5. Evaluation of male factor infertility

• 1.5 mL, 15 mill/mL, 40% motile, 4% strict morphology. ALWAYS tested

• Absence of fructose = obstructive. Congenital absence of vas deferens always shows up on CREOGs b/c of genetics tie-in.
  • DON’T use TESE-sperm to do IVF-ICSI on a patient w/ undiagnosed CFTR mutation & make an affected baby.
  • DO karyotype/Y chromosome microdeletions in nonobstructive azo-(15%) or severe oligo-(5%) spermia.
119. Donor sperm use

• Prognosis varies according to specific AZF microdeletion (a and b poor, c good w/ TESE)
• AZF mutations passed to male offspring
111. Retrograde ejaculation

- IUI’s from alkalinized urine specimens good if numbers ok, otherwise IVF
- Functional retrograde ejaculation: diabetic neuropathy, MS, spinal cord injury
38. Male factor (hyperprolactinemia)

- Hyperprolactinemia (idiopathic, tumoral, drug induced) can lead to ED, diminished libido, orgasmic or ejaculatory dysfxn (88%).
- Dopamine agonist (cabergoline/bromocriptine) treats hyperprolactinemia; if HPT axis permanently disrupted, may need HCG and HMG for spermatogenesis
- Testosterone supplementation=>hypogonadotrophic hypogonadism w/ improved libido, less sperm
- Clomiphene citrate in males requires functioning HPT axis
88. Primary hypogonadotropin hypogonadism

- If azospermia -> gonadotropins
- If low gonadotropins -> check TSH, prolactin, MRI
- Treat w/ hCG, HMG
77. Varicocelectomy

- Surgical repair of varicocele improves fertility odds
- Offer –ectomy if palpable & at least one abnormal semen parameter
79. SIN

- Salpingitis isthmica nodosa = fallopian tube diverticulae.
- Multifocal.
- Tubal surgery less successful if present.
- High risk for ectopic.
124. PID

- Laparoscopic surgery is more invasive than antibody testing, so Chlamydia antibody testing correct CREOG answer
- “Silent PID” can still cause tubal damage
12. Hydrosalpinges
35. & 87. Intrauterine microinsert f/u

- Hydrosalpinges are toxic to embryos/IVF. Cut ‘em out
  - maybe block them: intrauterine microinserts have been used off-label, 63% cumulative LBR/pt, 27% LBR/ET

- 25% of microinserts had complete tissue encapsulation by 13-43 month second-look hysteroscopy
- Tubal patency after 3 months 3.5% in review, 0.5% in academic institution
89. HSG complications

- Post-HSG PID rare but serious, more likely (10% vs 1-3%) if blocked, dilated tube(s).
- Give doxycycline x 5 days if hydrosalpinx seen on HSG.
- Prior iodine allergy, pretreat w/ antihistamines and steroids
Sometimes you don’t have to read the whole question stem

A 36-year-old nulligravid woman with primary infertility comes to your office for evaluation. She has been attempting pregnancy for 12 months and has had regular menstrual cycles. Hysterosalpingography is normal and basal antral follicle count is 15. Ovarian reserve testing reveals a follicle-stimulating hormone level of 6.5 mIU/mL and an antimüllerian hormone level of 2.5 ng/mL. Semen analysis concentration is 3 million/mL with 15% motility and 1% strict morphology. Repeat semen analysis is similar. Male karyotype, Y chromosome microdeletion, total testosterone level, and follicle-stimulating hormone level are all normal. You consider recommending in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI). **You counsel the patient that a complication unique to ICSI is**

(A) imprinting disorders
(B) multiple pregnancy
(C) ovarian hyperstimulation syndrome
(D) decreased fertilization rates
11. IVF & ICSI

- ICSI indications: few sperm (mod-severe male factor, surgically retrieved sperm), PGS/PGD (no extraneous genetic material/sperm), zona pellucida problems (prior failed/poor fert, frozen eggs). ICSI/epigenetic complications: still rare but increased imprinting disorders like Beckwith-Wiedeman, Angelman.
71. Preimplantation genetic screening

• Day 5 trophectoderm biopsy yields hundreds of cells for microarray, PCR, isothermal rolling-circle-based amplification, or complete genomic hybridization.

• Euploid embryos are more likely to have live birth, but using PGS not necessarily more likely to yield live birth, especially if low egg yield (failure to develop to day 5, no euploid embryo to transfer, risk of mosaicism/false result)
47. & 123. Fertility options after tubal

- AGE is (nearly) always most important in fertility!
- Fertility 54-87% in 12 months after reversal, lower w/ longer interval if after 36, but still reasonable option 40-45.

- Regret 20% if under 30 at time of tubal, 6% if over 30
- Laparoscopic band or clip > lap cautery > hysteroscopic insert or salpingectomy
  - Less tissue damage, longer tube remaining = better reversal prognosis
8. ART & ovarian hyperstimulation syndrome

- OHSS=VEGF mediated leaky vessels=>extravasation=>hemoconcentration=>reduced end-organ perfusion.
  - Mild: abd pain, N/V/D
  - Moderate: fluid on sono, Hct>41%
  - Serious: clinical ascites, SOA, oliguria, Hct>51%, Cr>1.6
  - Critical: DVT/PE, ARDS, shock
- Risk factors: PCOS, young, pregnancy (HCG triggers)
32. & 75. Fertility preservation (cancer pt)

- Embryo cryopreservation most effective
- Oocyte cryopreservation (by vitrification)
  - No longer experimental
  - No embryo custody/disposal issues
  - No partner/sperm donor required
- Ovarian tissue freezing experimental
- Ovarian transposition useful for pelvic radiation pts
- Gonadal suppression w/ GnRH agonist
  - Basis: chemo mostly attacks active cells
  - RCTs show mixed results
97. Amenorrhea & galactorrhea

- COCs can be used for galactorrhea for non-tumor-related hyperprolactinemia or microadenoma who do not desire pregnancy
- Dopamine agonists needed if pregnancy desired or macroadenoma
  - Cabergoline (more effective, better tolerated)
  - Bromocriptine
10. Macroadenoma & galactorrhea

- Pituitary macroadenoma + elevated prolactin, Ddx includes prolactinoma>GH-producing adenoma>thryotropin- corticotropin- or gonadotropin-secreting tumors.
  - Diagnose GH-producing tumors (acromegaly) by IGF-1.
46. Macroadenoma (Prolactinoma)

- Dopamine agonist (cabergoline, bromocriptine) + repeat MRI 3-6 months, if no improvement -> surgery.
- Risk of pituitary apoplexy, observation not appropriate
- Add somatostatin analog treatment if growth hormone involved (elevated IGF-1)
- Transphenoidal resection more likely if no prolactinemia
70. Sheehan syndrome

- Postpartum infarction of pituitary
- Can have abnl levels of some or all hormones originating from ant & post pituitary: growth hormone, prolactin, gonadotropins, ACTH, TSH
- Most morbid is ACTH deficiency leading to adrenal insufficiency; screen w/ early-morning cortisol levels
- If FSH/LH low, would need gonadotropins for infertility treatment. Oral OI agents require an intact HPO axis.
152-154. Testing for thyroid disease

- High TSH low T4: clinical hypothyroid
- High TSH normal T4: subclinical hypothyroid
- Low TSH high T4, TPO antibodies: hyperthyroid, likely Grave’s
114. Hypothyroidism

- Observe if subclinical hypothyroidism not trying for pregnancy
- Keep below 2.5 if trying for pregnancy
74. Hyperthyroid

- If Graves suspected, radioiodine uptake test
- U/s if that’s contraindicated/not available
53. Postpartum thyroiditis

- Transient autoimmune thyroid disorder (5-10%)
- Typical sequence hyper->hypo->euthyroid
- Risk factors (check TSH 3 & 6 mo postpartum)
  - TPO antibodies (50%)
  - DMI (25%)
  - Graves in remission
  - Chronic viral hepatitis
- Levothyroxine if symptomatic hypothyroid, trying for pregnancy, or persistently TSH>10 (then taper off)
- Treat if overt hyperthyroid
3. Antiphospholipid syndrome

- Clinical + lab 99th %tile x2/12 weeks = APS. Antiphospholipid antibodies of importance: lupus anticoagulant, anticardiolipin ab, anti-beta2-glycoprotein I ab. Clinical: thrombosis, preg morbidity (>10 wks normal fetus Sab/IUFD, <34 weeks PIH, 3x <10 weeks s/p excluding other cause).

- Secondary APS = other autoimmune disorder too (37% of SLE)

- RPL workup doesn’t include inherited coagulopathies (FVL, AT III).
21. & 69. Recurrent pregnancy loss

- Woman’s karyotype higher yield: 1) translocations more common in women than men 2) if different male partner
  - Reciprocal most common, but Robertsonian tends to produce more unbalanced gametes (=>miscarriages)
  - Robertsonian involves any 2 acrocentric chromosomes: 13, 14, 15, 21, 22

- Cytogenetic abnormalities 5% of RPL
- Start RPL workup after 2 losses

http://www.yourgenome.org/facts/what-is-a-chromosome-disorder
118. Luteal phase deficiency

- Two out-of-phase EMB results considered proof of luteal phase deficiency NO LONGER
- No good test
83. POF

- Turner, Swyer syndrome can present as premature ovarian failure.
- Due to cardiovascular/gonadoblastoma risk, karyotype is first priority
- *FMR1* premutation has risks to offspring if IVF successful, to family members’ and their offspring
6. Primary ovarian insufficiency

- Love FMR1 b/c REI/MFM crossover, & b/c classic triplet repeat disorder w/ premutation/expansion. Look for combination of primary ovarian insufficiency, (male) mental retardation/autism, elder tremor/ataxia syndrome in history.

- POI definition <40 yo, >4 mo amenorrhea, FSH >40 x2/weeks apart

- POI risk factors: 45XO, FMR1 premutation, enzyme defects (17alpha-hydroxylase, aromatase, galactosemia), chemo/rad, viral, autoimmune
131-133. Hereditary cancer syndromes

- BRCA 1/2 tumor suppressor genes: BRCA2 mutation in exon 11
- Peutz-Jeghers = STK11 gene mutation, autosomal dominant, hamartomatous polyps, skin discoloration, GI cancers, lung/breast/uterus/ovary cancers
- Lynch syndrome AD mismatch repair enzymes involving \( MLH1, MSH2, MSH6, \) or \( PMS2 \). Endometrium, ovary, gastrointestinal tract, upper urinary tract, and bile duct ca.
- \( RAD51C \) gene is involved in DNA double-strand break repair similar ovarian & breast ca rates to BRCA.
127. Breast cancer

BOX 127-1

Criteria Used to Calculate the 5-Year Risk of Breast Cancer According to the Modified Gail Model

- Current age
- Age at menarche
- Age at first live birth
- Number of first-degree relatives with breast cancer
- Number of previous breast biopsies
- Whether any breast biopsy has shown atypical hyperplasia
- Race

13. & 22. Cancer/contraception in BRCA

• BRCA1/2 breast ca risk of 65-74%
• BRCA1 ovarian ca 39-46%, BRCA 2 ovarian ca 12-20%.
• Risk reduction strategies:
  • COC’s -46% ovarian ca, no effect breast ca
  • Premenopausal BSO -85-90% ovarian ca, -40-70% breast ca
  • Mastectomy -90-95% breast ca
43. BRCA screening

- *BRCA1* and *BRCA2* carriers should have
  - Ovarian ca screening (by expert consensus)
    - TVUS & CA 125 periodically starting age 30 or 5-10 years earlier than youngest
  - Breast ca screening (more reliable)
    - Starting at 25 (or earlier based on youngest dx) semiannual clinical breast exams, annual mammography and breast MRI
120. Normal menopausal transition

- Change in cycle length ddx: perimenopause, thyroid, prolactin
28. Perimenopausal changes

- 2011 Stages of Reproductive Aging Workshop + 10

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<td>Symptoms</td>
<td>Likely VSM</td>
<td>Most likely VSM</td>
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31. R/B of hormone therapy (WHI)

- **Risks**
  - E+P: increased risk coronary heart disease (26%), stroke (20%), PE (45%), invasive breast ca (93%)
  - E only: increased risk of stroke (20%)

- **Benefits**
  - E+P: decreased risk of colon cancer (-18%), hip fracture (-10%)
  - E only: decreased risk of hip fracture (-12%)

- Absolute difference in risks small: total net adverse outcomes E+P 1.56/1000 women per year, E only 0.08/1000 women per year.

- Use HT for moderate-severe hot flashes. Estrogen good for osteoporosis but not first line.
34. Postmenopausal bleeding & HT

- TVUS or EMB if bleeding on HT after menopause
- If TVUS ES <4 mm, observe
- If >4 mm, sample endometrium
- If can’t get tissue on EMB, TVUS
72. Low dose estrogen therapy

• Systemic & vaginal hormone therapies both treat symptoms of urogenital atrophy
• Progestin is needed to prevent endometrial hyperplasia if uterus present & systemic estrogen desired
• Vaginal estrogen & estrogen ring do not require progestin therapy
113. Bioidentical hormones

• 17beta-estradiol & micronized progesterone are FDA-approved bioidentical hormones
• “Bioidentical hormones” is a marketing term
• Compounding has inherent risks
• Salivary hormone levels not reproducible
• Treat symptoms, not hormone levels
50. Alternative therapies for menopause

• Most effective treatment for VMS is estrogen, but in cases of estrogen-sensitive breast cancer or other reason for nonhormonal...

• Venlafaxine (SNRI) effective

• Fluoxetine, low dose paroxetine (SSRI) work, but may make tamoxifen less effective

• Gabapentin (less effective, but less GI side effects, worse mood, more dizzy than SNRI)

• Clonidine (didn’t reach statistical significance)
94. Low bone mass/bone physiology

- Bisphosphonates, estrogen (alendronate sodium, ibandronate sodium, risedronate sodium, and zoledronic acid), calcitonin, PTH, raloxifene are approved treatments to prevent fracture.

The National Osteoporosis Foundation recommends treatment if the patient has either:

- a personal history of hip or vertebral fracture,
- a DXA scan with a T-score less than −2.5, or
- a bone mass in the osteopenic range (T-score of −1.0 to −2.5) and a 10-year probability of a hip fracture of 3% or more or a 10-year probability of any fracture of 20% or more based on Fracture Risk Assessment Tool estimates.
58. DMPA and bone loss

- Gonadotropin suppression and hypoestrogenemia => osteoclast bone resorption greater than osteoblast bone formation. Transient, not associated with fracture risk.
- Smoking: bone loss 1.5-2.0 times greater
101. Osteoporosis & celiac

- Gluten-free diet improves celiac symptoms & bone mineral density in celiacs
- 40% of celiacs very low BMD in spine at dx, 15% in hip
24. Hysteroscopic complications

- Uterine perforation most common complication of hysteroscopy (0.7-3%)
  - Adhesiolysis > myomectomy > septum
- Excessive fluid 0.2-0.76% of cases
  - Adhesiolysis > myomectomy > septum, keep pressure below MAP
- Stop at deficit of 2500 mL (account for IVF and UOP), 1500 if nonelectrolyte media, check sodium level at 750, stop if hypoNa+
105. Complications of robotic

• Cochrane review 2012 robot for benign gyn, no change in intraop complications.

• Robot had increased postop complications of: UTI, SBO, wound infection, erosion, abdominal wall pain needing trigger point injection, abscess
159-161. Laparoscopic surgery complications

- Bowel injury: abdominal distention, diarrhea, ileus, leukocytosis
- Ureteral injury: fever, flank pain, elevated CRP, leukocytosis
- Gas embolism: tachycardia, hypotension, hypoxia, decreased ETCO2
143-145. Statistical analysis

<table>
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<tr>
<th>Goal</th>
<th>Categorical: Nominal, Ordinal</th>
<th>Score, Rank, Nonnormal Continuous</th>
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<tr>
<td>Description</td>
<td>Proportions, frequency tables</td>
<td>Median, interquartile range</td>
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<td>Kaplan–Meier curve</td>
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<td>Compare one group with a hypothetical value</td>
<td>Chi-square goodness of fit</td>
<td>Wilcoxon signed rank test</td>
<td>One sample t-test</td>
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<td>Compare two independent groups</td>
<td>Fisher exact test, chi-square test of independence</td>
<td>Mann–Whitney test</td>
<td>Unpaired t-test</td>
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<td>Compare two paired groups</td>
<td>McNemar test</td>
<td>Wilcoxon signed rank test</td>
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<td>Compare three or more independent groups</td>
<td>Chi-square test of independence</td>
<td>Kruskal–Wallis test</td>
<td>One-way ANOVA</td>
<td>Cox proportional hazards regression</td>
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<td>Examine association between two variables</td>
<td>Chi-square test of independence</td>
<td>Spearman correlation</td>
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Abbreviations: ANOVA, analysis of variance; SD, standard deviation.
57. Absolute risk vs. RR

- Absolute risk is a **number or rate**; relative risk is a **ratio**
- Positive/negative predictive value: likelihood that person who has positive/negative test actually does/doesn’t have disease (depends on prevalence)
- Sensitivity (esp. for screening, minimize false negatives)
- Specificity (esp. for confirming, minimize false positives)
- Type I error finding a difference when there is none (inflated ego)
- Type II error missing a difference when there is one
1. Ethical/legal IVF

• Unless compelling evidence otherwise, in CREOG ethics question, Patient autonomy > Nonmaleficence
• Helpful to have clinic policy for futile efforts
39. Donor sperm for same-sex couples

- 3rd party reproduction (especially with known donor) is complex. Respect everyone’s rights and choices, not just your fertility patient(s).
  - ASRM “Guidelines for Gamete and Embryo Donation”
  - FDA screening for communicable diseases
  - Psychological assessment/mental health professional
  - Extensive medical history, genetic screening
  - Genetic counseling important pre- and post-test
  - For both donor and intended parents
134-138. Lifestyle choices

- Bariatric surgery is risk for nutritional deficiency
- Losing weight can resume ovulation
- Smoking can cause decreased ovarian reserve
- Vitamin D deficiency during pregnancy leads to congenital Rickets
- Fetal alcohol syndrome includes facial dysmorphism & intellectual impairment
29. Preconception counseling donor egg

• Most important: the test that could prevent greatest M&M
  • In 2010, 38% of donor egg cycles were multiples
  • Complications of older conceptions: preterm labor, PPROM, GHTN, DM, preeclampsia, HELLP, abnl placentation.
  • w/ h/o uncontrolled HTN, echocardiogram could ID LVH, which could cause life-threatening cardiomyopathy in pregnancy
126. Donor oocyte use

- Risks to donor exist, but no documented long-term sequelae, no decrease in ovarian reserve
- Risk of inadvertant consanguinity is best reason to limit donor cycles
85. Psychologic effect of infertility

• Infertility is stressful. Depression is common after failed IVF, women>men.

• Meds may be indicated, but psychological counseling is indicated, potentially CBT.
115. Ambiguous genitalia

- If gender in question, use multidisciplinary team to assist in assignment. Avoid premature labels.
139-142. Hormonal changes in pregnancy

- In pregnancy, placenta is an endocrine organ
  - Human placental lactogen is increased & acts like growth hormone
  - Corticotropin-releasing hormone may play role in contractility
  - Thyroid-binding globulin increases parallel to total T4, so free T4 remains the same
122. Use of stem cells in reproduction

- Possible to transform fibroblast into something that looks a lot like an embryonic stem cell (won Nobel prize 2012)
- INDUCED PLURIPOTENT STEM CELLS could be differentiated into germ cells for use in fertility
40. Phantom HCG results

- Heterophilic antibodies react against the animal-derived antigens used in immunoassay testing.
  - Risk factor = exposure to animals/animal tissue
- 3 tests to test for phantom HCG
  - Urine: antibodies aren’t present in urine, so urine test should be negative
  - Serum w/ serial dilution: lack of linear curve = presence of antibodies
  - Serum + heterophilic blocking agent, should then be negative
QUESTIONS?

Thank you!

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<td>136) 111</td>
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