipation
- drowsiness
- blurred vision
- dizziness

Contraindications:
- narrow angle glaucoma
- hepatic/renal disease
Cochrane Review
OAB Rx Effectiveness

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<td>40-60%</td>
<td>20-40%</td>
<td>&lt; 0.05</td>
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<tr>
<td>Dry mouth</td>
<td>32%</td>
<td>14%</td>
<td>NS</td>
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</table>

32 trials; N=6800; *Meds very similar* Herbison 2003

Medication Prescribing Guideline
Appendix

Immediate Release
- Oxybutynin (Ditropan) →
- Tolterodine (Detrol) →
- Trospium (Santura)

Extended release
- Darifenacin (Enablex)
- Ditropan XL
- Solifenacin (Vesicare)
- Detrol LA
- Oxybutynin transdermal (Oxytrol)
- Mirabegron (Betanis)
What else?

- Combo treatment: Makes sense
  - UI
  - Behavioral to drug: 84%
  - Drug to behavioral: 89%
  
  *Bottom line: Be creative!*

Burgio 2000

Summary

*Simple Diagnosis - 3 IQ, UA*

- Reasonable expectations
- Ask patient what they want!
- Simple treatments
- Combine treatments, flexibility
  
  *Educate & Empower!*
New Oral Anticoagulants and Other Updates

Tracy Minichiello, M.D.
Associate Professor of Medicine
Chief, SF VA Anticoagulation & Thrombosis Service

Disclosures
I have none
Case

65 yo man with HTN is found on routine exam to be in AFIB. His meds include ASA, metoprolol, statin and ACE. He has normal renal function. What regimen will you suggest for stroke prevention?

1. ASA alone
2. ASA plus clopidigrel
3. Warfarin
4. Dabigatran
5. Rivaroxaban

NEW CHEST GUIDELINES

AFIB CHADS2=0 no therapy (2B); CHADS ≥1 anticoagulant (1B); if unsuitable for AC use asa+clopidigrel rather than asa (1B)
New Oral Anticoagulants

Warfarin
- Need for frequent monitoring
- Myriad of drug interactions
- Interaction with alcohol
- Requirement for dietary stasis
- Fluctuating INR is the norm

New Agents
- No lab testing required
- Few drug interactions
- Activity independent of vitamin K – no food drug interactions
- More predictable dose effect

Ansell, J. Hematology
### New Oral Anticoagulants

<table>
<thead>
<tr>
<th>Approval status</th>
<th>Dabigatran (Pradaxa)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Apixaban (Eliquis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonvalvular AFIB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonvalvular AFIB/DVT prevention</td>
<td></td>
<td></td>
<td>2012?</td>
</tr>
<tr>
<td>MOA</td>
<td>DTI</td>
<td>antiXa</td>
<td>antiXa</td>
</tr>
<tr>
<td>Renal metabolism</td>
<td>80%</td>
<td>30-60%</td>
<td>25%</td>
</tr>
</tbody>
</table>

### New Oral Antithrombotics

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran (Pradaxa)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Apixaban (n/a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1/2 hours</td>
<td>12-17</td>
<td>5-9</td>
<td>8-15</td>
</tr>
<tr>
<td>CYP3A4*</td>
<td>--</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>pGP</td>
<td>Yes</td>
<td>Yes</td>
<td>--</td>
</tr>
<tr>
<td>Antidote</td>
<td>None</td>
<td>None</td>
<td>none</td>
</tr>
<tr>
<td>Monitoring</td>
<td>ECT, TT, PTT</td>
<td>PT</td>
<td>Anti Xa</td>
</tr>
</tbody>
</table>
**RE-LY- DABIGATRAN v WARFARIN FOR STROKE PREVENTION IN AFIB**

Connolly SJ et al. NEJM 2009

**RE-LY Results**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>DABI 150% per yr</th>
<th>WARF % per yr</th>
<th>RR (95% CI)</th>
<th>NNT or NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/SEE (1° Endpt)</td>
<td>1.11</td>
<td>1.69</td>
<td>0.66* (0.53-0.82)</td>
<td>NNT=172</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>3.11</td>
<td>3.36</td>
<td>0.93 (0.81-1.07)</td>
<td>N/A</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>1.51</td>
<td>1.02</td>
<td>1.5* (1.19-1.89)</td>
<td>NNH=204</td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td>0.3</td>
<td>0.74</td>
<td>0.4* (0.27-0.6)</td>
<td>NNT=227</td>
</tr>
<tr>
<td>Myocardial infarction (MI)</td>
<td>0.81</td>
<td>0.64</td>
<td>1.27 (0.94-1.71)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
**ANALYSIS OF RELY TRIAL-TTR**

Wallentin, Lancet 2010

**TTR <57%**
- **57-65%**
- **65-72%**
- **>72%**

**Dabigatran : Drug Interactions**

- A substrate of p-glycoprotein
  - Inducers may decrease dabigatran levels (rifampin, St Johns wort AVOID)
  - Inhibitors could theoretically increase dabigatran (amio, dronedarone,ketoconazole, quinidine) USE CAUTION

- dronedarone / ketoconazole & CrCl 30-50 –use 75 mg twice daily
Rising Concerns....

Stop The Bleeding: FDA Probes Pradaxa Deaths

Less than a month after European regulators asked doctors to exercise caution about using the Pradaxa blood thinner, the FDA has decided to investigate post-marketing reports of serious bleeding events. As of November 6, the European Medicines Agency was aware of 356 cases of serious bleeding that resulted in patient deaths associated with the Boehringer Ingelheim blood thinner (see title). In announcing its review, the FDA notes that the Pradaxa labeling already contains a warning about significant and sometimes fatal bleeds. And a large clinical trial of roughly 10,000 patients that compared Pradaxa and warfarin, which has been the standard therapy for decades, major bleeding events occurred at similar rates.

Nonetheless, the reports of deaths have been causing concern for months. A recent report by the Institute for Safe Medicine Practices found that Pradaxa generated a large number of adverse event reports to the FDA (read this). And a flap erupted in New Zealand, where the government has been criticized for agreeing to provide reimbursement too quickly (read here).

Pradaxa, which was approved for preventing stroke in patients with atrial fibrillation, is

New FDA Communication

Pradaxa (dabigatran etexilate mesylate): Drug Safety Communication - Safety Review of Post-Market Reports of Serious Bleeding Events

UPDATED 11/02/2011. The FDA evaluated new information about the risks of serious bleeding associated with use of the anticoagulants dabigatran etexilate (Pradaxa) and warfarin (Coumadin, Jantoven, and generics). This assessment was done using insurance claims and administrative data from the Data Mini-Sentire pilot of the Sentire initiative. The results of this assessment indicate that bleeding rates associated with new use of Pradaxa do not appear to be higher than bleeding rates associated with new use of warfarin, which is consistent with observations from the large clinical trial used to approve Pradaxa (the RE-LY trial). FDA is continuing to evaluate multiple sources of data in the ongoing safety review of this drug. See the Data Summary in the 11/02/2011 Drug Safety Communication below for additional information.

FDA has not changed its recommendations regarding Pradaxa. Pradaxa provides an important health benefit when used as directed. Healthcare professionals who prescribe Pradaxa should carefully follow the dosing recommendations in the drug label, especially for patients with renal impairment (safety labels do not function normally) to reduce the risk of bleeding. Patients with atrial fibrillation should not stop taking Pradaxa without first talking to their healthcare professional. Stopping use of anticoagulant medications such as Pradaxa can increase the risk of stroke. Strokes can lead to permanent disabilities and death.

Posted 11/02/2011

AUDIENCE: Cardiology, Pharmacology
MI/ACS with Dabigatran

<table>
<thead>
<tr>
<th>Study, y</th>
<th>Dabigatran, No.</th>
<th>Control, No.</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-NOVATE II 2007</td>
<td>13</td>
<td>2266</td>
<td>9</td>
</tr>
<tr>
<td>RE-NEXTLE II 2007</td>
<td>10</td>
<td>1372</td>
<td>4</td>
</tr>
<tr>
<td>PETRO II 2007</td>
<td>2</td>
<td>443</td>
<td>0</td>
</tr>
<tr>
<td>RE-LY original 1-2 2009</td>
<td>175</td>
<td>11916</td>
<td>63</td>
</tr>
<tr>
<td>RE-COVER 2009</td>
<td>4</td>
<td>1289</td>
<td>2</td>
</tr>
<tr>
<td>RE-DREAM * 2011</td>
<td>32</td>
<td>1488</td>
<td>4</td>
</tr>
<tr>
<td>RE-NOVATE II 2011</td>
<td>1</td>
<td>1008</td>
<td>1</td>
</tr>
<tr>
<td>FE model</td>
<td>0.04</td>
<td>0.20</td>
<td>1.00</td>
</tr>
</tbody>
</table>


ROCKET AF- Rivaroxaban v Warfarin in AFIB

- 20mg QD
- Non Inferior to warfarin
- Major bleeding same
- ↑ risk fatal & intracranial bleed
- ↑ risk GI bleed
- CHADS2 score- 3-3.5
- TTR 55%
- No effect of TTR on efficacy
- ↑ CVA when △ back to warfarin

Patient Selection - Cautions

Dabigatran
- History of GI bleeding-unclear source
- Age > 80
- Concomitant therapy with P-gp inhibitors
- At risk for ↓renal function
- Problems with BID dosing

Rivaroxaban
- History of GI bleeding-unclear source
- Concomitant therapy with P-gp inhibitors/CYP3A4 inhibitors
- At risk for ↓renal function

Case

You decide to start your patient with new AFIB on dabigatran or rivaroxaban because he will be unable to get INR draws regularly due to his work/travel schedule.
Starting Dabigatran/Rivaroxaban

- Baseline labs-CBC, Cr, PTT/PT, LFTS
- Patient education-med guide
- Monitoring
  - Adherence
  - Adverse effects-GI
  - Bleeding/Stroke
  - +/-Labs

Follow up
- 2 weeks
- 1 month
- 3 months
- *continue monthly check in

Dabigatran :Prescribing Info

- Indicated for stroke prevention in non-valvular AFIB
- 150 mg po twice daily; 75 mg po twice daily if CrCl 15-30 ml/min or on dronaderone and CrCL< 50 ml/min.
- Not recommended if CrCl< 15ml/min
- Capsule cannot be broken or chewed
- When converting patients from warfarin therapy, discontinue warfarin and start dabigatran when the INR is below 2.0
Rivaroxaban-Prescribing Info

- Dose 20 mg q.h.s @ meal if CrCl > 50 ml/min
- Dose 15 mg q.h.s @ meal if CrCl 15-50 ml/min
  - (beware CYP 3a4-dilt, amio verapamil, dronaderone)
- When Δ from warfarin start rivaroxaban when INR is 3.0
- When Δ from rivaroxaban to warfarin consider stopping rivaroxaban, starting parenteral agent and warfarin together

Case

Which is a good candidate for dabigatran
a) 66 yo w/ AFIB, ESRD, poorly controlled INR admitted with TIA
b) 66 you with AFIB & MVR
c) 83 yo 50 kg woman with CRI (Cr Cl 30 ml/min) with new AFIB
d) none of the above
ARISTOTLE
Apixaban versus Warfarin in Patients with Atrial Fibrillation

Christopher B. Granger, M.D., John H. Alexander, M.D., M.H.S., John J.V. McMurray, M.D., Renato D. Lopes, M.D., Ph.D., Elaine M. Hylek, M.D., M.P.H., Michael Hanna, M.D., Hussein R. Al-Khalidi, Ph.D., Jack Ansell, M.D., Dan Ager, M.D., Alvaro Avezum, M.D., Ph.D., M. Cecilia Bahit, M.D., Rafael Diaz, M.D., J. Donald Easton, M.D., Justin A. Eckowitza, M.B., Ch.B., Greg Flaker, M.D., David Garcia, M.D., Margarida Geraldides, Ph.D., Bernard J. Gersh, M.D., Sergey Goldkyn, M.D., Ph.D., Shinya Goto, M.D., Antonio G. Hermosillo, M.D., Stefan H. Hohnloser, M.D., John Holowatz, M.D., Pueet Mohn, M.D., Ph.D., Petz Jansky, M.D., Brett S. Lewis, M.D., Jose Luis Lopez-Sendon, M.D., Prem Pais, M.D., Alexander Parkhomenko, M.D., Freek W.A. Verheugt, M.D., Ph.D., Jun Zhu, M.D., Lars Wallentin, M.D., Ph.D., for the ARISTOTLE Committees and Investigators

Granger CB, N Engl J Med
September 15, 2011

ARISTOTLE: APIXABAN V WARFARIN in AFIB

5mg BID
20% prior CV
↓ stroke 21%
↓ major bleed 13%
↓ death 11%*

### Then There Were Three... New Comers v Warfarin - Stroke

<table>
<thead>
<tr>
<th></th>
<th>DABIGATRAN</th>
<th>RIVAROXaban</th>
<th>APIXABAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ stroke</td>
<td>X</td>
<td>→</td>
<td>X</td>
</tr>
<tr>
<td>↓ INTRACRANIAL BLEED</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>↓ MORTALITY</td>
<td>X</td>
<td>X</td>
<td>X**</td>
</tr>
<tr>
<td>BLEEDING</td>
<td>↑ GI bleeding</td>
<td>↑ GI bleeding</td>
<td>↓ any cause</td>
</tr>
<tr>
<td>DRUG INTERACTIONS</td>
<td>Least-pGP</td>
<td>pGp &amp; CYP3A4</td>
<td>CYP 3A4</td>
</tr>
<tr>
<td>NUISANCE Side effects</td>
<td>10-20% dyspepsia</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>DOSING</td>
<td>BID</td>
<td>QD</td>
<td>BID</td>
</tr>
<tr>
<td>METABOLISM</td>
<td>80% RENAL</td>
<td>60% RENAL</td>
<td>25% RENAL</td>
</tr>
</tbody>
</table>

**AFIB TREATMENT COST**

<table>
<thead>
<tr>
<th></th>
<th>day</th>
<th>month</th>
<th>annual</th>
</tr>
</thead>
<tbody>
<tr>
<td>warfarin</td>
<td>&lt; 20 cents</td>
<td>$80*</td>
<td>$960</td>
</tr>
<tr>
<td>dabigatran</td>
<td>$6.75-8.00</td>
<td>$260</td>
<td>~$3000</td>
</tr>
<tr>
<td>rivaroxaban</td>
<td>$8.00</td>
<td>$260</td>
<td>~$3000</td>
</tr>
</tbody>
</table>
### Acute VTE Treatment

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Drug</th>
<th>Year Published</th>
<th>Overlap with heparin/LMWH</th>
<th>HR: Recurrent VTE vs. warfarin (95% CI)</th>
<th>HR: Major Bleeding vs. warfarin (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-COVER (DVT and/or PE)</td>
<td>dabi</td>
<td>2009</td>
<td>Yes</td>
<td>1.10 (0.65 – 1.84)</td>
<td>0.82 (0.45 – 1.48)</td>
</tr>
<tr>
<td>RE-COVER II</td>
<td>dabi</td>
<td>ONGOING</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EINSTEIN DVT</td>
<td>riva</td>
<td>2010</td>
<td>No</td>
<td>0.68 (0.44 - 1.04)</td>
<td>0.65 (0.33 – 1.30)</td>
</tr>
<tr>
<td>EINSTEIN PE</td>
<td>riva</td>
<td>2012</td>
<td>No</td>
<td>1.12 (0.75 – 1.68)</td>
<td>0.49 (0.31–0.79)</td>
</tr>
</tbody>
</table>

Schulman S NEJM 2009; Einstein Investigators NEJM 2010 & NEJM 2012

---

### EINSTEIN-Rivaroxan in Symptomatic DVT

**Vte rates**
- 2.1% rivaroxan
- 3% warfarin

**↓ DVT by 82%**

**Minor bleed**
- 5.4% v 1.2%
**Key Differences**

- **Dabigatran**
  - Direct thrombin inhibitor
  - Taken twice daily
  - 5 days of parenteral (e.g. LMWH) treatment needed

- **Rivaroxaban**
  - Direct FXa inhibitor
  - Taken twice daily for 3 weeks, then once daily
  - Can be used as monotherapy

---

**Rivaroxaban Gains FDA Indications For The Treatment And Prevention Of DVT And PE**

The FDA today expanded the indication for rivaroxaban (Xarelto, Johnson & Johnson) to include the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and to reduce the risk of recurrent DVT and PE.

The oral anticoagulant is already approved to reduce the post-surgical risk of DVT and PE after hip and knee replacement surgery and to reduce the risk of stroke in people with atrial fibrillation. The new indication was granted under the FDA’s priority review program.

---
**Case**

Your patient on dabigatran informs you that he is having a laproscopic cholecystectomy due to his recurrence episodes of cholecystitis next week. He wants to know when he should stop his dabigatran.

---

### Dabigatran–Perioperative Management

<table>
<thead>
<tr>
<th>Renal Function †</th>
<th>t½</th>
<th>Procedure associated with standard risk of bleeding (mild-to-moderate residual anticoagulant effect present at surgery)</th>
<th>Procedure associated with high* risk of bleeding (no or minimal residual anticoagulant effect is present at surgery)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-op</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl &gt;50 ml/min</td>
<td>13-15</td>
<td>Stop dabigatran 1 day before procedure (Take last dose 2 days before procedure)</td>
<td>Stop dabigatran 2–4 days before procedure (Take last dose 3–5 days before procedure)</td>
</tr>
<tr>
<td>CrCl 30–50 ml/min</td>
<td>15-18</td>
<td>Stop dabigatran at least 2 days before procedure (Take last dose at least 3 days before procedure)</td>
<td>Stop dabigatran 3–4 days before procedure (Take last dose 4–5 days before procedure)</td>
</tr>
<tr>
<td><strong>Post-op</strong></td>
<td>n/a</td>
<td>Consider resuming therapy 24–72 hrs or longer postoperatively and when hemostasis has been achieved, depending on bleeding risk of procedure and the patient’s thromboembolic risk ‡</td>
<td></td>
</tr>
</tbody>
</table>

Van Ryn, Thromb Haemostasis 2010; Douketis, Curr Pharm Design 2010
Rivaroxaban Perioperative Management

<table>
<thead>
<tr>
<th>Renal Function</th>
<th>Half-Life (hours)</th>
<th>Any procedure requiring interruption of anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal or mild renal impairment</td>
<td>5-9</td>
<td>Stop rivaroxaban 1 day before procedure</td>
</tr>
<tr>
<td>(CrCl &gt;50 ml/min)</td>
<td></td>
<td>(Take last dose 2 days before procedure)</td>
</tr>
<tr>
<td>Moderate renal impairment (CrCl 30-50 ml/min)</td>
<td>11-13 noted in elderly</td>
<td>Stop rivaroxaban at least 2 days before procedure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Take last dose at least 3 days before procedure)</td>
</tr>
<tr>
<td>Post-op (all patients)</td>
<td>n/a</td>
<td>Consider resuming therapy 24 – 72 hrs or longer post-operatively and when hemostasis has been achieved, depending on bleeding risk of procedure and the patient’s thromboembolic risk‡</td>
</tr>
</tbody>
</table>

Case

A 65 year old man with history of HTN and hyperlipidemia is admitted with a new PE. He is on ASA and statin. He is started on LMWH and bridged to warfarin. You

A) stop his aspirin now that he is on warfarin due to concerns of increased risk of bleeding
B) continue ASA for primary prophylaxis
Risk of Bleeding With Single, Dual, or Triple Therapy With Warfarin, Aspirin, and Clopidogrel in Patients With Atrial Fibrillation

Hansen M et al. Arch Intern Med. 2010

**NEW CHEST GUIDELINES**

- “For patients taking warfarin we suggest AVOIDING concomitant antiplatelet therapy except where benefit is likely to be greater than harm: valves, ACS, stents, CABG” (2C)
CASE

A 55 yo man with no PMHx was diagnosed with PE 3 months ago, treated with LMWH→warfarin. He has had no bleeding complications thus far. His work up for cancer is unrevealing.

Case

How long would you recommend he stay on anticoagulation?

a) 3 months
b) 6 months
c) 12 months
d) indefinitely
Risk of VTE Recurrence After Cessation of VTE

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>1st yr</th>
<th>Next 5 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal DVT</td>
<td>3% (6%)</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Major-transient</td>
<td>3%</td>
<td>10%</td>
</tr>
<tr>
<td>Minor-transient</td>
<td>5-6%</td>
<td>15%</td>
</tr>
<tr>
<td>Unprovoked</td>
<td>At least 10%</td>
<td>30%</td>
</tr>
<tr>
<td>Recurrent</td>
<td>&gt; 10%</td>
<td>&gt; 30%</td>
</tr>
</tbody>
</table>

Kearon, Blood 2005

Guidelines for Duration of Anticoagulation for VTE

<table>
<thead>
<tr>
<th>Indication</th>
<th>8th ACCP guidelines 2012</th>
<th>AHA 2010</th>
<th>ASH recommendations 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>First episode of VTE secondary to a transient risk factor</td>
<td>3 months (Grade 1B).</td>
<td>3 months (Class I Level A)</td>
<td>3 months</td>
</tr>
<tr>
<td>First episode of idiopathic (unprovoked) VTE</td>
<td>At least 3 months, prefer long-term treatment if risk/benefit ratio ok (Grade 2B).</td>
<td>At least 6 months, consider indefinite (Class I Level A)</td>
<td>6 months</td>
</tr>
<tr>
<td>Recurrent VTE</td>
<td>Long term (Grade 1B).</td>
<td>Indefinite (Class I Level A).</td>
<td>Long term if APLS, AT deficiency or recurrence</td>
</tr>
</tbody>
</table>

Clinical presentation predicts likelihood and type of recurrence

- Distal (calf vein thrombosis)
  - Low risk of recurrence/PE
- Proximal - nearly 5 fold increased recurrence risk over distal
- PE vs. DVT
  - Patients presenting with PE are 3x more likely to suffer recurrent PE than those presenting with DVT

Baglin T et al. J Thromb Haemost. 2010
Douketis Ann Intern Med 2010

Management Trial Using D-dimer Results to Determine Duration of Anticoagulation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Normal D-dimer Level (%&lt;99%)</th>
<th>Abnormal D-dimer Level without Anticoagulation (%&lt;10%)</th>
<th>Abnormal D-dimer Level with Anticoagulation (%&lt;10%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (%)</td>
<td>4 (6.2)</td>
<td>18 (31.5)</td>
<td>1 (7.9)</td>
</tr>
<tr>
<td>No. of events/100 person-yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of recurrent venous or pulmonary embolism — no.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>79</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Deep vein thrombosis with pulmonary embolism</td>
<td>3</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Isolated pulmonary embolism</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Major bleeding episode</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Systematic Review
- D-dimer +  8.9%
- D-dimer –  3.5%
Clinical Decision Rule

- Clinical predictors
  - Leg red or swollen or hyperpigment 5-7 mos after event
  - D-dimer >250 ug/L on AC
  - BMI >30kg/m²
  - Age > 65

- Female patients with 0-1 risk factor had recurrence risk of 1.6%: ≥2 = 14%

Rodgers et al. CMAJ August 2008

Impact of Thrombophilia on Recurrence Risk

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Recurrence of VTE per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>total</td>
<td>2.6%</td>
</tr>
<tr>
<td>1 thrombophilia defect</td>
<td>2.5%</td>
</tr>
<tr>
<td>Initial VTE provoked</td>
<td>1.8%</td>
</tr>
<tr>
<td>Initial VTE unprovoked</td>
<td>3.3%</td>
</tr>
<tr>
<td>Unprovoked with thrombophilia</td>
<td>3.4%</td>
</tr>
<tr>
<td>Unprovoked without thrombophilia</td>
<td>3.2%</td>
</tr>
</tbody>
</table>

Christiansen JAMA 2005

Shulman Amer j Med 1998
Individual Bleeding Risk on Anticoagulation

Bleeding Risk Factors
- Age > 75
- Previous GI bleed with no reversible cause
- Previous bleed on warfarin
- Renal/hepatic failure
- Antiplatelet therapy

Aspirin for Prevention of Recurrent VTE.

Recurrent VTE
- ASA 6.6%
- Placebo 11.2%

↓ VTE 40%
- No difference in major bleeding
Duration of Anticoagulation
Unprovoked VTE

- PTS
- D-dimer
- Bmi > 30
- Age > 65

IF DVT Get u/s and measure d-dimer. If d-dimer up continue AC

Consider ASA if anticoagulation stopped
Clinical Pearls in Allergy and Immunology

Katherine Gundling, MD
University of California, San Francisco
December, 2012

No industry affiliations
Unless otherwise specified, images and videos in this talk were obtained from sources within the public domain.

Three Topics 
(and an intermission!)

1. Allergies to animals
2. Food allergy and intolerance

*Intermission*
(Cool Immunology Stuff)

3. Hygiene hypothesis
Topic 1

Allergies to Animals
(Focus on Dogs)

Images: Wikipedia dogs
Which dog is the least likely to trigger a severe allergic reaction?

A. Peruvian *Hairless* Dog  
B. Chihuahua  
C. St. Bernard  
D. Labradoodle
Which dog is the least likely to trigger a severe allergic reaction?

A. Peruvian *Hairless* Dog
B. Chihuahua
C. St. Bernard
D. Labradoodle

*E. None of the above*

**Dog Allergy**

The allergens are proteins found in the -epithelial cells
-saliva
-urine

*Each animal is different!*
*Each human is different!*
What can a person do to minimize dog allergen in the home?

Maintain one animal free zone (bedroom)
Ensure a healthy diet for your dog
Bathe the dog (once a week?)
Use a high quality HEPA air filter
Protect your furniture and car seats
Why do some people have symptoms around dogs and cats even though they have negative allergy skin tests to these animals?

_They might be allergic to dust mites!_

Chronic or “Perennial” Symptoms

- Allergic rhinitis (“colds”)
- Asthma (“bronchitis”)
- Recurrent sinusitis
- Allergic conjunctivitis
- Atopic dermatitis
What to know about dust mite allergy

Symptoms can occur *any time of the year* in the Bay Area, and locations with constant humidity. Common treatments for allergic rhinitis can help. Watch out for the development of *asthma* in adulthood!

**Recommendations:**
- Learn about and undertake aggressive *environmental preventive measures* in the home.
- Consider *allergen immunotherapy* for refractory cases.

Key Points

- Dog allergy reactions are induced by proteins that exist in skin or saliva.
- There is no such thing as an “allergy-free” dog; a given individual might be very allergic to one dog and fine around another.
- Allergy testing can help distinguish whether a person is allergic to dogs, or whether the reaction is due to dust mite or other allergen.
A 32 year old woman presents with concern about food allergy. For the past three years she has noted increasing symptoms of itching, possible swelling and irritation in the mouth and throat upon eating certain foods, including apples, nectarines and plums. She asks whether food allergy testing is needed.
PMH:
– Generally healthy
– Infant eczema that resolved by age 5
– s/p appendectomy age 16
– Springtime hay fever symptoms including itchy, watery eyes, nasal congestion and drainage; occasional sinusitis with URIs

Meds:
– Oral contraceptives
– Calcium
– PRN ibuprofen for headaches and dysmenorrhea

Drug allergies: None known

FH:
– Father with HTN; mother with hypothyroidism, eczema
– One brother with exercise induced asthma

SH:
– Married, no children. Works as an attorney; no significant avocational exposures; non-smoker

ROS:
– Occasional generalized headaches
Physical exam:
Remarkable only for slight conjunctival injection and moderate edema of the nasal mucosa

What is the cause of her problems with food?
A. Food allergy
B. Pollen-Food syndrome
C. Ibuprofen sensitivity
D. Irritation from chemical constituents of the food
What is the cause of her problems with food?

A. Food allergy

B. Pollen-Food syndrome

C. Ibuprofen sensitivity

D. Irritation from chemical constituents of the food

Adverse Food Reactions

- Non-Immunologic
- Immunologic
Adverse Food Reactions

**Non-immunologic**

<table>
<thead>
<tr>
<th>Toxic/Pharmacologic</th>
<th>Non-Toxic/Intolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial food poisoning</td>
<td>Lactase deficiency</td>
</tr>
<tr>
<td>Heavy metal poisoning</td>
<td>Galactosemia</td>
</tr>
<tr>
<td>Scombroid fish poisoning</td>
<td>Pancreatic insufficiency</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Gallbladder / liver disease</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Hiatal hernia</td>
</tr>
<tr>
<td>Histamine</td>
<td>Gustatory rhinitis</td>
</tr>
<tr>
<td></td>
<td>Anorexia nervosa</td>
</tr>
<tr>
<td></td>
<td>Idiosyncratic</td>
</tr>
<tr>
<td></td>
<td>Carbohydrate malabsorption</td>
</tr>
</tbody>
</table>

Adapted from
Sicherer/Sampson
JACI 2006; 117:S470-475

**Immunologic**

- IgE-Mediated (most common)
  - Systemic (Anaphylaxis)
  - Oral Allergy Syndrome
  - Immediate gastrointestinal allergy
  - Asthma/rhinitis
  - Urticaria
  - Morbilliform rashes and flushing
  - Contact urticaria

- Non-IgE Mediated
  - Protein-Induced Enterocolitis
  - Protein-Induced Enteropathy
  - Eosinophilic proctitis
  - Dermatitis herpetiformis
  - Contact dermatitis

Pollen-Food Syndrome or Oral Allergy Syndrome

- Clinical features: rapid onset oral pruritus, rarely progressive
- Epidemiology: prior sensitization to pollens
- Key foods: raw fruits and vegetables
- Allergens: proteins that are heat labile
- Cause: cross reactive proteins pollen/food

Birch  Apple, carrot, celery, cherry, pear, hazelnut
Ragweed  Banana, cucumber, melons
Grass  Melon, tomato, orange
Mugwort  Melon, apple, peach, cherry

Adapted from AAAAI Food Allergy Teaching Slide

The diagnosis of Pollen-Food Syndrome can be made easily by asking the right question:

*Can you eat these apples baked into a pie?*

“Yes”  Pollen-Food Syndrome

“No”  Higher risk of major food allergic reactions
Why is this important?

Pollen-Food Syndrome is generally just annoying

*True food allergy can kill!*

If in doubt, prescribe epinephrine and consider referral to an Allergy/Immunology specialist

One more thing…

Serum IgG testing

Serum IgG testing for food allergy is

A. essentially irrelevant
B. specific but not sensitive
C. equivalent to prick skin testing
D. useful for eczema but not asthma
Serum IgG testing

Serum IgG testing for food allergy is

A. essentially irrelevant
B. specific but not sensitive
C. equivalent to prick skin testing
D. useful for eczema but not asthma
Key Point

IgG food testing is not helpful to define meaningful food allergies

Epinephrine Prescription

Dr. Gundling’s demonstration video:
http://www.youtube.com/watch?v=i6K2_kVmr3E&feature=g-hist

Example: Rx
Epinephrine auto injector
    (adult) or (child) #2

Use as directed
2 refills
Intermission!

Cool Immunology Stuff

Neutrophil behavior most closely resembles the behavior of which superhero?

A. Batman  
B. Superman  
C. Spiderman  
D. Mr. Incredible
Neutrophil behavior most closely resembles the behavior of which superhero?

A. Batman  
B. Superman  
C. Spiderman  
D. Mr. Incredible
A young woman who has asthma and atopic dermatitis is pregnant, and asks about whether her children will also suffer from atopic disease.

A discussion ensues about the genetics of these conditions, and the patient rightly wonders whether environmental exposures are important.
Which of the following early exposures is most associated with the prevention of atopic disease (atopic dermatitis, food allergy, allergic rhinitis, asthma)?

A. Barn animals
B. An older brother
C. A household dog
D. Dust mites in the pillow
Early exposure to barn animals is strongly associated with less atopy

Exposure to pets from infancy might also be helpful, as are older siblings

Exposure to dust mites is associated with increased atopic conditions


---

Farming, Bavarian Style

Courtesy of Erica von Mutius
Asthma Prevalence in the USA

Age **5-14**
- Male: 12%
- Female: 9%

Age **35-64**
- Male: 5%
- Female: 11%

Prevention of atopic conditions

**Clear:**
- Infants should be breast fed
- Early exposure to animals (especially barn animals) and older siblings is preventative
- Allergen immunotherapy can prevent the development of new sensitization and asthma

**Unclear:**
- What the pregnant mother should eat or avoid
- What the lactating mother should eat or avoid
- Whether an infant should be exposed to small amounts of common food allergens, or completely avoid common allergens
Summary of Today’s Clinical Pearls

Dog allergy: be skeptical about claims of “hypoallergenic”

Oral allergy syndrome (“food pollenosis”) can be diagnosed with one simple question.

*Prescribe and demonstrate the appropriate use of epinephrine!*

Spiderman behaves like neutrophils!

Dirt is GOOD for you!
Breast Cancer: Key Issues for the Non-Oncologist

Leah Karliner, MD MAS
Department of Medicine
December 2012

Controversies in Women’s Health

- I have no disclosures
OUTLINE

• Testing At Diagnosis
  – Abnormal mammograms
  – Hormone Receptors and HER2/Neu
  – Sentinel lymph node biopsy

• Treatment
  – Radiation
  – Anti-estrogen therapy
  – Reconstruction

• Survivorship
  – Surveillance
  – Therapy related complications
  – Risk reduction: exercise

Abnormal Mammogram

• Cumulative risk of false positive result: 49% after ten mammograms
  Elmore et al NEJM 1998

• False positive rates highest for women in their 40’s and 50’s
Case 1

- Your patient AH, a 56 yo woman, goes for her screening mammogram. A few days later, you get a call from the radiologist. The mammogram shows increased density and possibly a calcification on the right. The radiologist says they are reading it as a BIRADS 0 and the patient should get follow-up, could you please let her know?

What kind of follow-up does this patient need next?

1. A repeat mammogram in 3-6 months
2. A mammogram at the usual screening interval
3. A diagnostic mammogram with spot-compression views
4. A referral to the breast surgeon/clinic for a biopsy
American College of Radiology BIRADS category (breast imaging reporting and data system)

**Normal**
1: negative  
2: benign finding  

**Abnormal**
0: indeterminate  
3: low chance malignancy (~2%)  
4: >2-95% chance malignancy (a: low; b: intermediate; c: moderate)  
5: ≥95% chance invasive malignancy  

(normal follow-up)

(spot-compression views + u/s)

(short interval follow-up)

(3-6 months repeat mammo)

(biopsy)

Case 1

- Your patient AH, a 56 yo woman, goes for her screening mammogram. A few days later, you get a call from the radiologist. The mammogram shows increased density and possibly a calcification on the right. The radiologist says they are reading it as a BIRADIS 0 and the patient should get follow-up

....could you please let her know?
MQSA: Mammography Quality Standards Act

- Passed by U.S. Congress in 1992
- Mammography facility must send patient written report of her mammogram within 30 days of exam
- Report must be in words she can easily understand
- For BIRADS 4 or 5 results, facility expected to contact patient as soon as possible – ‘expectation’ within 5 days
- If verbal contact, still need to send letter

www.fda.gov/Radiation-EmittingProducts/MammographyQualityStandardsActandProgram/ConsumerInformation/ucm113968.htm

Why Do You Need To Get Involved?

- Good Practice: you ordered the test
- Malpractice:
  
  Failure to diagnose a breast cancer
  
  Most common cause of claim:
  - Premenopausal woman with a breast lump
  - Negative mammogram
  - No further evaluation
Communication Matters

• Adequate communication of abnormal results improves receipt of appropriate follow-up
  Poon et al, JGIM 2004

• Minority women report lower rates of adequate communication, and are less likely to know their abnormal mammogram results
  Zapka et al, Prev Med 2004

• Women who received their results verbally (in person or over the telephone) more likely to know that their mammogram was abnormal
  Karlner et al, JGIM 2005

Delays in Diagnosis

• 20-40% women undergoing breast cancer diagnosis experience delays to diagnosis or treatment

• Delay of ≥ 3 months (symptoms to treatment) associated with 12% lower 5-year survival
  – Most of this attributable to later stage disease
  Richards et al, Lancet 1999

• African-American women are more likely to suffer delays than White women
  Elmore et al, Med Care 2005

• Hospitals disproportionately serving non-English speaking and minority women have longer delays
  Karlner et al, Med Care 2011
Causes of Delay

• Mammogram Facility
  – Resource issues
  – Tracking systems
  – Appointment access
• Communication
  – Physician inaction (not contacting patient; not ordering follow-up tests)
  – Inadequate communication of abnormal results and need for follow-up
  – Language barriers
• Patient
  – Patient inaction (lack of knowledge / understanding, fear, anxiety)

Case 2

• You are seeing GL, a 50-year-old Chinese-American woman, for her routine annual exam. She tells you about a new lump she found in her breast, which you feel and find to be firm with regular borders.

• You send her for a diagnostic mammogram which shows an area of calcification BIRADS 4 and next she undergoes a core biopsy.
What Pathologic Staining Findings are Indicative of a Poor Prognosis Tumor?

1. ER/PR positive staining
2. ER/PR and HER2Neu positive staining
3. ER/PR/Her2Neu negative staining

Hormone Receptors and HER2

Assay for estrogen, progesterone receptors and HER2

- Perform on core biopsy specimen
- If negative on core specimen, should be repeated at definitive surgery:
  - up to 15% of cases with negative markers on biopsy specimen will be positive on larger surgical specimen

- ER/PR + cancers responsive to anti-estrogen therapy
- Over-expression of HER2/neu oncogene
  - worse prognosis
  - responsive to trastuzumab (Herceptin)
Poor Prognosis Tumors

- **Triple negative tumors**
  - ER- / PR- / HER2-
  - Unresponsive to anti-estrogen therapy and trastuzumab
  - Neo-adjuvant chemotherapy
  - Clinical trials investigating immune modulators and receptor-blockers for growth factors

- **African Americans, Latinas and BRCA1 carriers more at risk for triple negative tumors**

Sentinel Lymph Node Biopsy

- **Initial standard axillary staging procedure for invasive breast cancer**

- **SLN:** any node receiving drainage directly from the primary tumor (can be >1)

- **Technetium-labeled sulfur colloid or vital blue dye injection around tumor / biopsy cavity / subareolar**

- **Identifies SLN in 92-98% of patients**

- **97.5-100% concordance with complete axillary lymph node dissection (ALND)**
SLN biopsy and survival

- RCT of 5,611 women with invasive breast CA, 8-years of follow-up
  
<table>
<thead>
<tr>
<th></th>
<th>ALND in +SLN only</th>
<th>ALND in all</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival</td>
<td>90.3%</td>
<td>91.8%</td>
<td>0.12</td>
</tr>
<tr>
<td>Disease Free Survival</td>
<td>81.5%</td>
<td>82.4%</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Krag et al, Lancet Oncology 2010

If SLN negative then can avoid axillary dissection

SLN and Survival

- If SLN positive – medical necessity of ALND is at question –
  - RCT of no further axillary treatment vs. ALND
    - T1-T2 invasive breast cancer, no palpable adenopathy,
    - 1-2 SLN with mets
  - No difference in 5-year overall or disease free survival
  - Only able to enroll half target (891/1900 women)

Giuliano et al, JAMA 2011

- When ALND required, standard: removal of at least 6-10 nodes (level I and II dissection, not radical dissection)
Metastatic Work-up
**Mets are rare without symptoms**

- Physical exam: breasts, skin, lymph nodes, abdomen
- Diagnostic bilateral mammography; possible breast MRI
- CBC, LFTs
- Chest x-ray; possibly CT pre-radiation
- Staging CT – liver, pelvis, chest – and bone scan in stage III disease and above

In Situ Breast Cancer

- Stage 0
  - LCIS: increased risk of developing invasive ca later in life (up to 30-40% lifetime risk)
  - DCIS: 25-50% of untreated cases become invasive, but no mortality risk in and of itself

Early Stage Invasive Breast Cancer

- Stage 1: tumor <2cm, no lymph node involvement
- Stage IIA: no tumor in breast, but +LN non-matted, OR ≤2cm, and +LN non-matted, OR ≥2-5cm, no lymph node involvement
- Stage IIB: ≥2-5cm, and +LN non-matted, OR >5cm, no lymph node involvement
Standard Treatment

- Lumpectomy + radiation vs. mastectomy (with or without reconstruction)
- For HR+ tumors 5 years of anti-estrogen therapy
- For HER2+ tumors – trastuzumab plus chemotherapy
- Chemotherapy

Radiation Therapy

Goal: eradicate residual disease and so reduce local recurrence

- BCS without radiation risk of recurrence >20%
  - Whole breast radiation reduces this risk to around 7%
  Clark et al, Lancet 2005
- Post-mastectomy radiation to chest wall & regional lymph nodes
  - In women with risk factors for local recurrence:
    - ≥ 4 + axillary LN
    - Extracapsular nodal extension
    - Large primary tumor
    - Very close or +deep margins of resection
  Reduces risk of recurrence from 27% to 9%
EBCTCG, Lancet 2005
Anti-estrogen Therapy

For HR-positive tumors

- **Premenopausal women: tamoxifen**
  - 12% reduction in recurrence rate
  - 9% reduction in mortality (regardless of age or chemotherapy use)

- **Post-menopausal women: aromatase inhibitor (AI)**
  - Superior to tamoxifen in time to recurrence & possibly survival time
  - AI followed by tamoxifen ok if change necessary

  ATAC, Lancet 2005
  BIG, NEJM 2005; BIG 1-98, NEJM 2009

- Several regimens have been shown to be more effective than 5 yrs of tamoxifen alone
  - 5 yrs of adjuvant AI therapy
  - 2 to 3 yrs of tamoxifen, followed by 2 to 3 yrs of an AI
  - 5 yrs of tamoxifen, followed by 5 yrs of AI

Other Systemic Treatments

- For HER2+ tumors
  Standard: 1 year adjuvant trastuzumab (following 4 cycles of chemotherapy)
  - Reduces recurrence by 6%
  - Increases overall survival by 3%
  Smith et al, Lancet 2007

  Awaiting trial results of 1 year vs. 2 years (HERA) and 1 year vs. 6 months (INCA-PHARE)

- Axillary node + tumors: Chemotherapy
  - Anthracycline-based regimen
  - Followed by taxane

Breast Reconstruction

- Immediate vs. delayed
  - Patient preference
  - Need for chest wall radiation
  - Patient's underlying health

- Type of reconstruction: implant vs. tissue
  - Size of natural breast
  - Availability of tissue
  - Aesthetic considerations
  - Surgery issues (#, length, recovery)
• **Implants – usually saline with expanders**
  – Silicone also used; other materials/shells being studied
  – One-stage immediate
  – Two-stage (saline expander; after 4-6 months permanent implant)
  – Potential complications:
    • Rupture, leaking, infection, pain, capsular contracture, need for replacement

• **Tissue flap (tram and latissimus dorsi)**
  – Advantage: no replacement or rupture, own body tissue
  – Disadvantage: bigger surgery, 2 surgical sites

• **Nipple sparing mastectomy vs. nipple/areolar reconstruction**
  – Reconstruction a separate outpatient surgery
  – Nipple sparing not yet widely available

• **Alloderm (acellular donated skin)**
  – Used to extend & support implant, tissue flap, nipple reconstruction
  – No outcome studies

Case 2 continued

- GL, who had ER/PR+ stage I disease, has now completed her treatment of breast conserving surgery, breast radiation and is completing her 5th year taking an aromatase inhibitor. Her breast surgeon does not feel that GL needs to continue to see her on a regular basis and would like you to take over her follow-up care for her breast cancer.

What should GL’s follow-up care consist of?

1. Yearly mammogram, LFTs and bone scan to look for metastases
2. Yearly mammogram and breast MRI and physical exam with special attention to symptoms which indicate metastases or treatment complications
3. Yearly mammogram and physical exam with special attention to symptoms which indicate metastases or treatment complications
4. Nothing special beyond usual screening and primary care as her chances of recurrence are low since she had Stage I disease.
High Rates of Long-term Survival Among Breast Cancer Survivors

There are an estimated 2.5 million breast cancer survivors in the United States

![Graph showing long-term survival rates](image)

- 2,838 women Stage I-III treated with adjuvant or neo-adjuvant systemic therapy
- 1985-2001; disease free x 5 years
- Residual disease-free recurrence rate
  - 10 years post-diagnosis 89%
  - 15 years post-diagnosis 80%
- By stage residual risk of recurrence at 10 years
  - Stage I 7%
  - Stage II 11%
  - Stage III 13%  

Brewster et al JNCI, 2008
Surveillance After Therapy

Goals:

– Early recognition & treatment
  • disease recurrences
  • second primary breast cancers

– Screening for therapy related complications

– Detection of symptoms consistent with metastatic disease

• Intensive surveillance vs follow-up with regular physical exams & mammography
  – No survival or quality of life benefit for intensive approach
  
  De Bock et al J Clin Oncol 2004

• Testing should be guided by symptoms and findings
Surveillance After Therapy

- Ipsilateral local recurrence: 1-2% per year
- Contralateral 2\textsuperscript{nd} primary .5-1% per year (non-BRCA carriers)
  - BRCA carriers 29-40% over 10 years
- Only retrospective evidence to support use of mammography to prevent local recurrence or new primary

ASCO Guidelines for Follow-up of Breast Cancer Patients: Recommended Surveillance

<table>
<thead>
<tr>
<th>Type of Surveillance</th>
<th>Summary of Recommendations</th>
</tr>
</thead>
</table>
| History and physical examination |  - First 3 years after primary therapy: every 3 to 6 months  
  - Years 4 to 5: every 6 to 12 months  
  - Years 6+: annually |
| Breast self-examination       |  - Monthly                                                                                          |
| Mammography                   |  - 1st post-treatment mammography: 1 year after initial mammogram leading to diagnosis, but no earlier than 6 months after radiation therapy  
  - Subsequent mammograms as indicated for surveillance of abnormalities |
| Pelvic examination            |  - Regular gynecologic follow-up  
  - Patients taking tamoxifen should report any vaginal bleeding |

### ASCO Guidelines for Follow-up of Breast Cancer Patients: Recommended Surveillance (cont’d)

<table>
<thead>
<tr>
<th>Type of Surveillance</th>
<th>Summary of Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referral for genetic counseling</td>
<td>- Ashkenazi Jewish heritage</td>
</tr>
<tr>
<td></td>
<td>- Patient or family (1st-/2nd-degree relatives) ovarian cancer</td>
</tr>
<tr>
<td></td>
<td>- Family history of breast cancer</td>
</tr>
<tr>
<td></td>
<td>- 1st or 2nd degree relative diagnosed before 50 years of age</td>
</tr>
<tr>
<td></td>
<td>- Patient/relative with a history of bilateral breast cancer</td>
</tr>
<tr>
<td></td>
<td>- Male relative with breast cancer</td>
</tr>
<tr>
<td>Patient education: on symptoms of recurrence</td>
<td>Counseling should include: new lumps, bone pain, chest pain, abdominal pain, dyspnea, or persistent headaches</td>
</tr>
<tr>
<td>Coordination of care</td>
<td>- Continuity of care should be encouraged and should be performed by a physician experienced in surveillance of cancer patients and in breast examination</td>
</tr>
<tr>
<td></td>
<td>- If follow-up care is referred to a PCP, the PCP and patient need to be informed of the long-terms options for adjuvant hormonal therapy (may necessitate referral for periodic oncology assessments)</td>
</tr>
</tbody>
</table>

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### Treatment Plan/Summary and Survivorship Care Plan

- **Facilitates coordination of care among providers**
  - Ensures appropriate follow-up care

- **Helps patient-physician communication**

- **Empowers patients to take charge of their own survivorship**

Ganz PA, Hahn EE. *J Clin Oncol.* 2008;26:759-767

[http://www.cancer.net/patient/Survivorship/ASCO+Cancer+Treatment+Summaries]
Patient Name: Medical Oncologist Name: 

FOLLOW-UP CARE TEST RECOMMENDATION PROVIDER TO CONTACT

Medical history and physical (H&P) examination (see below)
Visit your doctor every three to six months for the first three years after the first treatment, every six to 12 months for years four and five, and every year thereafter.

Post-treatment mammography (see below)
Obtain a mammogram one year after your final mammogram that detects cancer, but no earlier than six months after radiation therapy. Obtain a mammogram every six to 12 months thereafter.

Breast self-examination
Perform a breast self-examination every month. This procedure is not a substitute for a mammogram.

Pelic examination
Continue to visit your gynecologist regularly. If you use tamoxifen, you have a greater risk for developing endometrial cancer (cancer of the lining of the uterus). Women taking tamoxifen should report any vaginal bleeding to their doctor.

Coordination of care
About a year after diagnosis, you may continue to visit your oncologist or transfer your care to a primary care doctor. Women receiving hormone therapy should talk with their oncologist about how often to schedule follow-up visits for re-evaluation of their treatment.

Genetic counseling referral
Tell your doctor if there is a history of cancer in your family. The following risk factors may indicate that breast cancer could run in the family:
- Ashkenazi Jewish heritage
- Personal or family history of ovarian cancer
- Any first-degree relative (mother, sister, daughter) diagnosed with breast cancer before age 50
- Two or more first-degree or second-degree relatives (grandparent, aunt, uncle) diagnosed with breast cancer
- Personal or family history of breast cancer in both breasts
- Personal or family history of breast cancer in a male relative

YEARN BREAST CANCER FOLLOW-UP & MANAGEMENT SCHEDULE

| Visit Frequency for H&P Years 1-3: | 3 months | 6 months (circle one) |
| Visit Frequency for Mammography: | 6 months | 12 months (circle one) |

Visit Frequency

2nd Month (if applicable)

5th Month (if applicable)

8th Month (if applicable)

11th Month (if applicable)

Notes:

- Risk: You should continue to follow-up with your physician because the risk of breast cancer returning continues for more than 15 years after remission, and because, if you have not had bilateral mastectomies, you are at higher risk to develop a new, unrelated breast cancer at some time in the future.

- Symptoms of Recurrence: Report these symptoms to your doctor: new lump, bone pain, chest pain, shortness of breath or difficulty breathing, abdominal pain, or persistent headaches.

- Not Recommended: The following tests are not recommended for routine breast cancer follow-up because they do not improve outcomes:
  - MRI
  - PET scans
  - Complete blood cell counts
  - Automated chemistry studies
  - Bone scans
  - Brain MRI
  - CA 15-3, CA 27.29, CA 125

Talk with your doctor about reliable testing options.

Therapy Related Complications

- Radiation late toxic effects
  - Radiation pneumonitis risk 1%,
    - increased with supraclavicular radiation (3%) or concurrent chemotherapy (8.8%)
  - Lymphedema
    - ALND alone 2-10% risk
    - ALND and axillary radiation 13-18% risk
  - Brachial plexopathy uncommon with more fractions (1%) with 30 vs. 6% with 15 fractions
  - Cardiac events with new techniques since 1990’s no longer big issue
  - Second malignancies
    - Rare sarcomas in treated field (0.2% at 10-years)
    - In smokers possible small increased risk ipsilateral lung
Acute effects of tamoxifen and AIs on menopausal symptoms

• Prospective study: 181 consecutive postmenopausal women starting hormonal therapy
  – Both first line tamoxifen and AIs increased occurrence and severity of hot flashes
  – Musculoskeletal pain and dyspareunia significantly increased with AIs
  – Sexual interest decreased significantly with tamoxifen
  – Younger age was associated with more hot flashes and vaginal dryness

Morales et al, Anti-Cancer Drugs 2004

Tamoxifen

• Increases risk of thromboembolic events & cerebrovascular disease approximately threefold
  (1-2% incidence DVT and PE; <1% incidence stroke)
  – Patients under the age of 50 do not appear to have a statistically significant increase in risk


• Concurrent chemotherapy & tamoxifen associated with a further increased risk of thromboembolism

• Other potential harms from tamoxifen
  – Endometrial cancer 2-7x greater (gyn eval for abnl bld)
  – Benign ovarian cysts (10%)
  – Possible increased risk GI malignancy under study
  – Reports of ophthalmologic toxicity (refer for eye complaints)

Aromatase Inhibitors
  – Reduce estrogen
  – Are associated with a decline in BMD and an increased risk of fracture
  – Exacerbate the normal progressive loss of BMD in postmenopausal women

• In contrast, tamoxifen may preserve BMD

• Patients with osteopenia/osteoporosis prior to initiation of AI therapy may be at the greatest risk
Check bone density within one year of starting an AI

- Normal BMD at baseline: take calcium & vit D, weight bearing exercise
- Osteopenia: recheck BMD one year later to assess change
- Osteoporosis at baseline or during follow up: consider bisphosphonate therapy

- AIs associated with joint symptoms/arthralgias
- Typical onset within 2 months of treatment initiation
  - Symptoms may resolve over time
  - The true etiology and the optimal treatment is not known
• **Trastuzumab**
  
  – Cardiotoxicity:
    - severe CHF 0.6%;
    - symptomatic CHF 1.7%
    - 3-year cumulative cardiac events 4.1% (compared with control 0.8%)

• **Chemotherapy**
  
  – Taxanes: peripheral neuropathy (20-30%), often dose-limiting
  – Anthracycline-based regimens: cardiotoxicity (3-5%)
    - Increases with age
    - Increases with underlying heart disease
    - Increases with higher BMI
    - Can be reduced with limiting cumulative dose, peak concentrations (via dosing schedule)

---

**Case 2 continued**

• GL is back in your care and she is now 7 years post-treatment. She confesses to you that she lays awake most nights worrying that her breast cancer might come back. During the day she is too busy to worry, but her poor sleep at night is causing her to be irritable with her family and she believes it may be affecting her performance at work as well.

• She hasn’t told you about this before because she is afraid you will tell her that there is nothing she can do to help prevent a recurrence of her breast cancer.
What can GL do to help prevent a recurrence?

1. Nothing beyond the treatment she had and regular check-ups with you to catch an early recurrence
2. She should eat a low-fat high-vegetable diet
3. She should do at least 3 hours of moderately strenuous exercise per week
4. She should eat a low-fat, high-vegetable diet and do at least 3 hours of moderately strenuous exercise per week

Need for Patient Education on Recurrence

2007 Harris Interactive Poll with Breast Cancer Patients (n=543)

- Recurrence concern: 78% Not sure, 22% Yes, 0% No
- Spoke to physician about recurrence: 45% Not sure, 55% Yes, 0% No
- Belief that they can impact recurrence: 47% Not sure, 30% Yes, 23% No


Slide courtesy of Dr. Michelle Melisko
High Vegetable/Lower Fat Diet: the WHEL Study

- Multi-site clinical trial
- 3088 women with early stage breast cancer
- Randomly assigned
  - high vegetable/fruit/fiber and low-fat diet
  - control group
- Followed for a mean 7.3 years
- No effect of diet on survival
- Post-hoc analysis: exercise associated with increased survival


Exercise and Mortality in U.S. Nurses Health Study

- 2987 breast cancer patients (Stage I-III)
- Diagnosed with early stage breast cancer between 1984-98
- Followed until 2002
- Doing at least 3-5 hrs/wk of brisk walking or similar exercise reduced deaths by 50%

Holmes et al. JAMA 2005;293:2479-86
Breast Cancer Mortality by Physical Activity (Nurses Health Study Cohort)


All-Cause Mortality by Physical Activity (Nurses Health Study Cohort)

Take Home Points

- Delays in diagnosis are common after an abnormal mammogram
- Improved communication of abnormal results improves receipt of appropriate follow-up
- SLN biopsy can help avoid axillary dissection and results can help determine need for chemo
- Anti-estrogen therapy increases survival in ER/PR+ tumors
- Trastuzumab increases survival in HER2/neu+ tumors

Goal of radiation therapy is lowering risk of local recurrence

- Metastases are rare without symptoms
- If a woman survives 5-years, her 10-year survival is very good (Stage I-III)
- Care coordination can be improved with treatment summaries and survivorship plans
- Surveillance by hx/PE/mammography; other testing should be guided by symptoms
- Be aware of long-term complications of different treatments
- Encourage breast cancer survivors to do 3-5 hours of moderate exercise per week
Best Practices in Contraception: Preventing the Unintended

Carolyn Sufrin, MD, MA
Dept. Ob/Gyn & Reproductive Sciences
University of California, San Francisco

Disclosure statement

• I have no relevant financial relationships to disclose.
Do you place intrauterine contraception in your clinical practice?

a. Yes
b. No

How comfortable would you be offering a woman an IUD if she had a history of Chlamydia and no current infection?

a. Very comfortable
b. Somewhat comfortable
c. Uncomfortable
Would you offer a 20 year-old woman with migraine the combined oral contraceptive?

a. Yes
b. It depends
c. No

Would you order a DEXA scan for a woman who has been on Depo-Provera for more than 2 years?

a. Yes
b. It depends
c. No
What percent of women of reproductive age prescribed Category D or X medications (dangerous in pregnancy) receive contraceptive counseling before starting the medication?

a. 25%

b. 50%

c. 75%

d. 85%

e. 100%

Objectives

At the end of this talk you will be able to:

- Remember to think about contraception in your clinical practice.
- To be comfortable using the CDC MEC for women with medical comorbidities.
- Instruct patients on correct method use
- Encourage women to use longer-term contraceptive methods.
- Address recent controversies and myths in contraceptive methods.
What we will not have time to address. . .

- Barrier methods
- Non-contraceptive uses of methods
- Fertility Awareness Based Methods
- Permanent sterilization

Jane is a 27 year-old gravida 0 woman taking combined oral contraceptive pills, who presents to your clinic for a health maintenance visit. She missed her last period and her pregnancy test is positive. She chooses to terminate the pregnancy, and wants to avoid another pregnancy for now.
6.4 Million US Pregnancies Annually

52% Intended
48% Unintended

6.4 Million U.S. Pregnancies Annually

52% Intended
23% Unintended No method used
25% Unintended Despite method use
Why did Jane get pregnant?

Jane tells you that she ran out of birth control pills last month, and that she tried to call the office for a refill, but the receptionist told her she was overdue for a pap smear. Today was the first day she could get an appointment.

Provider Barriers to Effective Contraception

• Requiring exam??
  – *Initiation*: BP check for estrogen-containing methods
    • Otherwise NO exam required
  – *Refills*:
    • Should not require pap smear to get refill!!
    • 1 year supply = 30% reduction in unplanned preg. than 3 mo supply¹

• Awareness about need for birth control
  – 48% using D or X med. counseled on contraception²

• Knowledge about contraindications
  – CDC Medical Eligibility Criteria

¹ Foster Obstet Gynecol 2011
Case: Counseling Issues

Jane has had migraine headaches since she was a teen. She has no aura and they have not changed with OCPs, but she wants to learn about other methods.

How do you approach counseling with her?

Helping patients choose the best method. . .

- **Safety**: Always balance against the risk of pregnancy
- **Efficacy**: Perfect use efficacy, Frequency of intervention
- **Non-contraceptive benefits**
- **Future pregnancy plans**
- **Patient Preference**: Convenience, Individual factors
Can my patient use this method???

CDC Medical Eligibility Criteria (MEC)

• Evidence-based guidelines for safety of methods with co-existing conditions
• Similar to WHO but US-specific
<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Can use the method</td>
</tr>
<tr>
<td>2</td>
<td>Can use the method</td>
</tr>
<tr>
<td>3</td>
<td>Should not use method unless no other method is appropriate</td>
</tr>
<tr>
<td>4</td>
<td>Should not use method</td>
</tr>
</tbody>
</table>
Synergistic effect of migraines, COC, aura: 

\[ OR = 8.7 \ (95\% \ CI 5.0-15.0) \]

Absolute risk of stroke is low!!

<table>
<thead>
<tr>
<th></th>
<th>No COC</th>
<th>COC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>6 per 100,000 ♀ /yr</td>
<td>12 per 100,000 ♀ /yr</td>
</tr>
<tr>
<td>Migraine</td>
<td>12 per 100,000 ♀ /yr</td>
<td>19 per 100,000 ♀ /yr</td>
</tr>
<tr>
<td>Migraine + aura</td>
<td>18 per 100,000 ♀ /yr</td>
<td>30 per 100,000 ♀ /yr</td>
</tr>
</tbody>
</table>

Stroke in pregnancy: 34 per 100,000 ♀ / year

Speroff & Darney Clinical Guide for Contraception 2005

Choosing a COC

[Images of various COC pill packages]
Choosing a COC

**Estrogen dose:**
- Low dose = < 50 mcg

**Progestin type:**
- 3rd generation progestin & VTE (desogestrel):
  - OR = 1.7 (1.4-2.0) [1]
- Drosperinone & VTE:
  - RR = 1.6 (1.3, 2.1) vs. No difference [3]

1. Kemmeren 2001 *BMJ*
2. Dinger 2007 *Contraception*
3. Lindegaard 2009 *BMJ*
4. Heinemann 2009 *Contraception*

ABSOLUTE RISK IS LOW!!
- Non-pregnant, no COCs: 4.4 per 10,000 ♀-yrs
- Desogestrel COCs: 6.5 per 10,000 ♀-yrs
- Drosperinone COCs: 7.8 per 10,000 ♀-yrs
- PREGNANCY: 29 per 10,000 ♀-yrs

**Unscheduled bleeding**

Choosing a COC

- Monophasic, Bi- or triphasic?
- Drosiprenone?
  - PMDD: fewer sx at 3 & 6 months – equivalent at 2 years
  - Acne: Overall, studies show equivalent to other pills

My initial approach:
- 30 or 35 mcg EE + 2nd generation progestin
- Monophasic

1. VanVliet Cochrane 2006
2. LaGuardia Contraception, 2003
3. Freeman Women's Health 2001
4. van Vloten Cuts 2002
Pill Instructions *

• Initiation:
  – If Sunday or Quick Start – backup for 7 days
  – System for remembering

• Continuation:
  – If miss one: take forgotten pill ASAP
  – If miss two: take forgotten pills every 12 hours
    • Continue and backup contraception x 7 days
    • If beginning of pack and unprotected sex: ECP
    • If extended cycle: no need for ECP
  – If miss more than two:
    • If unprotected sex: take ECP, restart OC next day
    • Backup for 7 days

• Antibiotics:
  – Rifampin is the only antibiotic which reduces efficacy of OCPs
  – Do not tell women to stop taking OCPs when they are on an antibiotic!!

How effective is the combined oral contraceptive for prevention of pregnancy?

Typical use ≠ Perfect use
Realities of Pill Use

New users:
Mean = 4.7 missed pills/cycle

Percent of Women (%)

Active Pills Missed

1. Potter Fam Plann Perspect, 1996
2. Hou Obstet Gynecol 2010

Contraception Methods

Least effective
Most effective

<83%
92%
94%
>99%

Permanent

Barrier
OCPs
Ring
DMPA (IM or SQ)
Progestin Implant
Copper IUD
LNG-IUS
Vasectomy
BTL
Hysteroscopic Vasectomy

Episodic
Daily
Weekly
Monthly
3 Mo's
3 yrs
5 yrs
10 yrs

Combined Hormonal
Progestin Only
IUC
Sterilization
Contraceptive Method Use, U.S.*

*Among the 38 million women currently using birth control

---

**Contraception Methods**

- Least effective
  - <83%
  - 92%
  - 94%
- Most effective
  - >99%

**Barrier**
- OCPs
- Patch
- Ring
- DMPA (IM or SQ)

**Progestin Only**
- Progestin Implant
- Copper IUD

**Combined Hormonal**
- LNG-IUS

**Permanent**
- BTL
- Vasectomy

---

Mosher Vital Health Statistics, 2010
Alan Guttmacher Institute, Facts In Brief, 2010.
<table>
<thead>
<tr>
<th>Intrauterine Contraception</th>
<th>LNG-IUS</th>
<th>Copper T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>5 years</td>
<td>10 years</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Lighter &amp; irregular</td>
<td>Same or heavier</td>
</tr>
<tr>
<td>Non-contraceptive benefits</td>
<td>• Menorrhagia &lt;br&gt; • Pelvic Pain &lt;br&gt; • Endo. hyperplasia</td>
<td>None</td>
</tr>
<tr>
<td>Hormone</td>
<td>Min. systemic absorption</td>
<td>No hormone</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Active cervicitis or PID</td>
<td>Severe anemia &lt;br&gt; Wilson’s disease &lt;br&gt; Copper allergy &lt;br&gt; Active cervicitis or PID</td>
</tr>
<tr>
<td>Efficacy</td>
<td>&gt;99%</td>
<td>&gt;99%</td>
</tr>
</tbody>
</table>

**IUD: Dispelling Common Myths**

- IUDs in fact:
  - DO NOT cause pelvic infection
  - DO NOT impair future fertility
  - CAN be used for nulligravidas
IUD and PID

- Current IUDs do NOT cause PID!!!
  - Transient increased risk at time of insertion with both IUDs
    - 22,908 insertions:
      - 9.7/1000 within 20 days
      - 1.4/1000 after 20 days
- Beyond time of insertion
  - Overall decreased risk with LNG IUS
  - No increased risk of Copper IUD

Farley Lancet 1992
Walsh Lancet 1998

IUC, Nulliparity & Infertility

- Nulliparity not a contraindication!!!
  - May have increased pain with insertion
  - May have increased risk of expulsion
- Case-control study of women with tubal factor 1° infertility
  - No association with prior IUD use (OR=1)

Is Jane a candidate for IUC? Who is?

Women of any reproductive age seeking long-term, highly effective contraception

- Contraindications to CHC or other methods
- No active cervicitis or PID
  - Screen women appropriately for GC/CT
  - Treat those with positive cultures

Every 3 years:
Single-Rod Implant

- Etonogestrel 60mcg/day
- Efficacy > 99%
- Very easy & well tolerated to insert
- 1 year continuation: 75%-90%

- Main side effect = bleeding (40%)
  - “irregularly irregular”

Blumenthal Eur J Contracept Reprod Health Care, 2008
Every 3 months:
Progestin Injection (Depo Provera)

• Medroxyprogesterone acetate 150 mg IM
  – One injection every 12-13 weeks

• Efficacy ~ 97%

• Side effects:
  – Delayed return to fertility (9-10 months)
  – Irregular bleeding, amenorrhea (50% at 1 yr)
  – Weight gain- 6 mo wt gain predicts future^1

• SQ low-dose (104 mg) version now available

---

DMPA & BMD

• BMD decreases by 1-2% per year

• FDA: limit to 2 yrs in young women.
  – WHO & ACOG do not agree w/ this!!
  – No clear evidence of increased fractures
  – Reverses by 12 mo’s after discontinuation.

• No indication for DEXA

• Weigh risks against risk of pregnancy

---

1. Bonny Contraception 2010
4. WHO 2005
5. ACOG 2008 Committee Opinion 415
Monthly: Contraceptive Vaginal Ring

- 15 mcg EE & 120 mcg desogestrel
- One ring each month:
  - “3 weeks in 1 week out”?
  - Ring out last 5 days of month
- Can stay out up to 3 hours
  - 20% expelled at least once during 3-week period

Ring Instructions

- Initiation:
  - First five days of menses – if not backup x 7 days
- The ring can be left in for up to 35 days
- May remove up to 3 hours (not recommended)
- If ring is out for more than 3 hours use back-up for 7 days
- Always have two rings on hand in case one is lost
- Rings may be stored at room temperature for up to 4 months
- Disposal: Fold over self. Place in solid waste. Do not flush down toilet.
- Ring floats in toilet

Miller Obstet and Gynecol, 2005.
Creinin Obstet Gynecol 2008
Weekly:
Transdermal Contraception “Patch”

- 20mcg EE & 150mcg norelgestromin
- One patch each week x 3 weeks, then week off
- Improved compliance than with pill (88% v. 78%)
- 46% experience at least one detachment in one cycle
- Less effective if > 90kg

Patch Instructions

- Initiation:
  - Prescribe replacement patches (up to 3)
  - If day other than first day menses – backup 7 days
- If the PATCH FREE interval is >9 days (late restart), apply a new patch and use backup contraception for 7 days
- No band-aids, tattoos, or decals on top of patch as this might alter absorption of hormones
- Smooth edges down when you first put it on
- Avoid the same site 2 consecutive weeks

Audet, JAMA, 2001
Creinin Obstet Gynecol/ 2008
Zieman M, Fertil & Steril, 2002
Patch Instructions

- Location of patch should not be altered mid-week
- Women should check the patch daily to make sure all the edges remain closely adherent to skin
- Single replacement patches are available through pharmacists
- Unlike pills, the time of day the patch is changed doesn’t matter
- Disposal: Fold over self. Place in solid waste. Do not flush down toilet

Emergency Contraception

**Levonorgestrel** 120 mcg x 1, up to **5 days**
- Behind the counter if > 17 yo

**Ulipristal Acetate** 30mg, up to **5 days** (FDA approved)
- Rx only

**Effectiveness:**¹,²
UPA is “non-inferior” to LNG:
1.4% vs. 2.2%
Meta-analysis of 3445 ♀
120 hrs: OR = .55 (.32-.93)

¹ Glasier 2010 Lancet
² Creinin 2006 Obstet Gynecol
Alternatives to LNG EC & Ulipristal acetate?

• **Copper IUD**
  – VERY effective (99%) as EC up to 7 days!¹
  – 1693 ♀: 0 pregnancies at 1 mo
  0.23/100 at 12 mo²

• Mifepristone (10, 25 or 50 mg)³
  – More effective than LNG

• Yuzpe regimen
  – More side effects and less effective³

¹. Belden 2011 Contraception
². Wu 2010 BJOG
³. Cheng 2008 Cochrane Database

Jane

• You counsel Jane about the other options available, emphasizing those with high efficacy that require less intervention. She ends up choosing a highly effective IUD which you place that same day.

Quick start
Rule out pregnancy, then start method immediately!!!
Summary

- Unintended pregnancy remains a common problem in the US
- CDC MEC help guide safe contraception choices
- Many effective, safe methods available!
  - Minimize barriers to contraception
    - Provider, systemic, and patient
  - Encourage more effective methods

References

- Many easily accessible resources exist to help solve contraception quandaries.
  - www.cdc.gov
  - www.acog.org
  - www.arhp.org
  - http://www.managingcontraception.com/
  - http://www.who.int/reproductivehealth/publications/family_planning
  - http://www.cochrane.org/
<table>
<thead>
<tr>
<th>Condition</th>
<th>Type</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key**
- Green: No contraindications.
- Red: Contraindications.
- Yellow: Precautions.

**Notes:**
- The chart only contains a subset of the recommendations for use.
- For complete guidance, visit [CDC's website](http://www.cdc.gov/reproductivehealth/).
Controversies in Women’s Health
December, 2012

New Guidelines for Menopause Management

Michael S. Policar, MD, MPH
Clinical Professor of Ob,Gyn, & RS
UCSF School of Medicine
policarm@obgyn.ucsf.edu

I have no commercial disclosures for this lecture
Key Points:
Position Statement
on Hormone Therapy


*Available at: menopause.org*

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full name</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET</td>
<td>Estrogen (E) therapy</td>
</tr>
<tr>
<td>EPT</td>
<td>Combined E+P therapy</td>
</tr>
<tr>
<td>HT</td>
<td>Hormone therapy (ET, EPT)</td>
</tr>
<tr>
<td>MHT</td>
<td>Menopausal hormone therapy</td>
</tr>
<tr>
<td>Progestogen</td>
<td>Progesterone or progestin (P)</td>
</tr>
<tr>
<td>CC-EPT</td>
<td>Continuous-combined E+P therapy</td>
</tr>
<tr>
<td>CS-EPT</td>
<td>Continuous-sequential E+P therapy</td>
</tr>
</tbody>
</table>
Let’s Get This Out of the Way….  

The WHI Re-analyzed

Act 1

Background: Late 1980s

• In 40 retrospective observational studies, both EPT and ET reduced the risk of heart attack by 50%
  – Most studies included women in their 50s
  – Women were self-selected for hormone use (or not); studies were subject to selection bias
• Conventional wisdom
  – All women should use HT for heart protection, unless there was a reason not to do so
  – Women with CVD risk factors, especially previous MI, stroke, HTN or diabetes, should use HT
Background: 1990s

• 1990: Wyeth requested that FDA add labeling to HT products that included cardioprotection
• FDA insisted that RCTs be performed to prove that HT improved CVD outcomes vs. placebo
• Two RCTs initiated to evaluate cardioprotection
  – HERS: secondary prevention trial
  – WHI: primary prevention trial
• Average age in both studies was 64 years old...necessary to measure differences in MI rates
• Women with menopausal symptoms excluded

Women’s Health Initiative (WHI)

• 1993-2005: RCT with 17,000 women
• Postmenopausal women 50-79 years old
  – 33%: 50-59 yrs old; 45%: 60-69 yo; 22% 70-79 yo
  – Average age: 64 years old
• End points
  – Primary prevention of MI and stroke
  – Hip fracture, various cancers
• Treatment arms
  – If uterus: CC-EPT (CEE+MPA) vs. placebo
  – If no uterus: ET (CEE) vs. placebo
**WHI: EPT Arm Study Results**
Released July 2002: Findings after 5.2 years

<table>
<thead>
<tr>
<th>Event</th>
<th>RR</th>
<th>Attributable Risk /10K/yr</th>
<th>Attributable Benefit/ 10K/yr</th>
<th>Number needed to harm or benefit/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart attack</td>
<td>1.29</td>
<td>7</td>
<td></td>
<td>1,100</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.41</td>
<td>8</td>
<td></td>
<td>1,200</td>
</tr>
<tr>
<td>Breast CA</td>
<td>1.26</td>
<td>8</td>
<td></td>
<td>1,300</td>
</tr>
<tr>
<td>TE event</td>
<td>2.11</td>
<td>18</td>
<td></td>
<td>600</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>0.63</td>
<td>6</td>
<td></td>
<td>1,700</td>
</tr>
<tr>
<td>Hip fractures</td>
<td>0.66</td>
<td>5</td>
<td></td>
<td>2,000</td>
</tr>
</tbody>
</table>

Discontinued early, as “risks greater than benefits”

**WHI : ET-Only Study Arm**
Released 2004: Findings after 7 years

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Change vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td>No difference in risk</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>No difference in risk</td>
</tr>
<tr>
<td>Stroke</td>
<td>Increased risk</td>
</tr>
<tr>
<td>Hip fractures</td>
<td>Decreased risk</td>
</tr>
<tr>
<td>Dementia, cognitive change (&gt; 65 years old)</td>
<td>Trend toward increased</td>
</tr>
</tbody>
</table>
The Women’s Health Initiative
- **Was** a drug study of the effect of hormones on CVD, cancer, fractures, and memory in older women (mainly in 60s, long post-menopausal)
- **Was not** a menopause study...
  - Only 3.5% subjects were “early menopause”
  - Excluded symptomatic menopausal women

**Should the WHI be used to evaluate the safety and efficacy of EPT in treating women with menopausal symptoms?**

**WHI: HT and Risk of CV Disease by Age and Years Since Menopause**

Roussow JE. *JAMA*. 2007: Combined secondary analysis

<table>
<thead>
<tr>
<th>Age at HT initiation</th>
<th>Heart attack</th>
<th>Stroke</th>
<th>Death from any cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–59 years</td>
<td>↓ 7%</td>
<td>↑ 13%</td>
<td>↓ 30%</td>
</tr>
<tr>
<td>60–69 years</td>
<td>↓ 2%</td>
<td>↑ 50%</td>
<td>↑ 5%</td>
</tr>
<tr>
<td>70–79 years</td>
<td>↑ 26%</td>
<td>↑ 21%</td>
<td>↑ 14%</td>
</tr>
</tbody>
</table>

“Women who initiated HT closer to menopause tended to have reduced CHD risk compared with the increase in CHD risk among women more distant from menopause, but this trend test did not meet our criterion* for statistical significance.”

*Statistically significant defined as p<0.01.
Clinical Implications: Unified Hypothesis

- **Mild cardioprotection**
  - Women in their early-mid 50s, who
  - Initiate HT soon after menopause, with
  - Few or no heart disease or stroke risk factors
  - And who use estrogen-only regimens

- **Increased heart disease risk**
  - Women in their mid-60s or later, who
  - Initiate HT long after menopause, who have
  - Heart disease or stroke risk factors
  - And who use estrogen and progestin regimens
HT & Venous Thromboembolism

- Oral HT increases VTE risk in menopausal women
- VTE risk emerges soon after HT initiation (1-2 y) and decreases over time
- Lower VTE risk with EPT or ET in women <60 y.o.
- Lower HT doses may be safer than higher doses, but no RCT evidence
- Possible lower VTE risk with transdermal than with oral ET, but no RCT evidence
- Risks fall into the “rare” category


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HT & Breast Cancer

- **EPT** use >4-5 years increased breast cancer risk
  - Increased absolute risk of EPT in WHI: “rare”
  - 4-6 additional cases/10,000/yr of EPT for ≥ 5 yrs
- **Estrogen only** regimens
  - WHI ET trial showed no increased risk after 7.1 yrs
    - 6 fewer cases/10,000 women/yr of ET use
  - Other studies showed that ET for < 5 yrs has little or no impact on breast cancer risk

Menopausal Hormone Therapy for the Primary Prevention of Chronic Conditions
USPSTF 2012

• The USPSTF recommends against the use of
  – EPT for prevention of chronic conditions in postmenopausal women
    • Grade: D Recommendation
  – ET for the prevention of chronic conditions in postmenopausal women who have had a hysterectomy
    • Grade: D Recommendation

Case Study

• Ms S is a 52 year old woman with moderate-severe hot flashes and difficulty getting to sleep
• Her menses were regular until one year ago, became irregular, and then stopped 6 months ago
• She has tried a number of herbal remedies, each of which helped for only a few months
• Her medical history, BP, physical exam are normal
• The hot flashes affect her work productivity and she wants to try something else
Would you recommend that she.....

1. Try a different over-the-counter supplement
2. Prescribe a SSRI or SNRI anti-depressant medication
3. Prescribe the lowest dose estrogen and progestin
4. Prescribe a “mid-range” dose of estrogen and progestin
5. Receive a consultation with an ObGyn to discuss this subject and have a treatment plan developed

Therapeutic Interventions

• Lifestyle changes
• Botanicals and PhytoSERMs
• Non-hormonal Rx medications
• Hormone Therapy (MHT)
Hot Flashes: Lifestyle Changes

- Exercise routinely, at least 3-4 days/week
- Cool room temperature, especially at night
- Dress in layers (remove outer layers if warm)
- Avoid hot and spicy foods
- Relaxing activities
- Avoid cigarettes
- Minimize alcohol

Botanicals and PhytoSERMs

*Probably better than placebo*
- Black cohosh

*No evidence of efficacy*
- Soy isoflavones
- Red clover isoflavones
- Evening primrose oil
- Dong quai
- Ginseng
- Vitamin E
- Chasteberry (Vitex)

- Not better than pbo
- Not better than pbo
- Not better than pbo
- Not better (as monox)
- Not better than pbo
- Not better than pbo
- No studies
**Botanicals: Black Cohosh**

- 14 trials reported, including 4 randomized trials using placebo and/or estrogen treatment arm
  - 3 of 4 RCTs found black cohosh to be beneficial
  - 12 of 14 trials reported *some* benefit
  - Currently, longest trial is 6 months
- NIH, large, randomized, prospective, 2-year trial
  - Preliminary data fail to show binding to E receptors
  - Binding to serotonin receptor noted

**Botanicals and PhytoSERMs**

- Positive effect of black cohosh vs placebo
  - Improvement is less than with estrogen
- Some of the impact is due to placebo effect, which is none-the-less therapeutic
- Relatively little risk of adverse effects
- **Reasonable first-line choice for women**
  - With mild menopausal symptoms
  - Who feel strongly about avoiding hormones
  - Who are willing to use medications that are not “proven” effective by EBM or regulated by FDA
### Non-Hormonal Hot Flash Therapies

<table>
<thead>
<tr>
<th>Medication</th>
<th>% treated patients with &gt;50% ↓HF</th>
<th>% placebo patients with &gt;50% ↓HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine</td>
<td>54-70%</td>
<td>30%</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>50-76%</td>
<td>35-57%</td>
</tr>
<tr>
<td>Sertraline</td>
<td>40-56%</td>
<td>21-41%</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>46-84%</td>
<td>27-47%</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>55%</td>
<td>36%</td>
</tr>
</tbody>
</table>

J Clinical Oncology 2009 (June)

### Gabapentin (GBP) and Hot Flashes (HF)

<table>
<thead>
<tr>
<th>Author</th>
<th>Dose</th>
<th>% HF↓ GBP</th>
<th>% HF↓ Placebo</th>
<th>% HF↓ Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butt DA 2008</td>
<td>300 mg TID</td>
<td>51%</td>
<td>26%</td>
<td>NA</td>
</tr>
<tr>
<td>Guttuso TJ 2003</td>
<td>900 → 2700 mg</td>
<td>54%</td>
<td>31%</td>
<td>NA</td>
</tr>
<tr>
<td>Pandya KG 2005</td>
<td>300 mg TID</td>
<td>46%</td>
<td>18%</td>
<td>NA</td>
</tr>
<tr>
<td>Reddy SY 2006</td>
<td>Up to 2400 mg</td>
<td>71%</td>
<td>54%</td>
<td>72%</td>
</tr>
</tbody>
</table>
**Prescription HT Options: ET and EPT**

<table>
<thead>
<tr>
<th></th>
<th>Oral</th>
<th>Transdermal</th>
<th>Intravaginal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ET</strong></td>
<td>• Micronized estradiol</td>
<td>• Patches</td>
<td>• Creams</td>
</tr>
<tr>
<td></td>
<td>• Conjugated equine estrogens (CEE)</td>
<td>• Gels</td>
<td>• Intravaginal tablet</td>
</tr>
<tr>
<td></td>
<td>• Synthetic conjugated estrogens</td>
<td>• Emulsion</td>
<td>• Rings</td>
</tr>
<tr>
<td></td>
<td>• Esterified estrogens</td>
<td>• Spray</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Estropipate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Estradiol acetate</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EPT</strong></td>
<td>• CC-EPT</td>
<td>• E+P combination patches</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CS-EPT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Hormone Therapy Regimens**

<table>
<thead>
<tr>
<th>Month 1</th>
<th>Month 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen Therapy (ET)</td>
<td>Estrogen</td>
</tr>
<tr>
<td>Continuous combined (CC) EPT</td>
<td>Progestin</td>
</tr>
<tr>
<td>Estrogen</td>
<td>Estrogen</td>
</tr>
<tr>
<td>Progestin</td>
<td>Progestin</td>
</tr>
<tr>
<td>Continuous-sequential (CS) EPT</td>
<td>Estrogen</td>
</tr>
<tr>
<td>Estrogen</td>
<td>Progestin 14d</td>
</tr>
<tr>
<td>Progestin 14d</td>
<td>Off for 14 d</td>
</tr>
<tr>
<td>Continuous-pulsed (CP) EPT</td>
<td>3d</td>
</tr>
<tr>
<td>3d</td>
<td>3d</td>
</tr>
</tbody>
</table>
Choice of HT Regimen

- If no uterus: estrogen only
- If uterus present
  - Goal is to avoid vaginal bleeding entirely, or, at least, to make it predictable
- Endometrial activity predicts bleeding pattern
  - Recent spontaneous or induced bleeding
    - Use continuous sequential
  - No bleeding for >2-3 cycles
    - Use continuous combined

OCs in Perimenopause

- Low-dose OCs (≤ 30 mcg estrogen) are commonly prescribed for perimenopausal women because they relieve menopausal symptoms and prevent pregnancy
  - Other benefits: cycle control, fewer ovarian cancers
- Other CHC (patch, ring) also may be helpful
- Progestin IUD and Depo Provera will not address vasomotor symptoms

NAMS position statement. Menopause 2007
Hormone Therapy Dosages

- Therapeutic goal is lowest effective estrogen dose (plus corresponding low progestogen dose for women with a uterus) consistent with individual treatment goals, benefits, and risks
- Lower doses better tolerated, may have more favorable benefit-risk ratio than standard doses
- Additional local ET may be needed for persistent vaginal symptoms


Hormone Therapy Starting Dosages

- Lower daily doses typically used with systemic ET
  - 0.3 mg oral CE
  - 0.5 mg oral micronized 17β-estradiol
  - 0.014-0.025 mg transdermal 17β-estradiol patch
- Typical lowest doses of progestogen
  - 1.5 mg oral MPA
  - 0.1 mg oral norethindrone acetate
  - 0.5 mg oral drospirenone
  - 50-100 mg oral micronized progesterone

**Choice of Estrogens**

- Start *low dose* transdermal or oral estrogen
- If suboptimal response, modify by
  - Change the estrogen dose (upward)
  - Change the estrogen preparation
  - Change delivery systems (oral → transdermal)
  - Consider an estrogen-androgen combination
- Injectable estrogen not recommended
  - Dosage equivalencies are not known
  - Estrogen cannot be discontinued easily

**HT Routes of Administration**

- No clear benefit of one route of administration for systemic ET
- Non-oral routes may offer both advantages and disadvantages compared with oral route
- *Transdermal ET may be associated with lower DVT risk than oral* (observational data, not RCTs)
- *Local ET preferred when solely vaginal symptoms*

**“First Line” Use: Transdermal Estrogen**

- Underlying medical conditions
  - History of DVT or PTE
  - High triglyceride levels
  - Gall bladder disease
- Need for “steady state” drug release
  - Daily mood swings (especially while on oral HT)
  - Migraine headaches
- Inability to use oral tablets
  - Stomach upset due to oral estrogen intake
  - Problems with taking a daily pill

**Off-Label EPT Uses**

- Insufficient endometrial safety evidence to recommend off-label use of
  - Long-cycle progestogen (ie, P every 3-6 months for 12-14 days)
  - Vaginal administration of progesterone
  - Levonorgestrel intrauterine system (Mirena)
  - Low-dose estrogen without progestogen
- Close endometrial surveillance recommended with these approaches

Compounded Hormone Therapy

• The *marketing* of compounded hormonal therapy
  – Only bioidentical hormones are used
  – Combination of 2 or 3 estrogens is more “natural”
  – Dosage is tailored to the individual
  – More “pure” than commercial products
  – Safer delivery systems (no dyes, etc)

• *The reality*
  – The *same* hormones are used in commercial and compounded 17b-E₂ and progesterone

Sources of Exogenous Hormones
Compounded Hormone Therapy

Compounded hormones will work about as well as commercial HT products, but...

- Value of adding E₁ + E₃ has not been evaluated
- Progesterone skin cream is not absorbed
- Compounded hormone doses are not standardized
- Salivary hormone levels are not useful
- FDA-approved HT products will offer
  - Bioidentical hormones
  - Choice of delivery systems
  - Formulary coverage/ lower out-of-pocket costs

Act 3

Practice Guidelines

How can your patient use these treatments safely, effectively, and conveniently?
Individualization of Therapy

- An individual risk profile is essential
- Each woman must be informed of her known risks
- Acceptance of HT risks varies with primary indication (e.g., relieve existing symptom or prevent disease)
- Benefit-risk ratio more acceptable for short-term symptom relief in a younger population
- Long-term HT or use in older women less acceptable
- Women with premature menopause have increased symptoms and risks if not treated


Explaining HT Risk

HT risk is related to

- A woman’s baseline disease risks
- Her age
- Age at menopause
- Cause of menopause
- Time since menopause
- Prior use of any hormone
- HT types, route of administration, doses used
- Emerging medical conditions during treatment

**Treatment of Hot Flashes**

- If mild symptoms, try lifestyle, CAM therapy
- Indications for hormone therapy
  - Moderate or severe symptoms
  - Non-hormonal treatments have failed
  - No interest in non-hormonal therapy
- Titrate estrogen dosage upward *if* needed
- When estrogen can’t be used, offer
  - SSRI or SNRI
  - Gabapentin, clonidine, a-methyldopa
  - Progestins alone
- Attempt discontinuation after 2 years

**Treatment of Sleep/ Irritability Symptoms**

- If mild symptoms
  - Lifestyle change, CAM therapy
- If severe symptoms or no response to above
  - Low dose HT, then titrate upward
  - If mood swings, transdermal E preferred
- Depression component, or no response to HT
  - SNRI or SSRI
HT and Vaginal Atrophy

- When HT is considered solely for this indication, local (not systemic) vaginal ET is recommended
- Progestogen generally *not indicated* with low-dose, local vaginal ET
- Vaginal lubricants often improve vaginal dryness and painful intercourse


### Vaginal Estrogen Therapies

<table>
<thead>
<tr>
<th>Product</th>
<th>Brand</th>
<th>Dosage</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated estrogen cream</td>
<td>Premarin cream</td>
<td>0.625 mg/ gram</td>
<td>Daily, then 1-3 time/wk</td>
</tr>
<tr>
<td>Estradiol cream</td>
<td>Estrace</td>
<td>0.01% (0.1 mg/ gm)</td>
<td>Daily, then 1-3 time/wk</td>
</tr>
<tr>
<td>Estradiol vaginal tablet</td>
<td>Vagifem</td>
<td>25 micrograms</td>
<td>Daily for 2 wks, BIW</td>
</tr>
<tr>
<td>Estradiol ring</td>
<td>Estring</td>
<td>7.5 mcg/ 24 hrs</td>
<td>Every 90 days</td>
</tr>
<tr>
<td>Estradiol ring*</td>
<td>Femring</td>
<td>0.05 mg/d 0.1 mg/d</td>
<td>Every 3 months</td>
</tr>
</tbody>
</table>

*Intended for use as *systemic* HT*
HT & Urinary Health

- Local ET may benefit some women with urge incontinence who have vaginal atrophy
- Unclear if ET by any route is effective for overactive bladder
- Controversial if local ET can improve stress incontinence (systemic ET may worsen or provoke it)
- Local vaginal ET may reduce risk of recurrent UTI
- No HT product approved for urinary health in US or Canada


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HT & Sexual Function

- Treatment of moderate to severe vaginal atrophy with systemic ET/EPT or local ET can relieve dyspareunia
- One oral systemic ET product FDA is approved for dyspareunia
- HT is not recommended as sole treatment of other sexual function problems (e.g., diminished libido)

HT & Cognitive Aging/Decline, Dementia

- HT not recommended at any age for the sole or primary indication of preventing cognitive aging or dementia
- HT seems to increase dementia incidence when initiated at ≥65 years old
- Inadequate data if HT started soon after menopause increases or decreases later dementia risk
- Limited data do not support HT for Alzheimer’s disease


HT and “Quality of Life”

- RCTs and retrospective studies show that HT has no effect on “quality of life” measures
- Many woman who wean from HT state that they “feel worse”...even after 20 years after menopause!
- Conventional wisdom
  - In women who “feel better on/ worse off” of HT, continue low dose HT if few or no risk factors
  - When (& how often) to re-attempt wean uncertain
  - Don’t start HT for solely for improving QOL
The Finale

Act 4

HT Discontinuance and Symptom Recurrence

• After 2 years of use, recommend drug vacation to determine whether HT is still needed
• Vasomotor symptom recurrence similar whether tapered or abrupt discontinuance
  – 25-50% chance of symptoms recurring when HT discontinued
• Decision to resume HT must be individualized

• Systemic HT is an acceptable option for healthy women up to age 59 or <10 years of menopause and who are bothered by moderate to severe menopausal symptoms.

• Individualization is key in the decision to use HT

• Consider quality-of-life priorities as well as her personal risk factors such as age, time since menopause, and her risk of blood clots, heart disease, stroke, and breast cancer.
**Plan**

- Palpable breast mass
- Non-Palpable breast mass
- Mastalgia
- Nipple Discharge
- Mastitis

**Gallup Poll: Leading Causes of Death in Women**

**Perceived**
- Breast CA: 38%
- Heart Dz: 18%
- Lung Ca: 9%
- Ovarian Ca: 9%
- Other: 17%
- Stress: 2%
- Lung Dz's: 1%

**Actual**
- Breast CA: 5%
- Heart Dz: 36%
- Lung Ca: 6%
- Ovarian Ca: 2%
- Other: 29%
- Lung Dz's: 9%
- Other Ca: 13%
Failure to diagnose breast cancer in a timely manner is a leading cause of malpractice claims

Common reasons:
- Unimpressive physical findings
- Failure to f/u with pt
- Palpable mass with negative mammo

Likelihood of Cancer in Dominant Breast Mass by Age

Of all discrete breast masses, about 10% are cancerous. (In contrast, 8% of abnormal mammos = cancer)
“Dominant Mass”?

- **Discrete or dominant mass** = stands out from adjoining breast tissue, definable borders, is measurable, not bilateral.

- **Nodularity or thickening** = ill-defined, often bilateral, fluctuates with menstrual cycle

- In women <40 referred for mass, only 1/3 had confirmed dominant mass

**Breast Mass: Diagnostic Options**

- Physical exam
- Ultrasound
- Mammogram
- Cyst aspiration
- Fine needle aspiration
- Core needle biopsy
- Excisional biopsy
A 42 yr old woman with no family or personal history of breast cancer has found a breast lump. She doesn’t know how long it has been there. It is not painful.

On exam, it is a discrete mass, 2 cm, relatively smooth, mobile and non-tender. She has no axillary lymphadenopathy.

What is your next step?

Q1: Palpable mass in 42 yo

Next step (pick one)?

A. Nothing now. Re-examine in 1-2 months
B. Ultrasound
C. Mammography
D. Office aspiration
E. FNAB
F. Core biopsy
Q1b: Palpable mass in 42 yo

A mammography was chosen and is negative. Next step (pick one)?

A. Re-examine in 1-2 months
B. F/u 1 year for annual exam
C. Ultrasound
D. Office aspiration
E. FNAB
F. Core biopsy

Q1c: Palpable mass in 42 yo

An ultrasound was chosen as the first step. It shows a cystic mass. Next step?

A. Re-examine in 1-2 months
B. F/u 1 year for annual exam
C. Office aspiration
D. FNA
E. Core biopsy
Step 1: Palpable Breast Mass

- **Determine if mass is cystic or solid**
  - Simple cysts are benign and don’t require further evaluation
  - 20-25% of palpable masses are simple cysts, most occurring in 40-49 yo’s
  - Options?: Ultrasound, office aspiration, FNA, core needle biopsy

Breast Exam

- Neither sensitive (50-60%) nor specific (60-90%) (even when done by experts)
- Cannot reliably distinguish cyst from solid
- Nonetheless, it is important for determining if mass is discrete (vs nodularity or thickening), is a necessary adjunct to mammogram and is required for follow-up of masses
- Perform in 2 positions, methodical, spirals or strips
- Mark mass prior to biopsy so others can find it
Ultrasound

- **Primary Use:** Classify mass as cystic or solid
- Guidance for cyst aspiration or biopsy
- Adjunct to evaluate symmetric densities detected by mammography
- Can be the first test performed & if cyst is confirmed—the only test required

**Fibroadenoma**
- Well-circumscribed, superficial

**Cancer**
- Irregular, deep

**Cyst**
- Anechoic, well-circumscribed,

Ultrasound is 98-100% accurate for diagnosis of simple cysts. However, for solid masses, it cannot reliably distinguish benign from malignant.
Cyst Aspiration

- **Simple office procedure:** 20-23 gauge needle and syringe, ultrasound guidance optional, specialized training not necessary
- **Primary Use:** Confirm mass is cystic
- **Secondary use:** Relieve pain/pressure due to symptomatic cyst
- **Benefits:** If cystic fluid obtained, establishes immediate diagnosis and provides symptomatic relief

---

1. Obtain oral consent from patient.
2. Clean area over the lump with an alcohol swab.
3. Immobilize the lump between the index and middle fingers of your nondominant hand.
4. Use a 23-gauge 1-in disposable needle with a semiopaque needle hub attached to a 3-mL or 5-mL syringe.
5. Introduce a small amount of air into the syringe barrel to break the seal.
6. Hold the syringe with your dominant hand, as you would a pen, and insert the needle into the centre of the lump (A).
7. Use the fingers of your nondominant hand to stabilize the distal aspect of the syringe while walking the fingers of your dominant hand up the syringe to pull back on the plunger to aspirate (B).

*Figure 2: Aspirating a breast lump. Reprinted, with permission, from Can Fam Physician 1999;45:1928.*
Cyst Aspiration (cont’d)

Adequate/reassuring if:
1. Cyst fully collapses (no residual mass)
2. Fluid is not brown/red (cloudy ok)
3. Does not re-accumulate (i.e. frequent f/u)

- If all are true, no need to send fluid.
- F/u in 1-3 months to ensure no reaccumulation or residual mass
- If no fluid or if bloody → further workup

Fine Needle Aspiration: QUIZ

- FNAB should be done by an experienced cytopathologist or breast surgeon? ....TRUE OR FALSE?

- A diagnosis of FATTY TISSUE on FNA means what?

- When should you FOLLOW-UP a woman with a palpable mass and negative FNA and mammogram?
### Fine Needle Aspiration Biopsy

- **Primary Use:** Diagnosis of solid masses
- Least invasive biopsy method
- Sensitivity is operator dependent:
  - For experienced personnel, 92-98%
  - For untrained personnel, 75% Average (as low as 65%).
- Experienced cytopathologist necessary to interpret
- Cannot diagnose DCIS, atypical hyperplasia or infiltrating carcinoma
- A non-diagnostic result in the setting of a discrete mass requires further work-up (possible sampling error)
Palpable mass: Diagnostic Mammography

- Cannot accurately differentiate benign from malignant masses or cystic from solid
- Poor sensitivity in young women due to density
- 15-20% of mammos are normal in women with palpable mass
- Primary use: Screen opposite breast (in women >40 yo) and identify other non-palpable suspicious areas
- Secondary use: Further classification of the palpable mass

**Even if the mammogram is normal, further work-up is required**

Breast Cyst

Can’t distinguish cyst from solid on mammogram

Cyst is anechoic on ultrasound
Breast Density

Spiculated mass

Small Cancer

Spiculated mass
Core Needle Biopsy

- **Primary Use:** Diagnosis of solid masses, f/u of non-diagnostic FNAB
- Unlike FNAB, it can distinguish DCIS from invasive disease and because it is a tissue specimen, interpretation is easier
- Few direct comparisons to FNAB for palpable lesions: Studies mixed for sensitivity—some showing FNA better and some with CNB better. Similar specificity.

Core Needle Biopsy (cont’d)

- Like FNAB, requires training to prevent false negatives due to sampling error
- Used instead of FNAB by consultant preference or where cytopathology service not skilled in interpretation
- Also preferred for evaluation of non-palpable lesions
Question 1

A 42 year old woman with no family or personal history of breast cancer has found a breast lump. She doesn’t know how long it has been there. It is not painful.

On exam, it is a discrete mass, about 2 cm, relatively smooth, mobile and non-tender. She has no axillary lymphadenopathy.

What is your next step?

So, what is the best first step?

• **First step = determine if cystic or solid.**
• How depends on your institution (availability and expertise of various services) and whether patient is symptomatic
• **FNAB:** Therapeutic, diagnostic and cost-efficient
• **U/S:** Similar in cost to FNAB, but FNAB more cost effective b/c 80% of masses are NOT cystic on U/S and will require FNAB to further evaluate
• **If FNAB not available:** U/S first will eliminate need for core biopsy in 20% that do have cysts
So, what is the best first step?

- **Office aspiration:** Reasonable 1st step esp if symptomatic. If not cystic, will require biopsy
- **Mammography:** not best 1st step b/c can’t reliably distinguish benign from malignant or cystic from solid (but is usually part of a complete evaluation)
- **F/U 1-2 mos:** Could be ok in young woman (<40) who will reliably follow-up. Discuss options, get agreement, document well. If mass persists, go to U/S or FNA.

Triple test

- Improved accuracy by combining:
  1. FNAB or core biopsy
  2. Mammography (or ultrasound)
  3. Physical exam
- When all 3 results concordant, 99% accuracy
- However, PE adds little b/c not specific. Its role is simply to document dominant palpable mass
- If any one is suspicious, core or excisional biopsy
Accuracy of triple test

Mass “benign “on Palpation

Step 2: for a cystic mass…

- If symptomatic, aspirate
- If diagnosed by ultrasound and no aspiration is done, f/u 1 year.
- If aspirated and fluid is not bloody, f/u 1-3 months to ensure no residual mass or re-accumulation
- For any patient >40, also get mammo for screening (>50 recommend, >40 shared decision)
**Step 2: for a solid mass**

**Biopsy** (FNA or core needle biopsy)

PLUS

**Mammogram** (to further characterize mass and to screen rest of breasts)

- If both are negative, f/u 3-6 months
- If either is equivocal or results are not concordant, refer to breast surgeon for further evaluation

---

**Ultrasound F/u instead of biopsy for solid mass?**

- 2 small retrospective cohort studies—largest n=312 with palpable mass & U/S= “probably benign”
- Mostly young women so low pretest probability of cancer (avg age 34yo)
- Strict criteria for calling lesion “probably benign”
- 2 of 312 were cancer. NPV=0.6%.
- Conclude ok to not biopsy and follow with q 6mo u/s for 2 yrs (sim to f/u of birads3 mammo)
- Caution: retrospective

Park, Acta Radiologica, 2008
How are we doing?

- In a study of women with a palpable mass and negative mammo, only 57% received any subsequent evaluation.
  - Latinas, obese and uninsured less likely to have any subsequent evaluation
- A recent study of delay in diagnosis found the most common reason was inappropriate reassurance of women with a lump and normal mammogram

Summary: Palpable Breast Mass

- Choice of work-up often depends on availability and expertise of FNA, U/S and core needle biopsy
- None of these tests is 100% accurate, maintain a high index of suspicion
- Triple test is gold standard. If any of the 3 tests is discordant continue work-up
- Frequent f/u even for masses thought to be benign to detect false negatives
**Domestic Breast Mass**

- **Simple cyst**
  - If aspirate and no residual lump, fluid not bloody then do CBE 4-6 wks. If u/s, no further w/u.

- **Solid or complex cyst**
  - Do FNA or core bx

  - **Cancer**
    - Treat
  
  - **Atypical, suspicious**
    - Core or excisional biopsy
  
  - **Benign**
    - Positive Mammo
      - More imaging, core or excision bx
    
    - Negative Mammo
      - CBE 3-6 mos
  
  - **Non-diagnostic**
    - Repeat FNA, core or excision biopsy

*Aspirate=office aspiration or FNAB*  
Adapted from Kerlikowske, Ann Int Med, 2003
Q1b: Palpable mass in 42 yo

A mammography was chosen and is negative. Next step (pick one)?

A. Re-examine in 1-2 months
B. F/u 1 year for annual exam
C. Ultrasound
D. Office aspiration
E. FNA
F. Core biopsy

Mammo cannot distinguish cyst from solid and is negative in 15% with palpable mass so need to proceed with work-up from Step 1 ie cyst vs solid

Q1c: Palpable mass in 42 yo

An ultrasound was chosen as the first step. It shows a cystic mass. Next step?

A. Re-examine in 1-2 months
B. F/u 1 year for annual exam
C. Office aspiration
D. FNA
E. Core biopsy

Simple cysts are benign and no further work-up is required. If the cyst is symptomatic, may aspirate in office.
### Non palpable lesions

**Pre/Post Test Probability of cancer based on mammo results and age**

**Table 4. Risk for Breast Cancer Based on Age and Mammographic Interpretation**

<table>
<thead>
<tr>
<th>Age and Type of Screening Examination</th>
<th>Risk for Breast Cancer before Mammography</th>
<th>Risk for Breast Cancer Based on Age and Mammographic Interpretation (BI-RADS Assessment)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Probable benign finding (3)</td>
<td>Suspicious abnormality (4)</td>
</tr>
<tr>
<td>40-49 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First screening</td>
<td>0.003</td>
<td>0.004</td>
</tr>
<tr>
<td>Subsequent screening</td>
<td>0.0015</td>
<td>0.0046</td>
</tr>
<tr>
<td>50-59 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First screening</td>
<td>0.006</td>
<td>0.007</td>
</tr>
<tr>
<td>Subsequent screening</td>
<td>0.0028</td>
<td>0.009</td>
</tr>
<tr>
<td>60-69 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First screening</td>
<td>0.012</td>
<td>0.016</td>
</tr>
<tr>
<td>Subsequent screening</td>
<td>0.0017</td>
<td>0.011</td>
</tr>
<tr>
<td>70+ y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First screening</td>
<td>0.014</td>
<td>0.017</td>
</tr>
<tr>
<td>Subsequent screening</td>
<td>0.0037</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* BI-RADS = Breast Imaging Reporting and Data System

† Based on the prevalence of breast cancer per 100,000 first screening examination for first screening (6) on Surveillance, Epidemiology, and End Results cancer statistics for incidence of invasive breast cancer for subsequent screenings (45), and on estimated likelihood ratios. Adapted with permission from Kerlikowske et al. (34); JAMA, 1996, 276(4):42. Copyrighted 1996, American Medical Association.

Kerlikowske, Annals Int Med, 2003
Follow-up of abnormal screening mammogram

If normal, repeat screen 6 mos then q 1-2 yrs
Consider breast exam to see if lesion is palpable & biopsiable

What about dense breasts?

- Recent law passed mandating all women be informed if they have dense breasts
- Breast density (birads 4 or 5) has 2.0 fold increase breast cancer risk
- Breast density assoc with decreased sensitivity on mammogram
- Digital mammography has higher sensitivity than traditional mammo in women with dense breasts
What to do about dense breasts?

- Recommend digital mammography
- Consider yearly instead of biennial mammography (no evidence)
- Ultrasound follow-up? no RCT’s in women with only breast density as risk factor, increases detection but much higher biopsy rate, unknown if increased detection leads to better mortality.
- Legislators should not practice medicine!
Breast Pain

- 2/3 - 3/4 report it
- > 1/2 of breast visits
- Etiology unknown: not associated with prolactin, estrogen or progesterone levels
- 2 types: cyclic & non-cyclic
- Both types chronic, relapsing especially if severe or early onset
- Severe breast pain interferes with sex (46%), activity (36%), social (13%), work (6%)

Mastalgia: Treatment

- Work-up: risk factor evaluation, exam, mammo if >40 years
- Determine effect on QOL
- 60-80% resolve spontaneously.
- Reassurance often sufficient
Mastalgia: Treatment

Proven in RCT’s:
- NSAID’s (topical and oral)
- Evening Primrose Oil
- Iodine
- Vitex agnus castus extract-containing solution (VACS)
- Gestrinone (N/A in US)
- Progesterone vaginal cream
- Bromocryptine
- Danazol
- Tamoxifen

No benefit (per RCT’s, though many are small and likely underpowered)
- Caffeine restriction
- Vitamin E
- Vitamin B6
- Diuretics
- Provera
- Soya protein
- Isoflavones

Other: Supportive, well fitting bra, bra at night, trigger point injections for localized pain, OCP’s—help some, make worse in others. If on OCP, try lower dose of Estradiol

Topical NSAID for mastalgia

Diclofenac topical (Voltaren) q 8hr vs placebo cream. Randomized, double-blinded

Table 2. Average Change in Pain Scores Between and Within Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Before treatment</th>
<th>After 6 mo treatment</th>
<th>p Value*</th>
<th>Change in pain score</th>
<th>p’ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclic mastalgia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment (Ia)</td>
<td>30</td>
<td>7.13 (1.38)</td>
<td>1.26 (1.25)</td>
<td>0.0001</td>
<td>5.87 (1.22)</td>
<td></td>
</tr>
<tr>
<td>Placebo (Ib)</td>
<td>30</td>
<td>7.23 (1.50)</td>
<td>5.93 (1.20)</td>
<td>0.0001</td>
<td>1.30 (1.34)</td>
<td></td>
</tr>
<tr>
<td>Non-cyclic mastalgia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment (IIa)</td>
<td>24</td>
<td>7.16 (1.09)</td>
<td>0.83 (0.91)</td>
<td>0.0001</td>
<td>6.33 (1.34)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Placebo (IIb)</td>
<td>24</td>
<td>7.37 (1.05)</td>
<td>6.25 (1.07)</td>
<td>0.0001</td>
<td>1.12 (1.11)</td>
<td></td>
</tr>
</tbody>
</table>

Data presented as mean values (standard deviation).
*Changes within groups (before versus 6 months after).
*Changes in pain within groups, Ia versus Ib and IIa versus IIb, respectively; Ia versus IIa, p = 0.53, Ib versus IIb, p = 0.96, respectively.

Colac, Journal of the American College of Surgeons, April 2003
Mastalgia: Prescribing Guide

Proven in RCT’s:

• **NSAID’s** (topical diclofenac q 8hr very effective in 3 RCTs; oral NSAIDs—moderately effective in some but not all RCTS)

• **Evening Primrose Oil**: 1000mg tid for at least 1 mo trial, >$2/day, mild nausea. Recent meta-analysis showed no benefit

• **Bromocriptine**: increase dose gradually to decrease side effects (nausea, dizziness, orthostatic hypotension, headache). 1.25 mg qhs, increase by 1.25 mg every week until 5 mg/day.

• **Danazol**: best of the endocrine agents but virulizing side effects make it less desirable, teratogenic, expensive. Start at 200mg qd. Taper down as tolerated to 100mg every other day or qd during luteal phase.

Proven in RCT’s (continued):

• **Tamoxifen**: 10 mg qd, hot flashes, expensive

• **Torimefin**: 30 mg qd, vag d/c, irreg menses

• **GnRH agonists**: very expensive, menopausal side effects, can only use for 6 months due to bone loss.

• **Local Injections**: trigger point injection of 1% lidocaine (1cc) and methyl prednisone (40mg). Half require second injection in 2-3 months.
Nipple Discharge

- Usually benign or malignant?  
  benign
- Most common cause of unilateral discharge?  
  intraductal papilloma
- Other causes: duct ectasia, nipple eczema, Paget disease
- If associated with mass, more likely to be cancer (but cancer rarely presents with nipple d/c)

Physiologic:
- Due to galactorrhea (ie increased prolactin) or nipple stimulation
- With compression
- Multiple ducts
- Clear, yellow, white
- No mass

Pathologic:
- Papilloma, cancer
- Spontaneous
- Single duct
- Bloody
- Mass present
### Nipple Discharge: Diagnosis

**Physiologic:**
- History: running, breast stimulation
- Prolactin, TSH
- Meds: Psychotropics

**Pathologic (Spont, unilat):**
- Isolate involved duct
- Hemoccult to confirm blood, cytology not useful
- Mammography with retro-alveolar views
- Galactography controversial
- Surgery referral

### Mastitis

- 2 types: lactating vs non-lactating
- Primary vs secondary (cellulitis, folliculitis, hyradinitis, sebaceous cyst)

### Cellulitis
Lactational Mastitis

- Suspect in any breast-feeding woman with a fever and malaise
- Often wedge shaped redness over involved duct
- Staph, Strept—(community acquired MRSA becoming more common so do culture of milk)

Non-Lactational Mastitis

- Difficult to treat
- Often chronic, recurrent
- Peri-areolar: young (avg 32), 90% are smokers, central pain, nipple retraction and discharge, often assoc with abscess
- Peripheral: elderly, usually associated with underlying disease (diabetes) or trauma
- Gram negatives, staph, strept, anaerobes
Mastitis Treatment

**Lactational**
- Increase feeding, warm compresses
- Keflex, Dicloxicillin
- IV if not better quickly
- Septra or Clinda for community acquired MRSA

**Non-Lactational**
- Include anaerobic coverage
- Clindamycin or Flagyl + Ancef or Nafcillin

**Biopsy if recurrent or doesn’t resolve**

Cancer can mimic mastitis

Inflammatory Cancer
Breast Abscess

- Suspect if “lump” on exam or if mastitis not responding to abx
- Ultrasound to confirm
- Get culture
- Aspiration now preferred over I&D
- Sometimes need repeated aspirations
- I&D often assoc with poor cosmetic result or fistula

The End…. Questions
Common Dermatologic Disorders: Tips for Diagnosis and Management

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University of California, San Francisco

DISCLOSURE OF CONFLICTS OF INTEREST

Lindy P. Fox, MD

I have no relevant conflicts of interest to disclose.
Outline

• Approach to the itchy patient
• How to really treat eczema
• Acne in the adult
• Rosacea
• Perioral dermatitis
• Hair 101
• Skin cancer (melanoma)
• Sunscreens

Approach to the itchy patient
Question 1

- 57 F with 3 months of itch
- started on lower extremities
- No response to antifungal creams and OTC hydrocortisone cream
- Showers 2 x/day with hot water, uses an antibacterial soap, and does not moisturize

Question 1: The Best Diagnosis Is

1. Asteatotic dermatitis
2. Pruritus of renal failure
3. Nummular dermatitis
4. Tinea corporis
5. Neuropathic pruritus
Question 2
68M with ESRD complains of generalized itch

Question 2: The Best Diagnosis Is

1. Asteatotic dermatitis
2. Pruritus of renal failure
3. Nummular dermatitis
4. Tinea corporis
5. Neuropathic pruritus
Pruritus = the sensation of itch

• Itch can be divided into four categories:
  1. Pruritoceptive
     • Generated within the skin
     • Itchy rashes: scabies, eczema, bullous pemphigoid
  2. Neurogenic
     • Due to a systemic disease or circulating pruritogens
     • Itch “without a rash”
  3. Neuropathic
     • Due to anatomical lesion in the peripheral or central nervous system
     • Notalgia paresthetica, brachioradial pruritus
  4. Psychogenic itch

Pruritus- History

• Suggest cutaneous cause of itch:
  – Acute onset (days)
  – Related exposure or recent travel
  – Household members affected
  – Localized itch
• Itch is almost always worse at night
  – does not help identify cause of pruritus
• Aquagenic pruritus suggests polycythemia vera
• Dry skin itches
Pruritus- Physical Exam

Are there primary lesions present?

- yes
  - Pruritoceptive

- no
  - Neurogenic, Neuropathic, or Psychogenic

Question 1

- 57 F with 3 months of itch
- Started on lower extremities
- No response to antifungal creams and OTC hydrocortisone cream
- Showers 2 x/day with hot water, uses an antibacterial soap, and does not moisturize

Nummular dermatitis
Case 2
68M with ESRD complains of generalized itch

Linear Erosions in “Butterfly” Distribution
Pruritus “Without Rash”

Causes of Neurogenic Pruritus
(Pruritus Without Rash)

• 40% will have an underlying cause:
  • Dry Skin
  • Liver diseases, especially cholestatic
  • Renal Failure
  • Iron Deficiency
  • Thyroid Disease
  • Low or High Calcium
  • HIV
  • Medications
  • Cancer, especially lymphoma (Hodgkin’s)
Linear erosions due to pruritus in patient with cholestatic liver disease

Workup of “Pruritus Without Rash”

- CBC with differential
- Serum iron level, ferritin, total iron binding capacity
- Thyroid stimulating hormone and free T4
- Renal function (blood urea nitrogen and creatinine)
- Calcium
- Liver function tests
  - total and direct bilirubin, AST, ALT, alkaline phosphatase, GGT, fasting total plasma bile acids
- HIV test
- Chest X-ray
- Age-appropriate malignancy screening, with more advanced testing as indicated by symptoms
Neuropathic Pruritus

- Notalgia paresthetica
- Brachioradial Pruritus
  - Localized and persistent area of pruritus, without associated primary skin lesions, usually on the back or forearms
- Workup= MRI!!
  - Cervical and/or thoracic spine disease in ~100% of patients with brachioradial pruritus and 60% of patients with notalgia paresthetica
- Treatment- capsaicin cream TID, neurontin
  - Surgical intervention when appropriate

Notalgia Paresthetica
Treatment of Pruritus

- Treat the underlying cause if there is one
- Dry skin care
  - Short, lukewarm showers with Dove or soap-free cleanser
  - Moisturize with a cream or ointment BID
    - Cetaphil, eucerin, vanicream, vaseline, aquaphor
- Sarna lotion (menthol/phenol)
- Topical corticosteroids to inflamed areas
  - Face- low potency (desonide ointment)
  - Body- mid to high potency (triamcinolone acetonide 0.1% oint)

Antihistamines for Pruritus

- Work best for histamine-induced pruritus, but may also be effective for other types of pruritus
- First generation H1 antihistamines
  - hydroxyzine 25 mg QHS, titrate up to QID if tolerated
- Second generation H1 antihistamines
  - longer duration of action, less somnolence
  - cetirizine, loratidine, desloratidine, fexofenadine
Systemic Treatments for Pruritus

• Doxepin - 10mg QHS, titrate up to 50 mg QHS
  – Tricyclic antidepressant with potent H1 and H2 antihistamine properties
  – Good for pruritus associated with anxiety or depression
  – Anticholinergic side effects
• Paroxetine (SSRI)- 25- 50 mg QD
• Mirtazepine- 15-30 mg QHS
  – H1 antihistamine properties
  – Good for cholestatic pruritus, pruritus of renal failure
• Gabapentin- 300 mg QHS, increase as tolerated
  – Best for neuropathic pruritus, pruritus of renal failure

Eczemas
Eczema (=dermatitis)

- Group of disorders characterized by:
  1. Itching
  2. Intraepidermal vesicles (= spongiosis)
     - Macroscopic (you can see)
     - Microscopic (seen histologically on biopsy)
  3. Perturbations in the skin’s water barrier
  4. Response to steroids

Eczemas

- Atopic Dermatitis
- Hand and Foot Eczemas
- Asteatotic Dermatitis (Xerotic Eczema)
- Nummular Dermatitis
- Contact Dermatitis (allergic or irritant)
- Stasis Dermatitis
- Lichen Simplex Chronicus
Asteatotic Dermatitis

Nummular Dermatitis
Eczema
Good Skin Care Regimen

- Soap to armpits, groin, scalp only (no soap on the rash)
- Short cool showers or tub soak for 15-20 minutes
- Apply medications and moisturizer *within 3 minutes* of bathing or swimming

Eczema
Topical Therapy

- Choose agent by body site, age, type of lesion (weeping or not), surface area
- For Face:
  - Hydrocortisone 2.5% Ointment BID
  - If fails, aclometasone (Aclovate), desonide ointment
- For Body:
  - Triamcinolone acetonide 0.1% Ointment BID
  - If fails, fluocinonide ointment
- For weepy sites:
  - soak 15 min BID with dilute Burrow's solution (aluminum acetate) (1:20) for 3 days
Eczema
Oral Antipruritics

• Suppress itching with nightly oral sedating antihistamine

• If it is not sedating it doesn’t help
  – i.e. Claritin, Allegra, Zyrtec not useful

• Diphenhydramine, Hydroxyzine 25-50mg, Doxepin 10-25mg

Eczema
Severe Cases

• Refer to dermatologist

• Do not give systemic steroids

• We might use phototherapy, hospitalization, immunotherapy

• Beware of making the diagnosis of atopic dermatitis in an adult - this can be cutaneous T cell lymphoma!
Question 3: The diagnosis is:

1. Acne
2. Rosacea
3. Seborrheic dermatitis
4. Perioral dermatitis
5. Contact dermatitis

Approach to the Adult Acne Patient
Acne Treatment Options- Topical

• Benzoyl peroxide
• Antibiotics- clindamycin, erythromycin, combination benzoyl peroxide and either of above
• Sulfur based preparations
• Azelaic acid
• Retinoids

Acne Treatment Options- Systemic

• Antibiotics
  – Doxycycline 100 mg po BID
  – Minocycline 50-100 mg po BID
  – Tetracycline 500 mg po BID
• Oral contraceptives
• Spironolactone
• Isotretinoin
Pathogenesis and Clinical Features of Acne

• Pathogenesis (treatment targets)
  – Excess sebum
  – Abnormal follicular keratinization
  – Inflammation from *Propionibacterium acnes*

• Clinical features
  – Non-inflammatory open and closed comedones (“blackheads and whiteheads”)
  – Inflammatory papules and pustules
  – Cystic nodules

Acne Treatment

• Mild inflammatory acne- benzoyl peroxide + topical antibiotic (clindamycin, erythromycin)
• Moderate inflammatory acne- oral antibiotic (tetracyclines) (with or without topicals)
• Comedonal acne - topical retinoid
• Acne with hyperpigmentation- azelaic acid
• Acne/rosacea overlap or if also has seborrheic dermatitis- sulfur based preparations
• Hormonal component- oral contraceptive, spironolactone
• Cystic, scarring- isotretinoin
  – Teratogenic, hypertriglyceridermia, transaminitis, chelitis, xerosis, alopecia (telogen effluvium)
Topical Retinoids

• Side effects
  – Irritating- redness, flaking/dryness
  – May flare acne early in course
  – Photosensitizing
  – Tazarotene is category X in pregnancy

Topical Retinoids- How to Use Them

• Warn patients of side effects
• Start with a low dose: tretinoin 0.025% cream
• Wait 20-30 minutes after washing face to apply
• Use 1-2 pea-sized amount to cover the whole face
• Start BIW or TIW
• Moisturize 30 minutes after applying
• If using another topical acne therapy, use on alternate days
• Sunscreen daily
Acne in Adult Women

• Often related to excess androgen or excess androgen effect on hair follicles
• Other features of PCOD are often not present—irregular menses, etc.
• Serum testosterone can be normal
• Spironolactone 50 mg-100mg daily with or without OCP’s can be very effective, especially in women with lower facial acne

Rosacea
Rosacea

- Chronic inflammatory condition of the central face (nose, cheeks, chin)
- Caucasians with fair skin
- F>M
- Middle age (30-50)
- Many types:
  - Telangiectatic- redness and telangiectasias
  - Papulopustular- no comedones
  - Rhinophymatous

Rosacea- Triggers

- Alcohol
- Sunlight
- Hot beverages (heat)
- Hot, spicy food
- If it makes you flush it can flare rosacea
- Rosacea is NOT related to androgens!!
Rosacea- Treatment

• Medical treatment - papular/pustular rosacea
  – Topical agents
    • Metronidazole
    • Sulfur/sulfacetamide
  – Oral antibiotics (months to years to life)
    • Doxycycline 100 mg BID
    • Cefadroxil 500 mg BID
    • Amoxicillin 500 mg BID
  – SUNSCREEN
• Surgical (laser)
  – Telangiectatic, rhinophymatous

Steroid Rosacea

• Topical steroids may exacerbate or induce an acneiform eruption resembling rosacea
• Treatment
  – stop the topical steroids
  – oral tetracyclines (doxycycline)
• Rosacea may flare severely when the steroids are stopped
Perioroficial Dermatitis

- Women aged 25-35
- Extremely common
- Tiny papules, papulovesicles in same stage of development
  - Grouped and might come together to form plaques
- May sting, itch, burn
- Perioroficial- eyes, mouth, upper lip, peri--nares
  - Narrow spared area around the lips
- May be triggered by topical steroid use to the face
Perioral Dermatitis- Treatment

• Discontinue topical steroids
• Topical
  – Clindamycin
• Systemic (4-6 week course)
  – Doxycycline 100 mg BID
  – Tetracycline
  – Minocycline
  – Erythromycin
  – Azithromycin
• Usually does not recur

Hair 101

Too little hair
Too much hair
Hair Stats 101

• Anagen 90-95%
  – Growing hair, lasts 2-6 years
• Catagen
  – Programmed cessation of hair growth, a few weeks
• Telogen 5-10%
  – Shedding, 3-4 months
• Length of hair is determined by length of anagen phase
• Normal amount of shedding- 50-150 hairs/day

Alopecias

Non-Scarring

• Focal
  – Alopecia areata
  – Trichotillomania
• Diffuse
  – Telogen effluvium
  – Androgenetic alopecia

Scarring

• Neutrophilic predominant
  – Folliculitis decalvans
  – Dissecting cellulitis of the scalp
• Lymphocytic predominant
  – Lichen planopilaris
  – Pseudopelade
Telogen Effluvium

• Increased shedding of normal telogen hairs
  – Response to pathologic or normal physiologic change in health status
  – Chronic form with no identifiable cause exists
• Shedding begins 3-4 months after event
• Physical exam
  – Diffuse thinning
  – Hair pull (gentle tug) positive ≥ 2 telogen hairs
• Prognosis- full recovery
• Treatment- remove trigger, minoxidil

Telogen Effluvium- Causes

• Postpartum (physiologic)
• Postfebrile
• Severe infections
• Severe, chronic psychological stress
• Post major surgery
• Endocrinopathy (thyroid)
• Extreme diets
• Medications
Telogen Effluvium - Workup

- CBC
- Fe
- Ferritin
  - Replete if ≤ 40ng/dl
- TSH
- 25,OH Vitamin D
- ANA
- RPR
- May be component of androgenetic alopecia, so consider scalp biopsy if above normal and doesn’t improve

Androgenetic alopecia

- Genetically determined sensitivity of the hair follicles to androgens
- Occurs age puberty to age 60
- Symmetric pattern of miniaturization of hair follicles
  - In women, presents as a widened part or thinning of the vertex with retention of the anterior hairline
- Treatment (women)- antiandrogens (arrest progression)
  - minoxidil 5% foam qd
  - finasteride 1mg (non-childbearing)
  - spironolactone
Androgenetic Alopecia

- Pathogenesis: Conversion of testosterone to dihydrotestosterone (DHT) by the hair follicle enzyme 5 alpha-reductase, type 2
- With each cycle the affected hairs have a shorter anagen phase and a narrower diameter ("miniaturized" hairs)
Androgenetic alopecia

• Systemic workup if:
  – Hirsutism
  – Virilization
  – Severe, scarring cystic acne
  – Irregular menses
  – Infertility

• Check:
  – Free and total testosterone
  – DHEAS
  – Prolactin

Hypertrichosis and Hirsutism

• Hypertrichosis
  – Excess hair all on any part of the body

• Hirsutism
  – Applies to women only
  – Excess growth of terminal hairs in a male pattern (face, chest, areola, linea alba, lumbosacral...)
  – Due to overproduction of or increased end organ sensitivity to androgens
Hirsutism- Etiology

• Increase in androgens- ovary or adrenal gland
• Increased end-organ sensitivity to androgens

• Patterns:
  – Ovarian- lateral face, neck, areola
  – Adrenal- central (pubic triangle to the upper abdomen and presternal area to neck and chin)
Skin Cancer

**Clinical Guidelines**

**Screening for Skin Cancer: U.S. Preventive Services Task Force Recommendation Statement**

**U.S. Preventive Services Task Force**

**Recommendation:** The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for skin cancer by primary care clinicians or by patient skin self-examination. ([I statement])
• Applies to adults without history of malignancy or premalignant conditions
• Clinicians should remain alert for skin lesions with malignant features noted in the context of the physical exam performed for other purposes
  – LOOK! for ABCDs, rapidly changing lesions, do a biopsy when indicated

• Know who is at risk:
  – Fair skin patients >65yrs
  – Atypical nevi
  – > 50 nevi
  – Positive family history of skin cancer
  – History of significant sun exposure and sunburns
Malignant Melanoma

- Most frequent cause of death from skin cancer
- Frequently occurs in young adults
  - #1 cause of cancer death in women age 30-35
- Intermittent, intense sun exposure (sunburns)

Melanoma Diagnosis and Prognosis

85% are cured by early diagnosis

- The prognosis is DEPENDENT on the depth of lesion (Breslow’s classification) and lymph node status
- Melanoma of < 1mm in thickness is low risk
- Sentinel lymph node biopsy is recommended for melanoma > 1mm (controversial)
- If melanoma is on the differential, complete excision or full thickness incisional biopsy is indicated
Malignant Melanoma

- Asymmetry
- Border
- Color
- Diameter
- Evolution
Acral Melanoma

- Suspect in African American, Latino, Asian patients
Skin Cancers: 
What to Refer to Dermatology

- ANY suspicious pigmented lesion
- Any bleeding skin lesion
- Any red spot that doesn’t clear in 6-8 weeks
- Any non-healing erosion or ulceration
- Persons with greater than 50 moles, atypical moles, or family history of melanoma
- Fair-skinned organ transplant recipients with prior sun exposure

Sunscreens 101
Why Sunscreens?

• Prevention of skin cancer
• Prevention of photosensitivity (UVA)
  – Medications
  – Diseases: e.g. lupus erythematosus
• Prevention of skin aging

UV-B and UV-A

**UVB (290-320nm)**
• Burning rays of the sun
• Filtered by the ozone layer
• Most carcinogenic
• Primary target of sunscreens
• SPF refers only to UVB blockade

**UVA (320-400nm)**
• Tanning rays
• Aging rays
  – a complete UVA blocker = anti-aging cream
• Cause of medication related photosensitivity (e.g. HCTZ)
• Harder to block
New Sunscreen Labeling (Summer 2012)

• Broad spectrum = blocks UVA and UVB
• SPF= UVB blockade
• For sunscreen to say can prevent skin cancer AND sunburn, must
  1. be broad spectrum
  2. SPF ≥ 15
• Water resistant for 40 min or 80 min
  – No more “water proof”, “sweat proof”
  – Suggests that always need to re-apply every 2h

Chemical vs Physical Sunscreens

• Chemical sunscreens have UV absorbing chemicals
  – Benzophenone, Parsol 1789, Mexoryl, etc
  – Chemical UVA blockers are photo-unstable (degrade)
    • Stabilizers are now common (e.g. Helioplex)

• Physical sunscreens scatter or block UV rays
  – Zinc and titanium are physical blockers
  – More photostable
  – Block UVA well
  – Inelegant (white film)
How to Apply Sunscreen

• Put it on every morning before leaving the house
  — at least 20 min before sun exposure
• For heavy sun exposure: reapply 20 minutes after exposure begins
• Reapply every 2 hours or after swimming/sweating/towel-drying
• Apply liberally
  — 1oz application = shot glass = covers the body

What to Tell Your Patients

• Use sunscreen, SPF ≥ 30 EVERYDAY
• Avoid mid-day sun/Short Shadow Seek Shade
• Wear protective clothing (hats)
• Put sunscreen on your children
• Ask your doctor to check your skin lesions (most persons with melanoma have been seeing doctors regularly for years)
• Vitamin D Supplement for those at risk for osteoporosis who obey stringent sun-protections practices
  • E.g. organ transplant patients
• The American Academy of Dermatology recommends that an adequate amount of vitamin D should be obtained from a healthy diet that includes foods naturally rich in vitamin D, foods/beverages fortified with vitamin D, and/or vitamin D supplements. Vitamin D should not be obtained from unprotected exposure to ultraviolet (UV) radiation.

• Unprotected UV exposure to the sun or indoor tanning devices is a known risk factor for the development of skin cancer.

• There is no scientifically validated, safe threshold level of UV exposure from the sun or indoor tanning devices that allows for maximal vitamin D synthesis without increasing skin cancer risk.

• To protect against skin cancer, a comprehensive photoprotective regimen, including the regular use and proper use of a broad-spectrum sunscreen, is recommended.

Taken from: American Academy of Dermatology website, 1/25/11
New and Emerging Therapies for Osteoporosis

Anne Schafer, MD
Assistant Professor of Medicine
Division of Endocrinology & Metabolism
December 7, 2012

I have nothing to disclose.
Outline

- Osteoporosis screening and diagnosis
- Nonpharmacologic strategies
- Pharmacologic therapy
  - Whom to treat
  - FDA-approved medications
  - Common patient questions
  - Future therapies

Osteoporosis Has Tremendous Medical and Economic Impact

- Mortality after hip fracture ~25% at 1 yr
  - Of survivors, only 50% recover pre-fracture functional status
- 1.5 million fractures per year in US
- Direct cost $18 billion

Osteoporosis Definition

- A chronic, progressive disease characterized by
  - low bone mass,
  - microarchitectural deterioration of bone,
  - bone fragility and a consequent increase in fracture risk
- Decreased bone *quality* as well as *quantity*

National Osteoporosis Foundation, 2008

Risk Factors for Osteoporosis

**Non Modifiable**
- Increasing age
- Female gender
- White or Asian race
- Family history
- Previous osteoporotic fracture

**Modifiable**
- Low BMI
- Current smoking
- Alcohol (≥3/day)
- Immobilization
- Glucocorticoids
- Sex hormone deficiency
- Falls
Screening for Osteoporosis

National Osteoporosis Foundation:
• Women age ≥ 65 and men age ≥ 70
• Younger postmenopausal women, and men age 50-69, with additional risk factors
• Adults with a condition or taking a medication associated with bone loss
• Adults who fracture after age 50

National Osteoporosis Foundation, 2008

Screening for Osteoporosis

US Preventive Services Task Force:
• Women age ≥ 65
• Younger women whose risk is equal to that of a 65 y.o. white woman who has no additional risk factors
  ▫ 9.3% ten-year risk for any osteoporotic fracture, by the US FRAX algorithm
• Current evidence insufficient to assess benefits vs. harms in men

United States Preventive Services Task Force, 2011
DXA Scanning

- Assesses 2-dimensional BMD
  - Lumbar spine, total hip, femoral neck
- Same machine, by same operator, for optimal longitudinal assessment
- Reports BMD (g/cm²), T-scores, Z-scores
  - T-scores: compared to sex-matched reference population of young adults
  - Z-scores: age- and sex-matched

WHO Definitions - 1994

- Normal
  - BMD within one SD of a “young normal” adult (T-score +1.0 to -1.0)
- Low bone mass (“osteopenia”)
  - T-score -1.0 to -2.5
- Osteoporosis
  - T-score ≤ -2.5

*For use in postmenopausal women and men age ≥ 50*

WHO, 1994
What about premenopausal women and men <50?

• Diagnose with care!
• ISCD:
  ▫ Use race-adjusted Z-scores, with low BMD for chronological age defined as Z-score ≤ -2.0
  ▫ Dx of osteoporosis not made on densitometric criteria alone
• Example of diagnostic challenge: Adolescent girl who has not attained peak bone mass

Simonelli et al., J Clin Densitom, 2008

Approach to Osteoporosis Treatment

1) Evaluate for secondary causes of bone loss/fracture
2) Institute nonpharmacologic strategies
3) Select pharmacologic therapy
Secondary Causes of Osteoporosis and/or Fracture

- Vitamin D deficiency
- Calcium deficiency
- Malabsorption (e.g., celiac disease, gastric bypass surgery)
- Hypogonadism
- Thyrotoxicosis
- Primary hyperparathyroidism
- Anorexia nervosa
- Multiple myeloma
- Rheumatoid arthritis
- Medications
  - Glucocorticoids
  - Aromatase inhibitors
  - Depo-Provera
  - Thyroid hormone excess
  - Thiazolidinediones
  - Phenytoin
  - Androgen deprivation therapy

How extensive a laboratory work-up does a patient need?

- Depends on degree of suspicion
  - Pre-menopausal women, men deserve more
  - Severe (e.g., multiple fractures, very low Z-scores)
- Basic: Serum Ca, alb, Cr, 25(OH)D, TSH, CBC, LFTs
- Next level: 24-hour urinary Ca, PTH, SPEP/UPEP, testosterone in men
- As clinically indicated: Celiac Abs, 24h urinary free cortisol/dexamethasone suppression test
Nonpharmacologic Strategies

- Calcium
- Vitamin D
- Weight-bearing & resistance exercise
- Smoking cessation
- Alcohol moderation
- Fall prevention measures
  - Home safety evaluation
  - Medication review
  - Hip protectors

New IOM Dietary Reference Intakes

<table>
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<th>AGE</th>
<th>CALCIUM (mg) (RDA)</th>
<th>CALCIUM (mg) (UL)</th>
<th>VITAMIN D (IU) (RDA)</th>
<th>VITAMIN D (IU) (UL)</th>
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<tr>
<td>19-50, pregnant/lactating</td>
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<td>2000</td>
<td>800</td>
<td>4000</td>
</tr>
</tbody>
</table>

Institute of Medicine, 2010
Vitamin D: The Controversy

- IOM: $25(OH)D \geq 20$ ng/mL adequate for bone health
  - Based on rigorous RCT evidence
  - Population-based recommendation
- Others insist $\geq 30$ ng/mL optimizes Ca absorption, suppresses PTH, protects against fractures/falls
- More than 600-800 IU daily may be needed to achieve $\geq 20$ (or $\geq 30$) ng/mL
  - Malabsorption, obesity

Institute of Medicine, 2010; Endocrine Society, 2011

Pharmacologic Therapy

NOF recommends osteoporosis medication for postmenopausal women and men $\geq 50$ with
- An osteoporotic hip or vertebral fracture
- T-score at the femoral neck or spine $\leq -2.5$ after secondary causes excluded
- Low bone mass (T-score $<-1.0$ but $>-2.5$) and FRAX 10-year risk of
  - major osteoporotic fracture $\geq 20\%$, or
  - hip fracture $\geq 3\%$

Tosteson, Osteoporos Int, 2008
FRAX

- Estimates 10-year absolute fracture risk
- Especially for those in low bone mass ("osteopenia") range
  - Example: 80 y.o. w/ prior fracture and taking prednisone, 52 y.o. with no risk factors, both with femoral neck T-score -2.0
- Applies to postmenopausal women and men ≥ 50 y.o., who are treatment naïve

Kanis, Osteoporos Int, 2008
Pharmacologic Therapy

- Antiresorptive agents
  - Bisphosphonates (oral or IV)
  - Raloxifene
  - Hormone therapy
  - Calcitonin
  - Denosumab
- Anabolic agents
  - Parathyroid hormone (PTH)

Bone Resorption

Bisphosphonates encourage osteoclast apoptosis

From Bob Josse, HealthPlexus 2010
Oral Bisphosphonates

- Alendronate, risedronate, ibandronate
  - Alendronate and risedronate: Decreased risk of spine, nonvertebral, hip fractures
  - Ibandronate: Decreased risk spine fracture
- Side effect: esophagitis
  - Full glass of water, do not lie down
- Inefficiently absorbed
  - Take on empty stomach

Black, 1996; Cummings, 1998; Harris, 1999; McClung, 2001; Chesnut, 2004

IV Bisphosphonates

- Zoledronic acid
  - Once yearly infusion
  - Decreased risk spine, nonvertebral, hip fx
  - Given within 90 days after hip fracture:
    Decreased risk of new spine and nonvertebral fx, and decreased mortality
- Side effect: transient flu-like symptoms
- Potential complication: osteonecrosis of the jaw
  - Risk 1-10/100 with IV therapy at cancer doses;
    ~1/100,000 with oral therapy for osteoporosis

Raloxifene, Estrogen, Calcitonin

- Raloxifene
  - Decreased risk spine fractures (not NVF)
  - Decreased risk breast cancer
  - Increased risk venous thromboembolism

- Estrogen or estrogen/progestin therapy
  - Decreased risk spine, nonvertebral, hip fxs
  - Other concerns

- Calcitonin
  - Decreased risk spine fracture (not NVF)
  - Analgesic benefit in pts with vertebral fxs?


Bone Resorption

Denosumab binds to RANKL and inhibits activation of RANK

Bob Josse, HealthPlexus 2010
**Denosumab**

- Monoclonal antibody to RANK-ligand
- Decreased risk of spine, nonvertebral, hip fractures
- SubQ injection q 6 months
- Expensive
- Can be used in renal failure
  - But be careful that you are treating osteoporosis, not CKD-MBD

*Cummings, N Engl J Med, 2009*

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**Teriparatide (PTH Therapy)**

- Sole anabolic agent currently available
  - Increases bone formation
- Decreased risk of spine and nonvertebral fractures
- Daily subQ injection
- Approved for 2 years of use
- Consider in severe disease, especially spine > hip
- Follow course with a bisphosphonate

You start Ms. O, a 70 y.o. woman with osteoporosis, on alendronate.

“How long will I take this medication?”

Duration of Bisphosphonate Therapy

- FLEX: After 5 years of alendronate (ALN), randomized to continued ALN vs. placebo
  - ALN group had continued reduction in clinical (but not radiographic) vertebral fx
  - Those in ALN group with femoral neck T-scores ≤ -2.5 had continued nonvertebral fx risk reduction

Black, JAMA, 2006; Schwartz, J Bone Miner Res, 2010
Duration of Bisphosphonate Therapy

• HORIZON-PFT extension trial: After 3 years of zoledronic acid (ZOL), randomized to continued ZOL vs. placebo
  ▫ Those with 3 years on, 3 years off had a small but significant decline in BMD
  ▫ Those with 6 years ZOL had fewer radiographic vertebral fractures (but no difference in other fracture types)

Black, JBMR, 2012

Duration of Bisphosphonate Therapy

• No formal guidelines
• One reasonable approach:
  ✓ Discuss with pt after ~5 yrs
  ✓ Repeat DXA
  ✓ If FN (or other?) T-score at that point is ≤ -2.5, or if very high risk of fracture (e.g., hx of hip or vertebral fracture), continuing therapy may be beneficial.
“My friend told me this medication actually causes fractures of the femur.”

Atypical Femur Fractures

Recent reports, some in setting of long-term bisphosphonate therapy

X-ray findings:
- Subtrochanteric
- Transverse
- Thick cortices

Atraumatic
- Fx before fall
- +/- prodromal pain

Neviaser, J Orthop Trauma, 2008
Atypical Femur Fractures

Is the connection to bisphosphonate therapy real? Should it change practice?

• Danish registry study:
  ▫ Similar associations between ALN use and atypical femur fracture, typical hip fracture

• Post-hoc analysis of RCT data:
  ▫ 12 fractures in 10 (of 14,195) women
  ▫ 2.3 per 10,000 person-years
  ▫ Wide confidence intervals, not stat sig
  

Atypical Femur Fractures

• If relationship is real, risk is very low:
  ▫ Treating 1000 women for 3 years would prevent 100 fxs, including 10 hip fxs, and could cause 1 atypical femur fx

• ASBMR Task Force:
  ▫ Causal association not established
  ▫ But, risk may ↑ with ↑ duration of med use

• Thoughtful decision-making about duration of therapy

  Black, N Engl J Med, 2010; Shane, J Bone Miner Res, 2010
“How will we know whether the medication is working?”

Monitoring response to therapy

- The challenge: Not all patients’ BMD will increase on therapy.
  - Treatment failure?
- Women adherent to ALN but with no change or a $\leq 4\%$ decrease in BMD still had fracture reduction compared to those taking placebo.
- Bisphosphonates also appear to improve bone quality, geometry.

Chapurlat, Osteoporos Int, 2005
Monitoring response to therapy

• One reasonable approach:
  ✓ Educate patient that while BMD helps decide whether to treat, it’s less useful for assessing treatment response.
  ✓ If repeating DXA, look for meaningful loss in BMD, and be prepared to explain this to patient.

• Meaningful loss → reassess adherence, secondary causes

Outline

• Osteoporosis screening and diagnosis
• Nonpharmacologic strategies
• Pharmacologic therapy
  ▫ Whom to treat
  ▫ FDA-approved medications
  ▫ Common patient questions
  ▫ Future therapies
Currently Approved Medications

- Antiresorptive agents
  - Bisphosphonates (oral or IV)
  - Raloxifene
  - Hormone therapy
  - Calcitonin
  - Denosumab
- Anabolic agents
  - Parathyroid hormone (PTH)
Goals for Future Therapies

- Greater fracture risk reduction than currently-approved therapies
- “Uncouple” resorption and formation such that resorption decreases while formation increases?

Cathepsin K produced by osteoclasts, is released during bone resorption and degrades collagen

National Osteoporosis Foundation, 2008
Cathepsin K inhibitor: Odanacatib

- Anti-resorptive
- Once weekly oral medication
- Appears to inhibit resorption more than formation
- Phase III trial stopped early: highly effective, good safety profile
- Fracture trial underway

Sclerostin

- Secreted by mature osteocytes
- Produced in response to decreased loading
- Inhibits osteoblasts
- Deficiency: very high bone mass
Anti-Sclerostin Antibodies

- Anabolic
- SubQ monthly or q 3 month
- Phase II trial: 12-month increases in spine BMD of 11%

Outline

- Osteoporosis screening and diagnosis
- Nonpharmacologic strategies
- Pharmacologic therapy
  - Whom to treat
  - FDA-approved medications
  - Common patient questions
  - Future therapies
Thank you for your attention!
Advances in Prevention and Treatment of Stroke: What Every Clinician Needs to Know

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The speaker has no disclosures

Disclosure
I have nothing to disclose
Case 1

- A 54 year-old woman with a history of HTN presented to the ED after being found at a park not moving her right side.
- Exam shows an expressive aphasia, R face and arm plegia as well as L gaze deviation and R homonymous hemianopsia.
- Her symptoms began at noon, it is now 2:15 p.m. There are no contraindications to tPA.

The 2012 Acute Stroke Timeline

- Time of onset= last time seen normal
  - 0-4.5 Hours IV-tPA Proven Approved
  - 0-6 Hours IA-tPA Proven Unapproved
  - 0-8 Hours Mechanical Embolectomy Unproven Approved
  - Greater than 8 hours Anticoagulants or Antiplatelets

Case 2

- A 78 year-old woman with a history of DM, HTN presents with 3 days of R sided weakness
- Examination shows R hemiparesis of face and arm greater than leg along with sensory deficits
- The patient is on clopidogrel daily
Standard Large-Vessel Stroke Workup

- Cardioembolic: afib, clot in heart, paradoxical embolus
  - 1. Telemetry
  - 2. TEE with bubble study
- Aortic Arch
  - 2. TEE with bubble study
- Carotids
  - 3. Carotid Imaging (CTA, US, MRA, angio)
- Intracranial Vessels
  - 4. Intracranial Imaging (CTA, MRA, angio)

And evaluate stroke risk factors

TEE vs. TTE

- 231 consecutive TIA and stroke patients of unknown etiology underwent TTE and TEE
- 127 found to have a cardiac cause of emboli, 90 of which (71 percent) only seen on TEE
- 38 of 46 “major risk factors” only found on TEE (most left atrial thrombi)
- TEE superior to TTE for: LA appendage, R to L shunt, examination of aortic arch

Atrial Fibrillation Detection

- EKG
- 48 Hours of Telemetry
- 30 day cardiac event monitor
  - 20% of patients with cryptogenic stroke otherwise unexplained had afib detected
  - Clearly changes management
  - Probably cost effective

Kamel H et al: Stroke 41:1514, 2010
Approach to Stroke Treatment

Acute Stroke Therapy?

No

Anticoagulants?

No

Antiplatelets

Shrinking Indications for Anticoagulation in Stroke

1. Atrial Fibrillation
2. Some other cardioembolic sources
   - Thrombus seen in heart
   - ?EF<35
   - ?PFO with associated Atrial Septal Aneurysm
3. Vertebral dissection
   - 2009: Questionable in carotid dissection
4. Rare hypercoagulable states: APLA
The Excitement Over the Demise of Warfarin

- We hope oral direct thrombin and Xa inhibitors lead to more patients with afib and risk factors being anticoagulated
- Stroke-specific concerns
  - Contraindications to tPA
  - What do we do with ICH patients or those who need rapid surgery?

Case 3

- A 62 year-old woman with a history of HTN, DM, smoking presents with 14 hours of right-sided weakness.
- The patient is on ASA 81mg daily
Approach to Stroke Treatment

Acute Stroke Therapy?

- No

Anticoagulants?

- No

Antiplatelets

Antiplatelet Options

- 1. ASA
  - 50mg to 1.5g equal efficacy long-term
- 2. Aggrenox
  - 25mg ASA/200mg ER Dipyridamole
    - ESPS-2, ESPRIT (Lancet 5/06)
- 3. Clopidogrel (Plavix)
  - MATCH (Lancet 7/04)
  - FASTER (Lancet Neurol 10/07)
Aggrenox vs. Plavix

• Aggrenox
  – Headache in first 2 weeks: 30% discontinue
  – Perhaps not compatible with cardiac antiplatelet goals or with unstable angina
  – Cannot be crushed in FT

• Plavix
  – Less evidence directly from stroke trials (until 2008)
  – Concerns regarding use in combination with ASA

PRoFESS Trial

• Randomized, double-blind trial of Aggrenox versus Plavix in over 20,000 patients with ischemic stroke

• Recurrent 4-year event rates basically identical between the two medications
  – HR for Aggrenox 1.01 (95% CI, 0.92-1.11)
  – Composite of stroke, MI, vascular death: 13.1% in each
  – Major hemorrhagic events higher in Aggrenox group

Antiplatelet Options

• If on no antiplatelet medication
  – ASA or Plavix vs. Aggrenox
• If already on ASA
  – Switch to Plavix vs. Aggrenox
• If already on Plavix or Aggrenox
  – ???

Other Acute Stroke Management

• Statins for (almost) all
  – SPARCL (NEJM 8/06), 80mg atorvastatin in stroke and TIA if LDL>100
• Tight Glucose and Fever control
• Enoxaparin for DVT prophylaxis
  – PREVAIL trial (Lancet 2007)
  – CLOTS trial 1 (Lancet 2009): Compression Stockings
Permissive Hypertension

• National Guidelines
  – To at least 220/120: Morbidity increases if lower in the acute setting
  – After IV tPA: less than 185 systolic for 24 hours
• Randomized trial of 2020 patients with acute stroke: candesartan vs placebo for 7d
  – Lower pressures with candesartan
  – No benefit to treatment
  – Higher risk of poor functional outcome with candesartan


Permissive Hypertension

• When to stop remains controversial
• Situations where more important
  – Large Vessel Occlusion
  – Fluctuating Symptoms
• We begin a medicine before discharge (~72h) and aim for normotension over a matter of weeks
  – Choose thiazides and ACEI first
Case 4

• A 61 year-old woman with HTN, DM comes to the ED after a 15 minute episode of right arm weakness that has since resolved.
• Exam is normal except bp 160/80

Differential for Transient Focal Neurologic Deficit

• The Big Three
  – 1. Stroke/TIA
  – 2. Seizure
  – 3. Complicated Migraine
TIA versus Stroke

• Up to 50% of TIA have infarct on imaging
• Conceptually the same disorder
  – Same workup, same treatment
• Pendulum swing
  – Pre-2001: Much more aggressive with Stroke
  – 2002-2007: TIA and Stroke equally aggressive
  – 2008-present: Moving to more aggressive approach with TIA

Risk of Future Stroke with TIA: ABCD² Score

• 7-day risk overall 8.6-10.5 percent
• Age
  – >60 =1 point
• Blood Pressure
  – SBP>140 or DBP>90 =1 point
• Clinical Features
  – Unilateral weakness =2 points
  – Speech disturbance without weakness =1 point
• Duration
  – >60 minutes =2 points
  – 10-59 minutes =1 point
• Diabetes=1 point

ABCD² Score

• 2-day risk of stroke
  – Score 6-7: 8.1 percent (high risk)
  – Score 4-5: 4.1 percent (moderate risk)
  – Score 0-3: 1.0 percent (low risk)


Aggressive Therapy for TIA

• Two key studies in October 2007
• 1. SOS-TIA trial
  – 1085 patients with TIA admitted to a 24-hour center
  – All treated with standard therapy
    • 74 percent discharged on same day, stroke risk reduced 80 percent from ABCD² prediction
• 2. EXPRESS study
  – 80 percent reduction in risk with urgent TIA clinic visit
    versus usual primary care visit in 1278 patients

When to Fix the Carotid?

• NASCET in early 1990s
  – Benefit of endarterectomy in patients with symptoms ipsilateral to 70-99% stenosis
    • Comparison: best medical management at the time
  – 50-69% symptomatic stenosis revascularization has limited benefit, especially in women
• In stroke management don’t miss carotid disease or atrial fibrillation

How to Fix the Carotid?

• Stenting +/- distal protection
  – SAPPHIRE (NEJM 10/04 and 4/08) in high-risk patients
  – Other small trials compare with NASCET data
  – Currently widely practiced: NeuroIR, vascular surgeons, BodyIR, Cardiologists
  – Unique risks: Hypotension, Bradycardia
Randomized Trial Results

• SPACE Trial (Lancet 10/06)
  – 1200 patients with recent stroke/TIA randomized to CEA vs. stenting
• EVA-3S (NEJM 10/06)
  – 527 patients with recent stroke/TIA randomized
• Both failed to demonstrate non-inferiority
  – In EVA-3S, stenting associated with significantly more short-term stroke and death

CREST Trial Results

• 4-year study of 1321 symptomatic and 1181 asymptomatic patients randomized to CEA or carotid stenting
• Combined endpoint of stroke, MI, death not significantly different
  – More strokes in first 90 days in stenting group, more MIs in surgical group
  – After 90 days, similar endpoints

Case 5

- A 54 year-old woman with a history of HTN comes to your office concerned as her mother just died after an ischemic stroke. She wants to know what primary preventative interventions can reduce his chances of having a similar event.
2011 Primary Prevention Guidelines

• Risk estimation schemes
• Treat vascular risk factors
• Anticoagulants for afib
  – CHADS2 score
    • 1-2=medium risk
    • 3 or higher=high risk
Asymptomatic Carotid Stenosis

• Some benefit for endarterectomy in asymptomatic stenosis
  – >60% or >80% cut-offs
  – Must have a very low perioperative risk of stroke and death to realize benefit (3%)
• Data much less convincing than symptomatic trials
• When to screen? Who to screen?

Transcranial Doppler to Predict Stroke risk

• 2-year study of nearly 500 patients with asymptomatic (>70%) carotid stenosis
• Embolic signals on TCD predicted risk of stroke
  – Hazard ratio of ipsilateral stroke with emboli compared to without: 5.57
  – Annual risk of stroke 3.6% vs. 0.7%
• Can we stratify those with greatest chance of benefit from surgery/stenting?

Markus HS et al: Lancet Neurol 9:663, 2010
Does aspirin prevent stroke?

- 2009 Meta-analysis of serious vascular event primary prevention trials
- 95,000 individuals at low-average risk
- ASA offered 12% reduction in vascular risk but mainly driven by MI
- Stroke risk reduction not significant (0.20% per year vs. 0.21% per year, p=0.4)

Every patient is an athlete:
Hot Topics in Sports Medicine 2012

Carlin Senter M.D.
Primary Care Sports Medicine
UCSF Internal Medicine and Orthopaedics

UCSF Controversies in Women’s Health
December 7, 2012

I have nothing to disclose.
In 40 minutes you will know

1. The return to play/work progression for concussion treatment.
2. Five questions to ask every athlete with hip pain.
3. Two keys to ordering knee radiographs.
4. Four principles in treating knee osteoarthritis.
5. How to write an exercise prescription.

Case #1

• 40 y/o woman presents to your office for ER follow-up one week after bike accident.
• Went over handle bars traveling on city streets.
• No loss of consciousness.
• Taken by ambulance to ER.
• Had trauma work-up including head CT (-).
• Diagnosed with clavicle fracture, nonoperative tx by orthopaedic surgeon, discharged home.
• Has headache, fatigue, dizziness, light sensitivity. Trouble staying focused at work, sleeping more than usual.
• Normal neurologic exam.
Diagnosis: Concussion

- H/o trauma
- Headache
- Fatigue
- Dizziness
- Light sensitivity
- Trouble staying focused at work
- Sleeping more than usual.

How would you treat the concussion?

1. Order urgent MRI brain to rule out subtle post traumatic bleed, return to clinic after MRI.
2. Rest from work and biking, return to clinic 1 week.
3. Return to work but rest from biking, return to clinic in a month.
4. Return to work and biking (assuming cleared by orthopaedic surgeon for clavicle fracture).
How would you treat the concussion?

1. Order urgent MRI brain to rule out subtle post traumatic bleed, return to clinic after MRI.

2. Rest from work and biking, return to clinic 1 week.

3. Return to work but rest from biking, return to clinic in a month.

4. Return to work and biking (assuming cleared by orthopaedic surgeon for clavicle fracture).

Concussion definition

- Blow to head, neck, body → force to head
- Rapid onset of neurologic impairment
- Symptoms usually short-lived and resolve spontaneously but in some cases can be prolonged
- Symptoms represent functional or metabolic change in CNS
- Graded set of clinical syndromes that may or may not include loss of consciousness
- Symptom resolution is sequential
- Standard neuroimaging is normal

Concussion symptoms


Concussion clinic evaluation

• History keys
  – Mechanism of injury
  – Symptoms initially and currently
  – If sports
    • Did they play through the symptoms?
    • Did they have a second hit (might make sx last longer)
  – Loss of consciousness (if many minutes then would expect transport and head CT)
  – PMH – associated with prolonged symptoms
    • ADHD, learning d/o
    • Depression, anxiety
    • Concussion
- Worsening headache
- Seizure
- Increasing drowsiness
- Focal neuro deficit
- Repeated vomiting
- Slurred speech
- Does not recognize people/places
- Increasing confusion/irritability
- Weakness/numbness arms or legs
- Neck pain
- Loss of consciousness >30 seconds


**SCAT2**

Concussion treatment

• Cognitive rest
• Physical rest
• Medication
  – Avoid aspirin and ibuprofen
  – Tylenol OK
• Avoid alcohol
• Avoid driving

Symptom resolution after sport concussion

• 50% recovered and returned to play in 1 week; 90% in 3 weeks (Collins et al. Neurosurgery, 2006.)
• Prolonged symptoms: > 4 weeks. Consider neurology or neuropsychology consult.
Return to work/play

- Asymptomatic
- Normal neurologic exam (SCAT2)
  - Cognitive
  - Balance
- Computerized neuropsychological testing


Step-wise activity progression

Asymptomatic

Clinician clearance

Light aerobic activity

Sport specific activity

Non-contact training

Full contact practice

Game play

Case #2

• 20 y/o collegiate cross country athlete
• Presents to clinic with right groin pain
• Started a few weeks ago, getting worse gradually
• Still able to run but pain gets worse the more she runs, hard to lift her leg due to pain

5 questions for every athlete with hip pain

1. Training: increased mileage?
2. Nutrition: Calories in versus calories out?
   History of eating d/o? Dietary restrictions?
3. History of stress fractures?
4. Family history of osteoporosis?
5. Menstrual history?
Our patient

- Increased mileage from 30 to 60 miles/week in last month without increased caloric intake
- No dietary restrictions or h/o eating d/o
- (+) h/o tibial stress fracture in high school
- No family history osteoporosis
- Menses regular until college but none since freshman year (18 months)

Locate the hip pain

- Anterior groin = hip joint, hip flexor
- Buttock = SI joint, lumbar spine
- Lateral hip = greater trochanteric bursitis, gluteus tendinopathy
- Radiating to thigh = could be hip joint
- Radiating to the foot = lumbar spine

Physical exam

- Walking with right-sided limp
- Tender right inguinal region
- Groin pain with passive ROM: flexion, internal, and external rotation of hip
- Neurologically intact lower extremities but pain with active hip flexion

Hip passive range of motion

- Flexion normal 120°
- External rotation normal 40-60°
- Internal rotation normal 30-40°

http://www.youtube.com/watch?v=5LNYdJjrWYo
Differential diagnosis
groin pain in runner

• Intraarticular hip problem
  – Impingement/labral tear
  – Osteoarthritis
  – Femoral neck stress fracture

• Extraarticular hip problem
  – Hip flexor strain

• GI/gyn problems


Hip impingement

NORMAL

CAM

PINCER

MIXED
Hip labral tear

What’s your leading diagnosis?

1. Hip flexor strain
2. Hip impingement or hip labral tear
3. GI/gyn problems
4. Osteoarthritis
5. Femoral neck stress fracture
What’s your leading diagnosis?

1. Hip flexor strain
2. Hip impingement or hip labral tear
3. GI/gyn problems
4. Osteoarthritis
5. **Femoral neck stress fracture**

High index of suspicion to prevent bad outcome

Female athlete triad

- Low energy availability with or without eating disorders (d/o)
- Osteoporosis
- Amenorrhea

PATHOLOGY

- Suboptimal energy availability
- Low bone density
- Irregular menses

Healthy energy status

- Healthy menstrual cycles
- Healthy bones

OPTIMAL HEALTH


Female athlete triad treatment

- Best treatment = prevention
  - Screen for risk factors
  - Finding 1 risk factor should prompt eval for others
- Increase energy availability
  - Increase dietary intake
  - Decrease exercise
  - Has been shown to restore menses
  - Has been shown to increase bone density
- Estrogen: does not improve BMD as much as if menses are restored with increased energy availability
- Multidisciplinary approach: primary care doctor, nutritionist, psychologist, eating disorder specialist, athletic trainer

Case #3

- 50 y/o woman presents for new patient appointment.
- Tired, lots of stress at work, doesn’t exercise due to right knee pain. H/o meniscus surgery in college due to soccer injury.
- BP 135/80, 5’8”, 220# (BMI 33), HR 80

Case #3 history

- Onset
- Provocation
- Quality
- Radiation
- Severity
- Timing
- Locking
- Swelling
- Instability
- Gradual
- Walking
- Generalized ache
- To thigh
- Worst at night, can prevent from falling asleep, stiff in AM < 30 min
- No
- Yes, more if walks on the beach
- When painful
Physical exam case #3

- **I**: large effusion, varus alignment of knees
- **P**: tender medial joint line and above/below medial joint line. Nontender patellar facets and lateral joint line
- **R**: 5-110, limited 2/2 pain and swelling
- **Other Tests**: (-) laxity on ligament testing, unable to perform McMurray due to limited flexion
Diagnosis

A. Medial meniscus tear
B. ACL tear
C. Osteoarthritis
D. Patellar dislocation
E. Septic arthritis
Radiographs:
2 keys to ordering knee x-rays

1. Minimum 2 views of every joint (AP and lateral)
   1. Knee has 2 articulations: want 2 views of each
      1. Patella – femur
      2. Femur- tibia
   2. Weight-bearing views to evaluate for arthritis
      – Arthritis is not painful if it’s not weight-bearing. Reproduce the painful situation to see the degree of cartilage loss.

Flexion **weight-bearing** PA view, aka “Notch view”
Patient standing, knees bent to 45 degrees.

- Evaluate medial and lateral compartments for OA
- Fractures
Lateral of the affected side

- Patellofemoral compartment
- Patellar fracture

Merchant view = axial view of the patella
Radiographic findings in osteoarthritis

1. Joint space narrowing
2. Subchondral sclerosis
3. Osteophytosis


4 components of non-operative treatment for knee OA

1. Patient education
   – Modules on exercise, healthy eating, medications, surgical treatment
   – Identify goals and action plans
   – Moderate effect size on pain relief
2. Exercise: low-impact aerobic → significant pain relief
3. Weight loss: 5% body weight → significant functional improvement, unclear effect on pain

4 components of non-operative treatment for knee OA

4. Pain control:
   - Nonpharmacologic
   - Glucosamine
   - Tylenol (<4gm/day) or NSAID unless contraindication
     • Significant reduction in pain compared to placebo
     • NSAIDs more effective than Tylenol but higher GI risk
   - Injections: steroid, viscosupplementation


Topical NSAIDs for knee and hand OA

• Diclofenac sodium 1% gel (Voltaren)
  – 4g 4x/day to the knee
• Diclofenac sodium 1.5% solution (Pennsaid)
  – 40 drops 4x/day to the knee
• Plasma levels of the drugs given topically < 5% of levels after taking drug orally
Topical diclofenac for knee and hand OA

• NNT 6.4 for solution, 11 for gel formulation
  – To achieve 50% pain relief over 8-12 weeks compared to placebo
• No difference between efficacy of oral vs topical diclofenac solution
• Increase in mild skin reaction when compare topical NSAIDs to placebo or oral NSAIDs
• GI events less common with topical compared to oral NSAIDs


Case #4

• 55 y/o woman presents for routine annual exam. No complaints but shocked that she gained 10# since she saw you last year. Takes no medications.
• BP 140/80, HR 80, Height: 5’3”, weight 170# (BMI 30)
• Labs:
  – HgA1c 6.3%
  – Fasting glucose 104
  – Total cholesterol 192, TG 119, HDL 50, LDL 118
What treatment would most benefit this patient now and in the long run?

Exercise

Strong evidence that physical activity associated with lower risk of

- Coronary artery disease
- Stroke
- High blood pressure
- High cholesterol
- Type 2 diabetes
- Colon cancer
- Breast cancer
- Falls

The exercise prescription: What’s the right dose of activity?

Physical activity recommendations: 4 types of activities
Physical activity recommendations: components of each activity

- **F**requency
- **I**ntensity
- **T**ime
- **T**ype

Estimating exercise intensity

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<th>Low</th>
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<td>Heart rate</td>
<td>&lt;50% max</td>
<td>50-70% max</td>
<td>&gt;70% max</td>
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<td>Talk test</td>
<td>Can talk and sing</td>
<td>Can talk but not sing</td>
<td>Can only say a few words before pause for breath</td>
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Exercise prescription:
Combine activity with components

- Frequency
- Intensity
- Time
- Type

CV fitness recommendations

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<th>Intensity</th>
<th>Time</th>
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<td>5x/week</td>
<td>Moderate</td>
<td>30 minutes</td>
<td>Major muscle groups</td>
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<td>3x/week</td>
<td>Vigorous</td>
<td>20 minutes</td>
<td>Major muscle groups</td>
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### Balance recommendations

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<td>2-3d/week</td>
<td>Unknown</td>
<td>20 minutes</td>
<td>Heel-toe walk, stand on 1 foot, Tai Chi</td>
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### Strength recommendations

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<td>Novice: 40-50%</td>
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<td>Experienced: 80%</td>
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# Flexibility recommendations

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<th>Type</th>
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<td>2-3d/week</td>
<td>Stretch to feeling of tightness</td>
<td>Hold 10-30 seconds</td>
<td>All major muscle-tendon units</td>
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# What makes a successful exercise program?

- **Program characteristics**
  - Moderate intensity
  - Supervised activity by experienced leader
  - Group support
- **Individually tailored program**
  - Goal-setting
  - Reinforcement: social support for behavioral change
  - Problem-solving
Pedometers

- Popular and effective for promoting physical activity
- 10,000 steps/day was old recommendation
- Update for 2011:
  - Pedometers don’t measure speed
  - May need <10,000 steps/day for sig health benefit
  - 100 steps/minute is rough estimate of moderate intensity exercise
  - Recommend using steps/minute and the number of minutes/session

ACSM Position Stand on Prescribing Exercise, Medicine & Science in Sports & Exercise, 2011.

Action plan: Exercise is Medicine

1. Identify potential health benefits of exercise.
2. Is the patient healthy enough to begin exercise?
3. Assess patient’s stage of change.
   1. Precontemplation
   2. Contemplation
   3. Preparation
   4. Action and maintenance
4. Write the exercise prescription.

Case #4

• 55 y/o woman presents for routine annual exam. No complaints but shocked that she gained 10# since she saw you last year. Takes no medications.
• BP 140/80, HR 80, Height: 5’3”, weight 170# (BMI 30)
• Labs:
  – HgA1c 6.3%
  – FPG 104
  – Total cholesterol 192, TG 119, HDL 50, LDL 118

Write the exercise prescription

- Frequency
- Intensity
- Time
- Type
Stationary bike
5/10 intensity
10 minutes each time
3 times a week

Exercise prescription resources

http://bleacherreport.com/articles/1189176-bay-to-breakers-2012-changes-the-race-must-make
Physical Activity for Everyone

How much physical activity do you need?
Regular physical activity helps improve your overall health and fitness, and reduces your risk for many chronic diseases.

Fitting regular exercise into your daily schedule may seem difficult at first, but the 2008 Physical Activity Guidelines for Americans are more flexible than ever, giving you the freedom to reach your physical activity goals through different types and amounts of activities each week. It’s easier than you think!

Physical Activity Guidelines

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<tr>
<th>Children</th>
<th>Adults</th>
<th>Older Adults</th>
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<td>6 to 17 years of age</td>
<td>18 to 64 years of age</td>
<td>65 years of age or older</td>
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If you are a healthy pregnant or postpartum woman, physical activity is good for your overall health. See our section on Healthy Pregnant or Postpartum Women.
**Stretches**

**Upper Body**
- **Hand Grip**
- **Wrist Curl**
- **Overhead Arm Raise**
- **Front Arm Raise**
- **Side Arm Raise**
- **Arm Curl**
- **Arm Curl with Resistance Band**
- **Seated Row with Resistance Band**

**Stretch It Out!**

Stretch gently after you warm up your muscles, and again after you cool down. Try doing the stretches listed below. Do not bounce or hold your breath when you stretch. Perform slow movements and stretch only as far as you feel comfortable.

**Side Reach**
Reach one arm over your head and to the side. Keep your hips steady and your shoulders straight in the side. Hold for 10 seconds and repeat on the other side.

**Wall Push**
Lean your hands on a wall and place your feet about 1 to 2 feet away from the wall. Bend one knee and point it toward the wall. Keep your back leg straight with your foot flat and your toes pointed straight ahead. Hold for 10 seconds and repeat with the other leg.

**Leg Curl**
Fold your right foot toward your buttocks with your right hand. Stand straight and keep your back knee pointing straight down. Hold for 10 seconds and repeat with your other foot and hand.

**Hamstring Stretch**
Sit on a sturdy bench or hard surface so that one leg is stretched out on the bench with your toes pointing up. Keep your other foot flat on the surface below, straighten your back, and if you feel a stretch in the back of your thigh, hold for 10 seconds and then change sides and repeat. If you do not feel a stretch, slowly lean forward from your hips until you feel a stretch.

**Knee Pull**
Lean your back against a wall. Keep your head, hips, and feet in a straight line. Pull one knee toward your chest, hold for 10 seconds, and then repeat with the other leg.
“All parts of the body if used in moderation and exercised in labors to which each is accustomed, become thereby healthy and well developed, and age slowly; but if unused and left idle, they become liable to disease, defective in growth, and age quickly.”

Hippocrates

Thank you!

Carlin Senter, M.D.
Primary Care Sports Medicine
UCSF Internal Medicine and Orthopaedics
<table>
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**Total Number of Attendees for MDM13M05:** 200
Save the Dates!

UPCOMING UCSF PRIMARY CARE CME COURSES

APRIL IN HAWAII
Primary Care Medicine: Update 2013
Wailea Marriott, Maui, HI
April 7 - 12, 2013

JULY IN HAWAII
Essentials of Women’s Health: An Integrated Approach to Primary Care and Office Gynecology
Hapuna Beach Prince Hotel, Hawaii’s Big Island
June 30 - July 5, 2013

AUGUST AT LAKE TAHOE
Essentials of Primary Care: A Core Curriculum for Adult Ambulatory Practice
Resort at Squaw Creek, North Lake Tahoe
August 4 - 9, 2013

FALL IN SAN FRANCISCO
Primary Care Medicine: Principles & Practice
Hotel Nikko, San Francisco
October 30 - November 1, 2013

DECEMBER IN SAN FRANCISCO
Controversies in Women’s Health
Hotel Nikko, San Francisco
December 12 - 13, 2013

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