UPDATES IN WOMEN'S HEALTH

Steve Brumfield, MD, FACOG
Obstetrician / Gynecologist
Valley Health Associates

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DISCLOSURES

- No relationships or financial interests to disclose

Objectives

- Understand latest updates in obstetrics regarding
  - Vaccinations in pregnancy
  - Timing of delivery
  - Pregnancy induced hypertension
  - Aneuploidy screening
  - Genetic carrier screening

Objectives

- Understand the latest updates in gynecology including:
  - Hereditary cancer screening & testing
  - Cervical cancer screening
  - Menopause management
  - Contraception
  - Screening & management of urinary incontinence

Vaccination in Pregnancy

- There is no evidence of adverse fetal effects from vaccinating pregnant women with
  - Inactivated virus
  - mRNA vaccine
  - Bacterial vaccine
  - Toxoid
- Live attenuated vaccines do pose a theoretical risk & should generally be avoided
  - Risk never demonstrated
  - MMR
  - Varicella
  - Live attenuated influenza (FluMist)

VACCINATION IN PREGNANCY - INFLUENZA

- Pregnant & recently postpartum patients are at higher risk for complications with flu
- Vaccination has been demonstrated to reduce rate of hospital admission
- **Seasonal influenza vaccination is "strongly recommended" for all pregnant & postpartum women including those who are breastfeeding**
- Use any inactivated vaccine at any point in pregnancy
  - Previous recommendation to use outside the first trimester has been changed
  - Those with history of mild-moderate egg allergy can get any vaccine in any setting
  - Those with history of anaphylaxis to eggs can get any vaccine but in supervised setting
- Reasonable but not necessary to use thimerosal free vaccines

VACCINATION IN PREGNANCY - INFLUENZA

- 2020 Healthy People goal from DHHS is 80% pregnant/postpartum women receive seasonal influenza vaccination
  - In 2016-17, this number was 53.6%
- **Emphasize opportunity to passively immunize the newborn via transplacental passage of antibodies & breastfeeding**
- Oseltamivir (Tamiflu)
  - Safe for use in pregnancy & breastfeeding
  - Post-exposure prophylaxis is recommended for pregnant/PP patients

VACCINATION IN PREGNANCY - TDAP

- Overwhelming majority of M&M from pertussis occurs in infants who are 3 mos of age & younger
  - But DTaP vaccination series does not start until 2 months of age
- **All pregnant women should received TDAP vaccine during EVERY pregnancy between 27-36 weeks gestation**
  - CDC's ACIP initially recommended "cocooning" approach in 2006 but this was revised to the above recommendation in 2013
- Safe for use in pregnancy & breastfeeding
- Vaccination NOT required for other family members so long as they are up to date
- Again emphasize passive immunization of the newborn through transplacental migration of antibodies & breastfeeding

VACCINATION IN PREGNANCY - COVID

- Pregnant/PP women are at increased risk of severe illness compared to non-pregnant peers
  - Hospitalization, ICU admission, need for mechanical ventilation / ECMO, & death
  - One analysis showed 18X higher risk for death from COVID in pregnancy
  - Also at increased for OB complications including preterm birth, C/section, & fetal demise
- **COVID vaccine strongly recommended for pregnant women**
  - Any vaccine at any point in pregnancy
  - Most up to date vaccine "booster" recommended
  - Provides passive immunization for the newborn
    - CDC found 61% lower risk for hospitalization for neonates if mother was vaccinated

VACCINATION IN PREGNANCY - COVID

- But is it really safe??
  - Pregnant women were not included in initial studies
  - Development & Reproductive toxicity (DART) studies by manufacturer in Europe do NOT indicate direct or indirect harmful effects to pregnancy, embryonic/fetal development, L&D process or post-natal development
  - As of Feb '22 >200K pregnancies were reported in the CDC V-SAFE post-vaccination tracking program with no indication to suggest risk to pregnancy
  - There is also a V-SAFE pregnancy registry with >23K women enrolled

VACCINATION IN PREGNANCY - COVID

Pregnancy Complication	Background Rate	V-SAFE Preg Registry Rate
Gestational Diabetes	7-14%	10%
Pregnancy Induced HTN	10-15%	15%
Eclampsia	0.27%	0%
Fetal Growth Restriction	3-7%	1%

VACCINATION IN PREGNANCY - COVID

Neonatal Complication	Background Rate	V-SAFE Preg Registry Rate
Preterm Birth	8-15%	9.4%
Congenital Anomalies	3%	2.2%
Small for Gestational Age	3.5%	3.2%
Neonatal Death	0.38%	0%

VACCINATION IN PREGNANCY - COVID

- What about the reproductive problems??
  - **Issues with infertility have been definitively disproven**
  - No increased risk for miscarriage/spontaneous abortion
  - Could be minimal, transient effect of menstrual cycle
    - Alteration in cycle timing of <1 day that resolves by 2nd cycle after vaccination
    - No change in length of bleeding
    - Small increase in volume of bleeding that resolves within 1 cycle
  - Transient lymphadenopathy is postulated to change interpretation of screening mammogram
    - RSNA expert panel recommends delaying screening mammogram 4-6wks after vaccination

VACCINATION IN PREGNANCY - RSV

- Bivalent RSV vaccine approved in Aug '23 by FDA for use in pregnant women to reduce risk of severe RSV disease in newborns for the first 6mos after birth
  - Abrysvo is the ONLY RSV vaccine approved for use in pregnancy
  - Recommended for those 32-36wks gestation who will deliver during RSV Season
  - There is also a neonatal monoclonal RSV antibody (Nirsevimab) that is alternative to maternal vaccination
    - Rare, high risk situations both can be used
    - Generally, it's either / or.

VACCINATION IN PREGNANCY - RSV

- Abrysvo can be given with other vaccinations such as flu, COVID & TDAP.
- Typical side effects for vaccines
- No fetal or neonatal adverse effects in study of 3500 pregnant women
- Trial showed increased risk for preterm delivery(5.7%) with vaccine compared to placebo (4.7%) but only in low to middle income countries
  - Thus recommendation to not give until 32wks

VACCINATION IN PREGNANCY - RSV

- Efficacy
  - Approximately 3500 pregnant women received vaccine & similar number received placebo
  - Vaccination reduced risk for severe lower respiratory tract RSV in newborns by 81.8% and 69.4% at 90 and 180 days after birth respectively
    - When limited to those who were vaccinated at 32-36wks these numbers were 91.1% and 76.5%

Timing of Delivery

- Standard of care was 42wks & expectant management of pregnancy up to this gestational age is still NOT unreasonable
- Induction of 41wks was associated with reduced risk of
  - Perinatal death (RR = 0.31)
  - Cesarean section (RR = 0.89)
  - Meconium aspiration syndrome (RR = 0.5)
  - Trend to lower risk of stillbirth with induction but not statistically significant
- **No elective induction prior to 39wks!!**

Timing of Delivery

- ARRIVE Trial from 2018
  - RCT of induction at 39wks vs expectant management in nulliparous women
  - No significant difference in composite adverse perinatal outcome
    - Trend to lower risk with induction group
  - Lower risk for cesarean section & PIH in the induction group

Timing of Delivery

- JAMA Systematic Review
  - Induction vs expectant management in both parous & nulliparous women
  - Lower risks in the induction group:
    - 3-4th degree lacerations
    - Operative vaginal delivery
    - Macrosomia
    - Low apgar scores
    - Emergency cesarean section
  - Non-significant reduction in risk with induction for:
    - Shoulder dystocia
    - NICU admission
  - Higher risk for shoulder dystocia in nulliparous women only with induction

Timing of Delivery

- Conclusion: It's safe & reasonable to induce labor at 39wks, and could potentially be beneficial

Management of Hypertension in Pregnancy

- Updated terminology
  - No longer "mild" and "severe" pre-eclampsia
  - Use "pre-eclampsia" and "pre-eclampsia with severe features" (PESF)
- Delivery by 37th week for everyone with PIH or chronic hypertension
  - Can consider expectant management of PESF up to 32-34wks
- Superimposed pre-eclampsia is no longer managed as severe disease by default
  - Same criteria for diagnosis of "superimposed pre-eclampsia" and "superimposed PESF"
- Use magnesium for seizure prophylaxis only with PESF or eclampsia
- Aspirin for prevention!

Low dose aspirin to reduce risk for pre-eclampsia

- Modest reduction in risk for pre-eclampsia with LDASA initiated after 16wks
  - RR = 0.81
- Much more significant reduction in risk if LDASA is initiated prior to 16wks
  - RR = 0.47
- Also lower risk for fetal growth restriction
  - RR = 0.56

Table 1. Clinical Risk Factors and Aspirin Use[*]

Level of Risk	Risk Factors	Recommendation
High[†]	• History of preeclampsia, especially when accompanied by an adverse outcome • Multifetal gestation • Chronic hypertension • Type 1 or 2 diabetes • Renal disease • Autoimmune disease (ie, systemic lupus erythematosus, the antiphospholipid syndrome)	Recommend low-dose aspirin if the patien has one or more of these high-risk factors
Moderate[‡]	• Nulliparity • Obesity (body mass index greater than 30) • Family history of preeclampsia (mother or sister) • Sociodemographic characteristics (African American race, low socioeconomic status) • Age 35 years or older • Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)	Consider low-dose aspirin if the patient ha more than one of these moderate-risk factors[§]
Low	• Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

Management of Pregnancy Induced Hypertension

- Chronic Hypertension and Pregnancy (CHAP) study in 2022 showed improved outcomes with more aggressive control of BP in pregnancy
  - Previously goal was <160/105
  - CHAP showed better outcome with goal of <140/90
- Antihypertensive therapy in pregnancy
  - Generally continue antihypertensive medication if patient is well controlled with exception of ACE inhibitors / ARB's
    - Risk of adverse effects on fetal kidneys with resulting IUGR, oligohydramnios, renal failure & death
  - Beta blockers & calcium channel blockers preferred.
  - Thiazides are not preferred but are not teratogenic
  - Use of alpha methyl-dopa is safe but largely ineffective
  - Atenolol has adverse effect on utero-placental blood flow with resulting effect on fetal growth & is thus not recommended

ANEUPLOIDY SCREENING – CELL FREE DNA

- **CFDNA IS THE CURRENT GOLD STANDARD FOR SCREENING AS SIMPLE MATERNAL BLOOD TEST**
- OFTEN REFERRED TO AS NON-INVASIVE PRENATAL TESTING OR SCREENING (NIPT / NIPS)
- SCREENING, NOT DIAGNOSTIC TESTING
- UNIQUE TO EVERY PREGNANCY
- ALSO CAN TEST FOR MICRODELETION SYNDROMES
- CAN BE USED IN TWIN PREGNANCY BUT LESS WELL STUDIED FOR HIGHER ORDER MULTIPLES
- **HIGH DEGREE OF SENSITIVITY & NEGATIVE PREDICTIVE VALUE (>99%) FOR AUTOSOMAL ANEUPLOIDY**

ANEUPLOIDY SCREENING

	Detection Rate	False Positive Rate
Trisomy 21 / Down	99.5%	0.05%
Trisomy 18 / Edwards	97.7%	0.04%
Trisomy 13 / Patau	96.1%	0.06%
Monsomy X / Turner	90.3%	0.23%
47XXY / 47XYY / 47XXX	93%	0.14%

Carrier screening

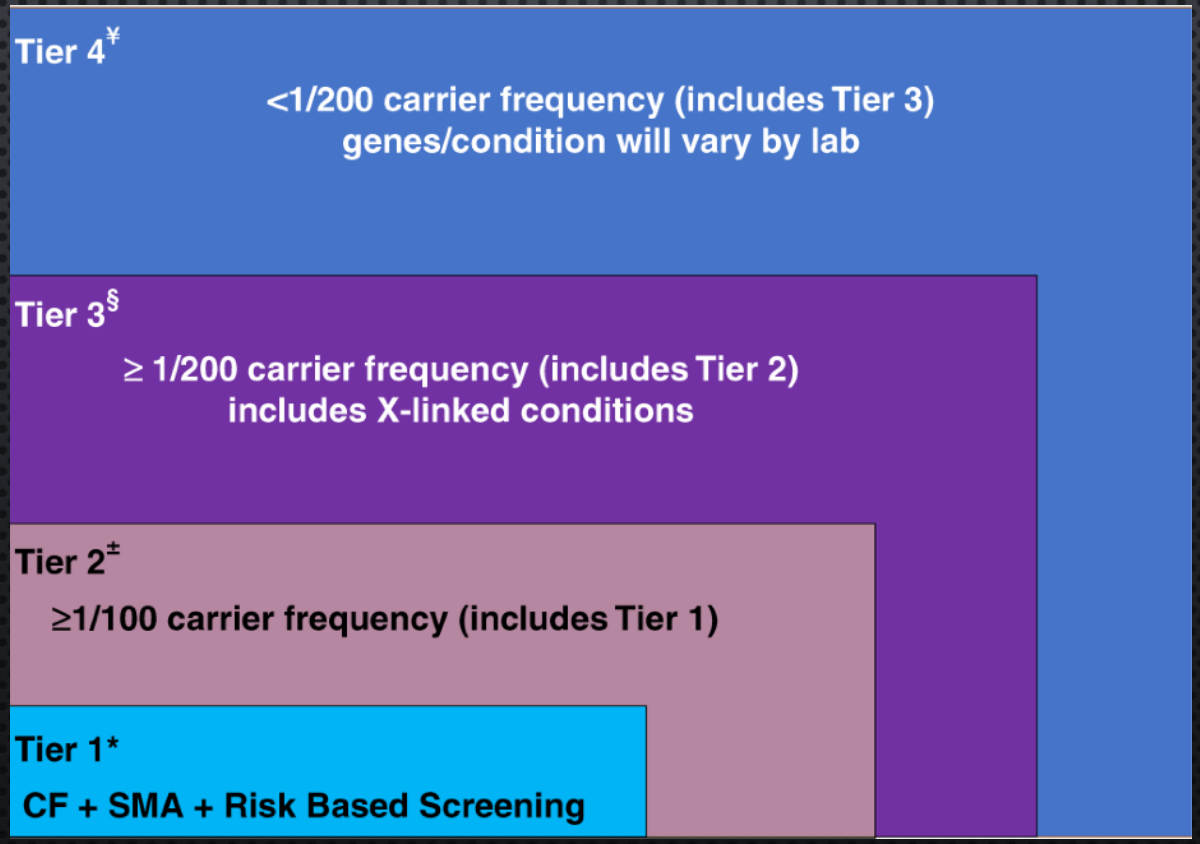
- Goal is identify heritable mutations that could be passed to offspring
- Classically done for recessive disorders inherited via standard Mendelian genetics of which a carrier would have no symptoms/disease.
- Carrier screening in the past….
  - Limited due to cost & availability
  - Limited options for management
  - Based on race / ethnicity along with personal & family history
    - "Targeted Carrier Screening"
- Carrier screening today…..
  - Widely available & far less costly due to advances in genetic testing lab techniques
    - "Expanded Carrier Screening"
  - This allows for wider range of conditions for which testing is done
  - NOT based on race / ethnicity as definitive categorization is increasingly difficult
  - More available treatment / management options

Carrier screening

- Requires pre-screen counseling
  - Written documents seem to be helpful
  - Informed consent is necessary
  - Many commercial labs offer free online genetic counseling
- Federal law prohibits employers & health insurers from discriminating based on genetic testing
  - "Genetic Information Nondiscrimination Act"
- **Ideally done prior to conception as this allows more options for managing a genetic mutation that could be passed on to offspring**
- Most carrier screening does not completely exclude the possibility that a person carries a mutation but reduces the likelihood of this.
  - Current testing paradigms test for some number of the most common mutations but not all
  - Results in "residual risk"
- Only ever needs to be done once (i.e., results never change).
- Does not replace newborn screening

CARRIER SCREENING

- ACGM RECOMMENDS TIER BASED SCREENING BASED ON CARRIER FREQUENCY
  - RECOMMENDATION IS THAT EVERYONE BE OFFERED TIER 3 CARRIER SCREENING



Carrier screening

- What to do with positive result
  - Counsel patient on results
  - Test reproductive partner
    - Would need to calculate fetal risk based on "residual risk" of reproductive partner
  - Refer to genetic counselor or other provider with expertise
  - Recommend testing for family members
    - But maintain confidentiality!

Carrier Screening

- **Modern reproductive medicine now offers several management options for couples at risk of passing on some genetic disease**
  - **Donor gametes from non-carrier**
    - Most commonly use donor sperm with insemination as this is far less invasive & costly
    - However, donor egg is also possible
  - **Pre-implantation genetic diagnosis**
    - Using IVF techniques the polar body corresponding to a given egg can be tested
      - Want to use the egg corresponding to polar body that tests POSITIVE for the given mutation
  - Adoption
  - Pregnancy management & post-natal testing if already pregnant.
  - Roll the dice!

Hereditary Cancer Syndrome Screening & Testing

- Hereditary Breast & Ovarian Cancer Syndrome
- Lynch Syndrome
- Li Fraumeni Syndrome
- Cowden Syndrome
- Peutz-Jeghers Syndrome
- Hereditary Diffuse Gastric Cancer Syndrome

Hereditary cancer syndrome screening & testing

- **Hereditary cancer syndrome screen should be done & updated / documented annually**
- May consider ethnicity for some hereditary cancer syndromes
  - Such as higher risk of BRCA in those of Ashkenazi Jewish descent
- Tools such as "My Family Portrait" available from office of U.S. Surgeon General can be helpful
- Screening/testing has become far more accessible due to advances in genetic testing laboratory techniques
  - First BRCA tests available at ONE lab were around $7500, now cost about $200

Clues & Indications of Possible Hereditary Cancer Syndrome

- Cancer diagnosed at an unusually early age (personal or family history)
  - Less than age 50 for breast, uterine, colon & ovarian
- Several different types of cancer in same person
- Multiple different primary tumors in same organ
  - Particularly breast or colon
- Several first or second degree relatives with same cancer on same side of the family
- Unusual presentation of a specific type of cancer
  - Such as male breast cancer
- Presence of benign problems known to be associated with hereditary cancer syndrome
  - Specific skin lesions or skeletal abnormalities

Hereditary Cancer Syndrome Screening & Testing

- Once a patient is identified as possible carrier of hereditary cancer syndrome (HCS)
  - Counsel her on the possible hereditary cancer syndrome including best assessment likelihood of her having this based on family history & mode of inheritance
  - Counsel her on risk of passing this on to offspring if present
  - Counsel her on management options if diagnosed with HCS
  - Remind her that results of genetic testing cannot be used against her in regard to employment, educational opportunities, health insurance coverage, etc.
  - Third party payers usually require genetic counseling before covering this testing
    - Provide this yourself with documentation
    - Refer to genetic counselor or to another physician/provider with expertise in this area of genetics
    - Most labs who do this type of testing offer free online genetic counseling (Legit!)

Hereditary cancer syndrome screening & testing

- What to do with a positive result
  - Counsel on implications / risks of this positive test
    - Consider referral to genetic counselor or other provider with expertise
    - Most labs offer free online genetic counseling
  - Set up plan for surveillance or preventative treatment
    - Such as prophylactic mastectomy, hysterectomy / oophorectomy for BRCA
    - Or hysterectomy/oophorectomy with serial colonoscopy with Lynch syndrome

Cervical cancer screening

- No longer pap every year
- **Screening does not begin until age 21**
  - No exception to this
  - Though all sexually active women <25 yoa should be screened for gonorrhea & chlamydia annually (usually urine, self swab also valid)
- **Widespread availability of HPV testing has changed guidelines & allowed to space screening**
- Can stop screening after age 65 under certain conditions
  - No history of high grade dysplasia / cervical cancer & no risk factor (e.g., HIV)
  - Adequate recent negative screening
    - 3 negative cytology screens, 2 negative co-testing screens or 2 negative primary HPV screens
- **No screening after hysterectomy unless there is history of high grade cervical dysplasia**

Cervical cancer screening

- ACOG, ASCCP, SGO endorse USPSTF guidelines for screening
  - Cytology only every 3 years from age 21-29
  - Age 30-65 with no history of high grade dysplasia & absence of other risk factors can have either
    - Cytology alone every 3 years (Not recommended)
    - Co-testing (cytology & hrHPV screening) every 5 years
    - hrHPV testing only every 5 years
      - Must be FDA approved HPV test for primary screening (Cobas 4800 by Roche & BD Onclarity)
      - Self screening has been validated & is likely the future of cervical cancer screening
      - Not widely available

Cervical cancer screening

- Follow-up of abnormal results
  - Adhere to most recent ASCCP guidelines, updated in 2019 to risk based approach
    - Use online tool / App (https://app.asccp.org/)
  - Expedited treatment (ie, skip colposcopy & biopsy) preferred for highest risk results & acceptable for medium risk results
  - ASCUS with negative HPV does not require colposcopy, just repeat in 12mos
  - Glandular abnormalities are more worrisome than squamous abnormalities & require different follow-up
  - Colposcopy for positive HPV 16 or 18, even if cytology is negative
    - Typically plan to repeat pap & HPV in 12mos if other HPV subtypes

Menopause Management

- Natural process so no treatment is required
- Average age in North America is 51, definitely by age 57
- "Post-menopausal" by 12mos from last menstrual period
  - **Any bleeding after this point should be evaluated to exclude endometrial pathology including hyperplasia or malignancy**
- Bone health should be addressed
  - 1200-1500mg calcium daily
  - 500-1000IU vitamin D daily
  - "Weight bearing" exercise
  - Screen for osteoporosis at 65, sooner if increased risk based on formal clinical risk assessment tool
    - Validated formal risk assessment tools include FRAX, SCORE, ORAI, OSIRIS, OST
    - Repeat testing in 2-5 years for osteopenia
    - Repeat testing in 5-8 years after normal screen

Menopause Management

- Vasomotor symptoms
  - Affect up to 81% with most having daily hot flashes
  - Can adversely affect job performance / productivity, mood, sexual functioning, quantity & quality of sleep as well as overall health and quality of life
    - Treatment improves these measures
  - Symptoms usually begin 1-2 years prior to final menstrual period
    - Low dose combined oral contraceptive pill is good choice for those still menstruating but having vasomotor symptoms
    - Knowing when to stop the OCP is tricky
  - Mean duration is 7.4 years

Menopause Management

- Treatment for vasomotor symptoms
  - **Estrogen is most effective**
    - Previous use was widespread and long-term until 2002 Women's Health Initiative Study
  - Neurokinin 3 Receptor Antagonists (NK3R)
    - **Fezolinetant (Veozah)** approved in May '23
    - Elinzanetant is in development
  - SSRI/SNRI
    - Low dose **paroxetine** is FDA approved
  - Progesterone
  - Testosterone
  - Gabapentin / Pregabalin
  - Clonidine
  - Herbal products such as soy & black cohosh based products
  - "Tissue selective estrogen complexes"
    - Combination of an estrogen plus selective estrogen receptor modulator

Menopause Management

- Estrogen Replacement Therapy
  - **Must combine with progesterone in women who still have uterus to protect endometrium from overstimulation and resulting hyperplasia or malignancy**
  - Therapy decreases symptom frequency by 75% and severity by 87%.
  - Improves sleep quality & quantity
  - Also FDA approved for treatment & prevention of osteoporosis
  - **Overall, all cause mortality is lower prior to age 60.**

Menopause Management

- Women's Health Initiative study (2002) Estrogen & Progesterone arm
  - RCT of conjugated equine estrogens + medroxyprogesterone acetate over 5+ years with >16k women with uterus
  - Increased coronary heart disease (RR = 1.29, CI = 1.02-1.63) or 7 more events per 10K person years
  - Increased breast cancer (RR= 1.26, CI = 1.00-1.59) or 8 more cases
  - Increased PE (RR = 2.13, CI = 1.39-3.25) or 8 more cases
  - Increased stroke (RR = 1.41, CI = 1.07-1.85) or 8 more events
  - Decreased hip fracture (RR = 0.66, CI = 0.45-0.98) with 5 fewer fractures
  - Decreased colorectal cancer (RR = 0.63, CI = 0.43-0.92) with 6 fewer cases
  - No change in endometrial cancer (RR = 0.83, CI = 0.47-1.42)
  - No statistically significant effect on death from all other causes

Menopause Management

- Women's Health Initiative Study (2004) Estrogen only arm
  - RCT of ERT in >10k women with prior hysterectomy (no progesterone) followed for 6.8 years
  - No increased risk for CHD (RR = 0.91, CI = 0.75-1.12)
  - No increased risk for breast cancer & possible trend to lower risk (RR = 0.77, CI = 0.59-1.01)
  - Increased risk for stroke (RR = 1.39, CI = 1.10-1.77)
  - No increased risk for PE (RR = 1.34, CI = 0.87-2.06)
  - No change in risk for colorectal cancer (RR = 1.08, CI = 0.75-1.55)
  - Decreased risk for hip fracture (RR = 0.61, CI = 0.41-0.91)
  - No overall effect on all cause mortality (RR = 1.08, CI = 0.88-1.22)

Menopause Management

- Cochrane Systematic Review 2017
  - Some increased risk for cardiac events, stroke, VTE, breast cancer, gallbladder disease & maybe lung cancer with prolonged use of varying lengths
  - BUT only increased risk for women 50-59 was VTE.
  - **All cause mortality data favors use in women <60 yoa or within 10 yrs of menopause**
  - Risks increase with prolonged use & after age 60
    - But there is NO data that HRT/ERT must be routinely stopped after age 60-65.

Menopause management

- Contraindications to use of menopausal HRT/ERT
  - Unexplained vaginal bleeding
  - Liver disease
  - Prior estrogen sensitive cancer (eg, breast or endometrial) or pre-cancerous condition (endometrial hyperplasia)
  - Prior CHD / MI, stroke, VTE or known thrombophilia
- Transdermal dosing may have lower risk for VTE
- Side effects are usually not significant
  - Nausea
  - Bloating
  - Weight gain
  - Fluid retention
  - Breakthrough bleeding
  - Breast tenderness
  - Mood lability (likely related to progesterone specifically)

Menopause management

- Bottom line on use of HRT / ERT
  - **With no contra-indication, use hormones for relief of vasomotor symptoms when these adversely affect quality of life, but use the lowest effective dose for the shortest time needed**

Menopause Management - Alternatives to HRT/ERT

- SSRI / SNRI's
  - **Paroxetine 7.5mg daily was only non-hormonal FDA approved med until 2023**
  - Desvenlafaxine has shown efficacy as well with 62% reduction in symptoms in RCT
- Clonidine
  - Small but positive effect in systematic review
- Gabapentin
  - Reduction of 45% in symptom frequency & 52% in symptom severity
- Phytoestrogens
  - Soy, red clover
  - No benefit for symptom frequency / severity in 2010 Cochrane meta-analysis
- Black Cohosh
  - No strong benefit in multiple low quality studies
  - Risk of liver toxicity

Menopause Management

- Not Effective / Recommended by NAMS:
  - Compounded hormones
  - Paced respirations
  - Nutritional supplements
  - Herbal remedies
  - Acupuncture
  - Cooling techniques
  - Exercise
  - Yoga
  - Trigger avoidance
  - Clonidine
  - Mindfulness based intervention / meditation

Menopause Management – Alternatives to HRT/ERT

- Tissue selective estrogen complexes
  - Combination of estrogen & SERM (agonist & antagonist)
  - conjugated estrogens & bazedoxifene (Duavee) is only one available
  - The SERM provides adequate protection of the endometrium so no progestin is needed
  - Reduction of 75% in frequency of hot flashes
  - No effect on breast tissue
    - May be good choice for those with breast tenderness on other ERT products
  - Still increases risk for VTE

Menopause Management – Alternatives to HRT/ERT

- Neurokinin 3 Receptor Antagonists (NK3R)
  - Fezolinetant (Veozah) is only FDA approved agent in this class
  - Works at the hypothalamus with different mechanism of action than estrogen
  - **Good choice for those with contra-indications to HRT/ERT**
  - No risk for VTE, stroke, CHD, breast cancer
  - No effect on bone mineral density or on vulvovaginal tissue
  - Reduction in hot flash frequency of about 64%
  - Safe & well tolerated
    - Limited number of women with increased LFT's in early trials
    - FDA requires monitoring of LFT's at baseline & every 3mos for the first 9mos of use

Menopause Management

- Genitourinary Syndrome of Menopause (GSM) / Vulvovaginal Symptoms
  - Up to 40% will experience bothersome vulvovaginal symptoms
    - Dryness, burning, irritation, discharge, bleeding & dyspareunia
    - Leading cause of sexual dysfunction in menopausal women
  - Alteration in vaginal pH & microbiome can result in increased risk for UTI's
- Treatment options
  - Vaginal estrogen
  - Vaginal DHEA
  - Oral SERM
  - Vaginal moisturizers / lubricants

Menopause Management – Treatment of GSM

- Vaginal lubricants & moisturizers
  - Moisturizers are used on a regular basis usually 2-3 times per week
    - Replens, RepHresh, KY Liqui-beads, Vagisil, etc.
    - Poor quality data shows some efficacy, possibly similar to estrogen therapy
  - Lubricants are used at the time of sexual activity
    - Oil, silicone or water based
    - Astroglide, Slippery Stuff, Pjur, Simply Slick, etc.
    - KY gets tacky/sticky after a few minutes

Menopause Management – Treatment of GSM

- Vaginal Estrogen
  - **Probably most effective treatment**
  - Restores vaginal pH & microbiome, thickens / increases vascularity of the epithelium, increases vaginal secretions & natural lubrication with resulting decreased dyspareunia, irritative symptoms & UTI risk
  - Available in creams, tablets & rings
    - Similar efficacy
    - Creams & tablets usually used 1-3 times per week
    - Ring is used for 90 days at a time
  - **Systemic absorption is minimal so little no risk for CHD/CVA/VTE/Etc.**
    - No need to treat with progestin for those with intact uterus
    - Can be used in those with contra-indications to systemic estrogen therapy selectively
  - **Considered first line treatment for post-menopausal women with recurrent / frequent UTI's**
  - Can be used in conjunction with systemic ERT

Menopause Management – Treatment of GSM

- Ospemifene (Osphena)
  - Oral SERM with estrogenic effects on the vulvovaginal tissue
    - No estrogenic effect on endometrium or breast
    - No increased risk for VTE seen but data insufficient
    - May have inhibitory effect on growth of breast carcinogenesis but data insufficient
    - May have positive effect on bone mineral density but data insufficient
  - Modestly effective in placebo controlled trials, never compared to estrogen
- Vaginal DHEA
  - Prasterone (Intrarosa)
    - Daily vaginal suppository
    - Effective compared to placebo for improving dyspareunia
    - Increases serum DHEA, testosterone & estrone levels though not estradiol levels
      - Not studied but concern for use in those with estrogen sensitive malignancy, using aromatase inhibitors

Contraception

- Use WHO Medical Eligibility Criteria for Contraceptives to guide counseling & safe prescribing
  - Online (https://www.who.int/publications/i/item/9789241549158)
  - Wheels
  - App
- **Should be addressed regularly with ALL women of childbearing age regularly**
- Still about 50% pregnancies in the US are unintended, unplanned with some recent improvements.
  - Certain demographics have higher risk
    - Ages 18-24
    - Low income
    - Non-Hispanic black & African American women
    - Women co-habituating but not married
    - Women who had not completed high school
  - Among active duty military women rates of unplanned / unintended pregnancy is 38-62%
    - Calls into question the conventional wisdom that cost & access to contraceptive health care is root cause of unplanned/unintended pregnancy

WHO MEDICAL ELIGIBILITY FOR CONTRACEPTIVES WHEEL

Contraception – Combined Oral Contraceptive Pills

- Most commonly & easily used
- Generally do not start before 4-6wks postpartum & avoid in breastfeeding moms (decreased supply)
- Generally avoid for those with history of VTE events, thrombophilia, those at higher risk for CVD / CVA
- Contra-indicated for smokers >35yoa due to higher risk for VTE/CVA
- **"Quick start" right away but use back-up method if other than first day of menstrual cycle**
- **Trend is lower dose estrogen with shorter pill free interval**
  - Shorter, lighter periods
- Remember menstrual period with pill is artificially induced
  - **Very reasonable to skip the placebo pills & thus monthly withdrawal "menstrual" bleed particularly for those with menstrual problems**
  - This has been documented safe up to 1yr (no studies beyond this but no reason to suspect risk beyond this time frame)
- **For those who want/do well with OCP but have difficulty taking this daily consider weekly patch or monthly contraceptive ring**
- Novel pill approved by FDA in 2021 with drosperinone & estetrol which is a novel estrogen
  - Has selective estrogenic effects on tissues with longer half life, less effect on hemostasis parameters & minimal 1st pass metabolism
- **Non-contraceptive benefits include menstrual cycle control, decreased risk for endometrial & ovarian cancer, less acne**

Contraception - Progestin only oral contraceptive pills ("mini pill")

- Most commonly used during postpartum period for breastfeeding moms
- Little / no risk for VTE
- Can start sooner postpartum
- Good choice for those who like / want OCP but have concerns for VTE/CVD/CVA
- SLIGHTLY less effective than combined OCP
- Most are norethindrone which works largely by thickening cervical mucus
  - Newly approved drosperinone pill that works by preventing ovulation
- FDA approved norgestrel OCP (Opill) as first over the counter daily contraceptive in Jul '23

Contraception - injections

- Depot medroxyprogesterone acetate (DMPA) or Depo-Provera
  - Little no risk for VTE so can be started immediately postpartum
  - Safe for breastfeeding
  - **Really the only contraceptive associated with weight gain**
    - Related to increased appetite
    - Limited effect in most studies
  - Probably has highest amenorrhea rates
  - **Highly effective but longest delay in return of fertility**
    - Can be up to 1yr

Contraception – Rings & Patches

- Same concerns, side effects, contra-indications & non-contraceptive benefits for OCP
- **Useful for women who need cycle control of, like OCP but have difficulty taking daily**
- Nuvaring is estrogen/progesterone based monthly ring worn for 3wks then discarded
- Annovera is similar but the same ring is used each month & does not require refrigeration
- Xulane is weekly contraceptive patch with EE/Norelgestromin with no patch worn on week 4
- Twirla is used similarly but contains less estrogen & levonorgestrel, approved in Feb ‘22
    - Less breakthrough bleeding?? Less VTE risk??

Contraception - Implants

- Nexplanon is progesterone only (etonogestrel) implant placed in office in the upper medial arm & highly effective for up to 3yrs
- No concern about VTE & safe with breastfeeding
  - Can be initiated immediately postpartum
- Less predictable effect on frequency of menstrual bleeding
- Relatively quick return to fertility
- Weight gain does not seem significant

CONTRACEPTION – IUD'S

- **HIGHLY (MOST??) EFFECTIVE WITH QUICK RETURN TO FERTILITY FOLLOWING REMOVAL**
- HISTORICAL CONCERNS ABOUT INFECTION ARE NEGLIGIBLE WITH MODERN IUD DESIGN
- SEEM TO WORK THROUGH SPERMICIDAL STERILE INFLAMMATORY REACTION WITHIN THE ENDOMETRIUM…..**NOT** ABORTIFACIENTS
- EVEN HORMONAL (LEVONORGESTREL) IUD'S CARRY NO CONCERN FOR VTE & ARE SAFE FOR BREASTFEEDING
  - CAN BE INITIATED IMMEDIATELY POSTPARTUM
  - EVEN VALIDATED IN THE DELIVERY ROOM, BUT HIGHER RISK FOR EXPULSION
- MIRENA (52MG LNG)
  - MOST COMMONLY USED & RECENTLY EXPANDED FOR RELIABLE USE UP TO 8YRS
  - ALSO FDA APPROVED FOR TREATMENT OF HEAVY MENSTRUAL BLEEDING
- LILETTA (52MG LNG) IS SIMILAR TO MIRENA & RECENTLY EXPANDED DURATION UP TO 8YRS
- KYLEENA (19.5MG LNG) IS SMALLER LEVONORGESTREL IUD EFFECTIVE FOR UP TO 5YRS
- SKYLA (13.5MG LNG) IS SMALLEST, LOWEST DOSE LEVONORGESTREL IUD EFFECTIVE FOR UP TO 3YRS & INTENDED PRIMARILY FOR NULLIPAROUS WOMEN (OR NO VAGINAL DELIVERY)
- PARAGARD IS NON-HORMONAL COPPER IUD EFFECTIVE FOR UP TO 10YRS
  - APPROVED FOR USE AS EMERGENCY CONTRACEPTION WITHIN 72HRS OF INTERCOURSE
- **LEVONORGESTREL IUD'S CAN PROVIDE THE PROGESTERONE PROTECTION OF THE ENDOMETRIUM WITH POST-MENOPAUSAL HORMONAL REPLACEMENT THERAPY & REDUCE RISK FOR THOSE AT HIGHER RISK FOR ENDOMETRIAL CANCER (EG, PCOS)**

Contraception – "On Demand" Methods

- Condoms have higher failure rates (15% per year) but do protect against STI's
- Diaphragms must be fit by provider & have higher failure rates
  - 6% with perfect use & 12% with typical use
  - Should be used with spermicide
  - Rarely used
- Caps & sponges are rarely used
- Nonoxynol-9 is OTC spermicide that must be inserted 10min prior to intercourse
  - 18% pregnancy rate with perfect use & 20% with typical use
- **Phexxi (lactic acid/citric acid/potassium bitartrate) is prescription spermicide that can works by altering pH of the vagina and can be used 5-60min prior to intercourse**
  - About 10-13% pregnancy rate
  - Can cause vulvovaginal irritation
  - Insurance coverage is inconsistent

URINARY INCONTINENCE SCREENING & TREATMENT

- CMS "recommends" urinary incontinence screening for all women >65yoa
  - "Do you ever leak urine?"
- Prevalence is VERY high & increases with age
  - 3% in women <35yoa
  - 7-10% of women 50-60yoa
  - Up to 70% of women over 65yoa
  - Associated with lower quality of life, higher risk for falls, depression, isolation, sexual dysfunction & increased mortality
- Many women see this as "normal" with aging / after childbirth & are unaware of available treatments
  - Women often spend $750-1200/yr on protective pads/garments & as much as $20K before getting treatment
- Basic evaluation includes history, exam, urinalysis & measurement of post-void residual volume
  - "What makes you leak?" & "how often do you leak?" & "are you bothered by leaking?"
  - Urinalysis: UTI?? Hematuria??
  - PVR assessment can be done via ultrasound or catheterization to r/o overflow incontinence which has higher risks
  - Exam: Presence of prolapse?? Urethra hypermobile??
  - **VAST** majority is stress or urge incontinence or combination (mixed) of these

URINARY INCONTINENCE SCREENING & TREATMENT

- Stress incontinence treatment / management options
  - Pessary
    - Low level of patient satisfaction (≤ 50%)
    - Consider for women with episodic UI (such as with exercise), or those with medical co-morbidities that make them high risk for surgery
  - Pelvic floor physical therapy
    - "Kegels" are the most basic form but OT/PT's provide more advanced care with better outcomes
    - Around 50-60% cure rate & high rate of patient satisfaction
  - Surgery
    - Most effective treatment & thus associated with highest rates of patient satisfaction
    - **Mid-urethral sling is highly effective (80-90%), minimally invasive outpatient procedure with low rate of complications, patient satisfaction as high as 95% and is now gold standard treatment for SUI**
    - Urethral bulking injections are also effective (about 65%)
      - Avoids mesh
      - May need to be done repeatedly

Urinary Incontinence Screening & Treatment

- Urge incontinence management options
  - Diet
    - Avoid triggers for detrusor instability including alcohol & "5 C's" (Coffee, caffeine, cola, chocolate, & citrus)
  - Medications
    - Anticholinergic medications
      - **Oxybutynin is probably least effective (ANECDOTAL), has more side effects & has to be taken more often**
      - Consider solfenacin, trospium, tolterodine, or fesoterodine
      - Typical anti-cholinergic side effects with most worrisome being cognitive impairment / dementia
      - Contra-indicated with gastric retention, narrow angle (only) glaucoma & SVT
    - Beta-3 Agonists
      - Mirabegron (Mybetriq) & Vibegron (Gemtesa)
      - Similar efficacy to anti-cholinergic medications but different mechanism of action & likely fewer side effects
    - Can use meds from the two classes synergistically
  - Sacral nerve stimulation is highly effective (86%) treatment for refractory UUI with implantable stimulator at S3 level
    - Also indicated for fecal incontinence, refractory overactive bladder & non-obstructive urinary retention
  - Tibial nerve stimulation is percutaneous treatment done via 12 weekly 30min treatment sessions in office with efficacy around 40%
  - Bladder botulinum toxin injection done via cystoscopy with cure rates similar to SNM with high rates of patient satisfaction
    - Typically requires repeated injections every 3-18mos (usually 9-12)
    - Risk of urinary retention & UTI

REFERENCES

- American College of Obstetrics & Gynecology Practice Advisory, "COVID Vaccination Considerations for Obstetric-Gynecologic Care". Dec 2020.
- American College of Obstetrics & Gynecology Practice Advisory, "Maternal Immunization". Jun 2018, Reaffirmed 2021.
- Brioschi Dos Santos AP, Vicente CR, Cola JP, Tanaka LF, Garbin JRT, Dell'Antonio LS, Dell'Antonio CSDS, Miranda AE. The impact of COVID-19 on maternal death and fetal death, a cohort study in Brazil. PLoS One. 2023 Aug 17;18(8):e0290343. doi: 10.1371/journal.pone.0290343. PMID: 37590217; PMCID: PMC10434867.
- American College of Obstetrics & Gynecology Practice Advisory, "Maternal Respiratory Syncytial Virus Vaccination". Sep 2023.
- "Labor Induction vs Expectant Management in Low-Risk Nulliparous Women" N Engl J Med 2018; 379:513-523
DOI: 10.1056/NEJMoa1800566

REFERENCES

- "Comparison of Maternal Labor-Related Complications and Neonatal Outcomes Following Elective Induction of Labor at 39 Weeks of Gestation vs Expectant Management: A Systematic Review and Meta-analysis". JAMA Network Open. 2023 May 1;6(5):e2313162. doi: 10.1001/jamanetworkopen.2023.13162. PMID: 37171818; PMCID: PMC10182428.
- American College of Obstetrics & Gynecology Practice Advisory,"Updated cervical cancer screening guidelines". Apr 2021.
- "ASCCP 2019 Risk Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors." Journal of Lower Genital Tract Disease. 2020;24, pp 102-131
- Writing Group for the Women's Health Initiative Investigators. Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial. *JAMA*. 2002;288(3):321–333. doi:10.1001/jama.288.3.321

References

- Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. JAMA. 2004 Apr 14;291(14):1701-12. doi: 10.1001/jama.291.14.1701. PMID: 15082697.
- Long-term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev. 2017 Jan 17;1(1):CD004143. doi: 10.1002/14651858.CD004143.pub5. PMID: 28093732; PMCID: PMC6465148.
- 2022 Hormone Therapy Position State of the North American Menopause Society. Menopause: The Journal of the North American Menopause Society. 2022 May; Vol 29, No. 7, pp 767-794.

QUESTIONS???

Thank You!!