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Exclusion criteria:

- Children > 1 year of age

If prenatal concern, see [communication strategies](#) and provide [resources](#) (Pediatric Endocrine Society, 2025)

Concerns for Differences of Sex Development (DSD)

- Atypical genital appearance following birth
- Discordance between prenatal testing and postnatal phenotype

Adrenocorticotrophic Hormone (ACTH) Stimulation Test

- Infants with adrenal insufficiency often present in adrenal crisis at 7 - 10 days of life
 - If there is a high suspicion for adrenal insufficiency, an ACTH stimulation test should be performed prior to discharge from the nursery
 - If not completed, close follow-up with Primary Care and Endocrinology is warranted
- The ACTH stimulation test at Children's Mercy includes progesterone, 17-OH progesterone, 11-desoxycortisol, cortisol, DHEA, and testosterone at 0 and 60 minutes
- For those with suspected undervirilized male genitalia (46,XY), the addition of 17-OH pregnenolone to this panel may provide additional information about 3-beta-hydroxysteroid dehydrogenase deficiency
- The addition of deoxycorticosterone can provide information about 17-hydroxylase deficiency in those with more typical female genitalia, though 46,XY chromosomal make-up

This testing should be considered in collaboration with a pediatric endocrinologist

Patient presents with a concern for differences of sex development

Physical Exam

Complete physical exam (i.e., full body assessment with detailed genital exam) with particular attention to:

- Midline defects (including cleft lip/palate, omphalocele, heart murmur)
- Gonad location (or noting if not palpable)
- Clitorophallus size (obtain [stretched length](#), if possible, and width)
- Urethra location
- Vaginal and urethral openings (separate or not)
- Skeletal anomalies
- Anus patency and location (if concern for anorectal anomaly or cloaca, involve Colorectal Team)

Communication

Discuss concerns with parents/guardian and obtain consent for genetic testing

- Use gender-neutral terms and avoid assigning sex or gender
- Emphasize patient's overall health or address acute medical concerns without solely focusing on atypical genitalia or sex assignment. Balance medical details with affirmations of the child's unique qualities
- Provide accurate terminology for families to use

Link to suggested [communication strategies](#) and [resources](#)

Laboratory Testing

- BMP within 36 hours of life
- Monitor blood glucose (POC)
- Karyotype with FISH for X and Y (including SRY)

Imaging

- Ultrasound of scrotum/labia
- Ultrasound of pelvis

Sonographer and radiologist **should be familiar** with newborn pelvic anatomy. If needed, refer to Children's Mercy Radiology

Consults or Referrals

If positive newborn screen for congenital adrenal hyperplasia (CAH) or electrolyte derangement, admit to inpatient

- **Inpatient:** Consult Endocrinology, Genetics, and Urology
 - Consider consult to GUIDE psychologist
 - If recommended by Endocrinology or Urology, consult Gynecology
 - Outpatient referrals as recommended (consider [GUIDE Clinic](#) for children with differences of sexual development)
- **Outpatient:** Refer to Endocrinology (within 2 weeks if < 1 month of age; within 4 weeks if ≥ 1 month of age). Endocrinology will coordinate referral to Genetics and Urology and/or Gynecology
 - Consider referral to [GUIDE Clinic](#)
 - Laboratory evaluation may be delayed until the Endocrinology visit, unless there is a concern for adrenal insufficiency or a delay in endocrine care beyond 6 months of life
 - If possible, obtain pelvic and/or scrotal ultrasound prior to the Endocrinology visit

Are male gonads palpated or identified on ultrasound (US) in either inguinal canal or labioscrotal folds?

Yes

No

Is a uterus present on US?

Yes

Complete XY Hormone Evaluation

- Consider 7-dehydrocholesterol level
- Consider **ACTH stimulation test**
- After 1 week and before 6 months of age in an effort to capture minipuberty window: (link to [supporting literature](#))
 - Luteinizing Hormone (ultrasensitive assay)
 - Follicle-Stimulating Hormone (ultrasensitive assay)
 - Testosterone
 - Dihydrotestosterone
 - Anti-Müllerian Hormone

Complete XX Hormone Evaluation

- Evaluate for CAH
 - 17-OH **progesterone** (Alert: sound alike lab - do NOT order 17-OH pregnenolone)
 - Consider **ACTH stimulation test**

Do labs reveal a diagnosis?

Yes

No

Consider Additional Genetic Testing

- Exome sequencing
- Consider long-read genome sequencing in the presence of additional syndromic features, such as hypotonia

Are labs consistent with CAH?

No

Yes

- **Admit** to inpatient, if outpatient
- **Treat** in collaboration with Endocrinology

- **Treat** accordingly, in collaboration with subspecialists as needed
- **Refer** to genetic counseling, if indicated

Ongoing Care

- Decide on sex/gender of rearing, in collaboration with subspecialists and family (this is a dynamic decision and may occur after discharge from the hospital)
- Ensure follow-up with relevant specialties (e.g., [GUIDE Clinic](#), genetic counseling)