

# Prenatal Atypical Genitalia

Provider Quick-Reference Cheat Sheet

Chukwuma Onyeije, MD · Maternal-Fetal Medicine · Atlanta Perinatal Associates

Full 27-slide deck: [openmfm.org/decks/prenatal-atypical-genitalia](https://openmfm.org/decks/prenatal-atypical-genitalia)

## Terminology

- **Atypical genitalia** describes phenotype — what is seen on imaging or exam.
- **DSD** (disorder of sex development) describes atypical chromosomal, gonadal, or anatomical sex development — a broader category.

## Triggers for Evaluation

- Atypical external genital morphology on ultrasound.
- cfDNA–ultrasound sex discordance.

Prenatal suspicion is uncommon; associated anomalies are frequent once referred — treat as a sentinel finding.

## Step 1 — Confirm Before Labeling

- Repeat targeted imaging with an expert operator before counseling the family.
- Optimize fetal position, magnification, orthogonal planes, and cine clips.

## Step 2 — Describe Systematically

- **Phallic structure:** size · contour · curvature.
- **Labioscrotal region:** fold fusion · urethral position.

**Signs are clues, not diagnoses:**

- Blunt, incurved phallus → clue for hypospadias.
- Bifid labioscrotal folds → clue for severe undervirilization.

## Step 3 — Survey Beyond the Perineum

- GU/abdominal: renal/urinary anomalies · OEIS complex · cloacal malformation.
- Other systems: cardiac · CNS · abdominal wall · spine.

## Differential by Karyotype

- **46,XX:** androgen excess (e.g., CAH) · SRY-related testicular development.
- **46,XY:** gonadal, androgen synthesis, androgen action, or anatomic disorders.

## History Clues for Discordance

- Prior sex-screening results · vanishing (co-)twin.
- Maternal transplant or transfusion · maternal disease.

## Why cfDNA Can Mislead

- **SNP platforms:** may misinterpret mosaicism or microchimerism.
- **Whole-genome (MPS) platforms:** blind to microtranslocations below resolution.
- **cfDNA** reflects placental + maternal DNA — biologic false positives possible.
- **Amniotic fluid** evaluates fetal DNA directly — bypasses CPM and maternal microchimerism.

Neither cfDNA platform is diagnostic for structural or single-gene DSD.

### ■ Golden Rule

Do not adjudicate screening with screening. A discordant or high-risk cfDNA result escalates to **diagnostic** testing — not a repeat cfDNA.

## Diagnostic Testing Ladder

- Genetic counseling first — testing is **offered**, not mandated.
- Offer amniocentesis for fetal DNA: karyotype + CMA.
- Rapid sex-chromosome assessment; full karyotype when structure/mosaicism matters.
- SRY FISH/PCR/sequencing — only for suspected SRY deletion, duplication, or translocation.
- Suspected CAH → CYP21A2 sequencing + deletion/duplication analysis.
- Unexplained DSD → multigene panel.
- Fetal MRI complements — does not replace — expert ultrasound.

## Build the Team Before Delivery

- MFM · Genetics/Genetic Counseling · Pediatric Endocrinology · Urology/Surgery.

## Delivery & Postnatal Confirmation

- Atypical genitalia alone does **not** mandate cesarean delivery.
- Anticipate salt-wasting crisis risk (CAH) when choosing the delivery center.
- Postnatal: expert exam + electrolytes/glucose · 17-OHP/targeted hormones · pelvic/abdominal ultrasound.

## Applied Example

### Y detected by cfDNA + apparently female ultrasound

- ≠ a “false-positive male” result.
- ≠ an indication for repeat cfDNA.
- = confirm anatomy → survey fetus → reconcile history → counsel → offer diagnostic testing.

## Five Take-Home Principles

1. Describe phenotype — not a premature sex label.
2. Confirm with expert imaging before counseling.
3. Search for associated anomalies with a full survey.
4. Offer diagnostic — not repeat screening — testing.
5. Build the multidisciplinary team early.