GYN Care in CAH

Samantha Erin Vilano, MD
Medical Director of Pediatric & Adolescent Gynecology, Riley Hospital for Children
Assistant Professor of OB/GYN and Pediatrics, Indiana University
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Why Gynecology ??

- GYNs often serve as primary care providers for women.
- Girls with CAH often make the transition to adult providers during adolescence.  
  - A time that poses a number of challenges in the management of CAH.
- GYNs are trained to discuss a variety of concerns common in CAH.
- GYNs can play an important role in team-based approach to CAH care.
What do we talk about?

• Anatomic concerns/sexual function
• Sexual health and intimacy
• Personal sexual expression
• Menstrual period irregularity
• HPV screening/prevention
• Fertility
• Reproductive options
The Gynecologic Aspects of CAH

LET’S TAKE A TOUR
The First Gynecologic Visit

- American College of OB/GYN
  - Recommends a 1st visit for ALL girls between the ages of 13 and 15
Puberty and CAH

• Changing hormones can lead to inadequate suppression of adrenal androgens
  – Increased enzyme expression (cytochrome b5) produces more adrenal androgens
    • Unwanted hair growth
    • Worsening acne
    • Irregular menstrual periods
Puberty and CAH

• Puberty also changes the metabolism of cortisol
  – Increased clearance from the body (especially in girls)
  – Decreased utilization of supplemental cortisone

• Teen Girls often need more cortisol replacement!

BUT....
Puberty and CAH

• Adherence to medication schedules can pose a challenge as teens increase their independence
  – Switching to longer-acting glucocorticoid
  – Dexamethasone should be avoided in young women at risk of pregnancy

• Higher doses of glucocorticoids can lead to weight gain
  – Further reduces compliance for teen girls
  – Close monitoring in partnership with endocrinologist is important
Managing Pubertal Hormones

• Adding more cortisol can lead to weight gain

ANTI-ANDROGENS

Spironolactone

• Inexpensive and effective anti-androgen
• Difficult to use in Classic 21-OHD because it may cause salt loss
  • May need to increase dose of fludrocortisone
Ovarian Androgen Production

- ~25% of the body testosterone is normally made in the adrenal
- ~25% of the body testosterone is normally made in the ovaries
Secondary Polycystic Ovaries

Ovarian Androgens
Irregular Menstrual Periods

- Polycystic ovaries are associated with overproduction of OVARIAN androgens
  - Therefore high testosterone does not always indicate poor adrenal control
  - Irregular periods are common even for women who are on adequate glucocorticoid replacement

This is when girls most commonly end up in a gynecology office!
Oral contraceptive pills (OCPs)

- Oral Contraceptive Pills
  - Reduce amount of testosterone made in the ovary
  - Decrease symptoms of hyperandrogenism
    - Acne
    - Hair growth
  - Provide contraception
- Patch (weekly)
- Vaginal ring (monthly)

May take ≥ 6 months to improve symptoms
Adolescence and CAH

- Sexuality and sexual function become increasingly important during adolescence and young adulthood
  - Genital surgery often done in early childhood
  - New post-surgical concerns may arise with the onset of menstrual periods and sexual activity
COMMON ANATOMIC CONCERNS IN ADOLESCENCE
Anatomic Features of CAH in Girls

- Girls with classic CAH are born with
  - Clitoral hypertrophy (enlarged clitoris)
  - Anteriorly displaced labia majora or fused labia
  - Absent labia minora
  - Urogenital sinus
    - Urethra and vagina fuse to a common pathway which goes to the skin

Feminizing Genitoplasty

• Early surgery may involve:
  – Clitoral reduction (nerve-sparing)
  – Labioplasty
    • Repositioning and separation of the majora
    • Construction of labia minora
  – Vaginoplasty
    • Separation of the urethra and vagina
Post-Surgical Concerns

• Clitoral pain
  – More common with older surgical techniques prior to 1996
  – Trapped erectile tissue may grow with increasing androgens or swell with sexual stimulation

• Persistent Clitoral enlargement
  – Poor androgen control can result in growth of the clitoris
  – May be managed with clitoroplasty and medication optimization

• Decreased/absent clitoral sensation
Clitoral Enlargement

• Most patients express satisfaction with the appearance of their genitals
• Clitoral appearance was rated lower
• Higher satisfaction with clitoral function was reported the younger the age at clitoral surgery
  – Role of development of body image
Leakage of Urine

- Vaginal voiding is common
  - Urine exiting the urethra enters the vagina
    • Daytime wetting/dampness
    • Usually shortly after voiding
  - May be functional/postural
    • Managed by sitting with legs apart or sitting backward
  - May be due to poor separation of the urethra and vagina
    • Managed by surgically repositioning the urethra

- Urinary incontinence
  - Girls with h/o total urogenital mobilization need urologic evaluation

Post-Surgical Concerns

- Vaginal hair-bearing tissue
  - Surgery in early childhood generally involves the use of skin flaps
    - These flaps may develop hair during puberty
    - Less common today
  - Professional hair removal
  - Flap removal and replacement with a buccal graft (from inside of the cheek)
Vaginal Caliber/Function

• GYN assessment prior to the start of menstrual periods is common
  – In-office
  – Under a general anesthetic
• The gynecologist will assess the vaginal caliber for:
  – Unobstructed passage of menstrual blood
  – Ability to insert and use a tampon
  – Adequacy for comfortable sexual intercourse
Vaginal Caliber/Function

• Mild vaginal narrowing may be treated with vaginal dilation and estrogen cream
  – Placing a tampon
  – Penetrative sexual activity

• More severe narrowing may require
  – introitoplasty (revision of the vaginal opening) or
  – vaginoplasty (surgical augmentation or replacement of the vagina)
Surgical Planning for Vaginal augmentation

• Many centers employ a multi-disciplinary approach
  – Urology
  – Gynecology
  – Colorectal surgery (if bowel graft needed)

• Preliminary work-up may involve
  – Discussion of goals of treatment
  – Discussion of timing of treatment
  – Assessment of readiness to dilate (to maintain the space)
  – Vaginoscopy in the OR
    • Vagina may not be accessible to office exam
    • Allows visual evaluation of the existing vaginal tissue
Transitioning to Adult GYN Care

Involves a discussion and review of:

a) Prior surgeries
   - clitoroplasty
   - vaginoplasty/introitoplasty
   - labioplasty
   - urogenital sinus mobilization
   - adrenalectomy

b) Genetic testing
   - CYP21A2 gene mutation

c) Current medications
   - Corticosteroids
   - Mineralocorticoids
   - Oral Contraceptive Pills
   - Anti-androgens

d) Labs and tests
   - 17-hydroxyprogesterone
   - Testosterone, free+total
   - Bone density
Transitioning to Adult-GYN Care

Involves a GYN-targeted health assessment

**Clitoris** - appearance
- sensation

**Vagina** - depth and caliber
- adequacy for menses, tampon use
- adequacy for intercourse
- ? hair-bearing tissue in the lower vagina

**Ovaries** - irregular menstrual periods (anovulation)
Transitioning to Adult-GYN Care

Cervix – routine pap testing
  -- is the cervix easily accessible
  -- HPV vaccination for teens/young adults

Breast – routine screening

Bone health – Bone density scan, Calcium, VitD

Serum – every 1-2yr lipid profile, diabetes screen, thyroid screen
Fertility

• Women with CAH also accumulate progesterone which can lead to irregular, infrequent periods
  – Thickens cervical mucus
    • Inhibits sperm getting past the cervix
  – Inadequate growth of the endometrium
    • Reduced embryo implantation

• For women with CAH attempting to conceive, the single most important parameter is maintaining the progesterone <0.6 ng/mL
  – May require small evening dose of long-acting prednisolone and in rare cases dexamethasone***

*** crosses placenta  J Clin Endocrinol Metab, July 2013, 98(7):2645–2655
Fertility and Classic CAH

• Rates of pregnancy for women with classic CAH are between 33% and 60%
• Consultation with a reproductive endocrinologist is advised
  – Hydrocortisone is typically used to treat mom because it is inactivated by the placenta
  – Increasing steroid repletion to three times per day
  – Medical ovulation induction
Pregnancy

• Lower uterine volumes in women with CAH
  – May be due to imbalance between estrogens and androgens during adolescence
  – Excess of androgens during fetal development may affect uterine development

• Lower fertility rates
• Higher rates of miscarriage and premature birth

Johannsen et al. Intnl J Ped Endo 2010
Labor ? ? And Delivery

• Rates of cesarean delivery are high 67-72%
  – vaginal stenosis
  – preservation of prior genitoplasty / cosmesis
Reproductive concerns

• Increased risk of having a child affected by congenital adrenal hyperplasia
  – Classic CAH – 1 in 120 chance
  – Non-classic CAH – 1 in 360 chance

• Studies however, show the actual rate to be much higher
  – Classic CAH – 2.5%
  – Non-classic CAH – 14.8%
Role for Prenatal Therapy?

• Male and female reproductive organs are indistinguishable until ~ 6-7 weeks of pregnancy
  – In girls with CAH, the adrenal gland inappropriately produces too much androgen (testosterone) during this crucial time

  ‘virilizes’ (masculinizes) the female genitals

[Images of stages 1 to 5 showing virilization development]
Role of Prenatal Therapy

- Doctors have tried to use a glucocorticoid early in pregnancy to try and prevent this masculinization of the genitals
  - Cortisol does not cross the placenta
  - DEXAMETHASONE has been used

- US-based study of 49 treated pregnancies with classic CAH
  - 25 female fetuses treated < 9 weeks of pregnancy
    - 11 had normal female genitals
    - 11 had minimal virilization (Prader 1-2)
    - 3 were more virilized (Prader 3)
  - 24 female fetuses treated > 9 weeks of pregnancy
    - Average Prader 3
  - Untreated female fetuses
    - Average Prader 3.75

Success rate across several studies for improving genital virilization is about 80 – 85%
But there’s a catch......

• Maternal Effects
  – Increased weight gain
  – More striae
  – Increased swelling

• No increased risk of serious pregnancy complications like
  – High blood pressure
  – Pre-eclampsia
  – Diabetes of pregnancy

• Fetal Effects
  – Dexamethasone is a Category C drug

• What’s the risk??
  – Cleft lip / palate
  – Slightly lower birthweights
    • Potentially higher risk of adult-onset high blood pressure, diabetes, heart disease
  – No effect on intelligence or long-term memory
    • Poorer verbal working memory
What’s the Debate

Prenatal treatment does

• Improved cosmetic outcome
• Decreased need for genital surgery
• ? Improved psychologic / emotional consequences
• Decreased parental distress
• Have some risks.....

Prenatal treatment does NOT

• Preserve life or intellect
• Change the need for life-long steroid replacement
• Prevent life-threatening salt-losing crises

• Exposes many *unaffected* female and male fetuses unnecessarily
  – Unethical
  – Not warranted
• Endocrine Society 2010 Guidelines for CAH

  – Prenatal dexamethasone is experimental
  – There are NO recommended treatment plans
  – Benefits do not warrant the risks
  – Prenatal dexamethasone should NOT be used
A Few Words about Non-Classic CAH

• Mildest form of CAH
• Partial 21OHD (20-50% enzyme activity)
• ~1/1000 general population

• Most have normal genitals at birth
• No salt-wasting

Girls and Women come to Gynecology at 3 times –

1. Childhood -- Early puberty
2. Adolescence – Acne, hirsutism, irregular periods
3. Adulthood – Fertility concerns
Non-classic CAH Women

• Symptoms often managed with oral contraceptive pills
  +/- spironolactone

• Glucocorticoids may be used at specific times
  – If started in childhood, continue at least 2-3 years after menarche (allow for regular menses to establish)
  – Pre-pregnancy treatment may
    • increase fertility
    • reduce the chance of miscarriage post-conception
Fertility and Non-classic CAH

- Infertility is the presenting symptom for many

- ~90% achieve pregnancy

- If conception is achieved without steroids, steroid treatment is usually not required while pregnant

- ~2/3 of patients with non-classic CAH are carriers of a classic mutation
  - Pre-conception genetic screening important
References