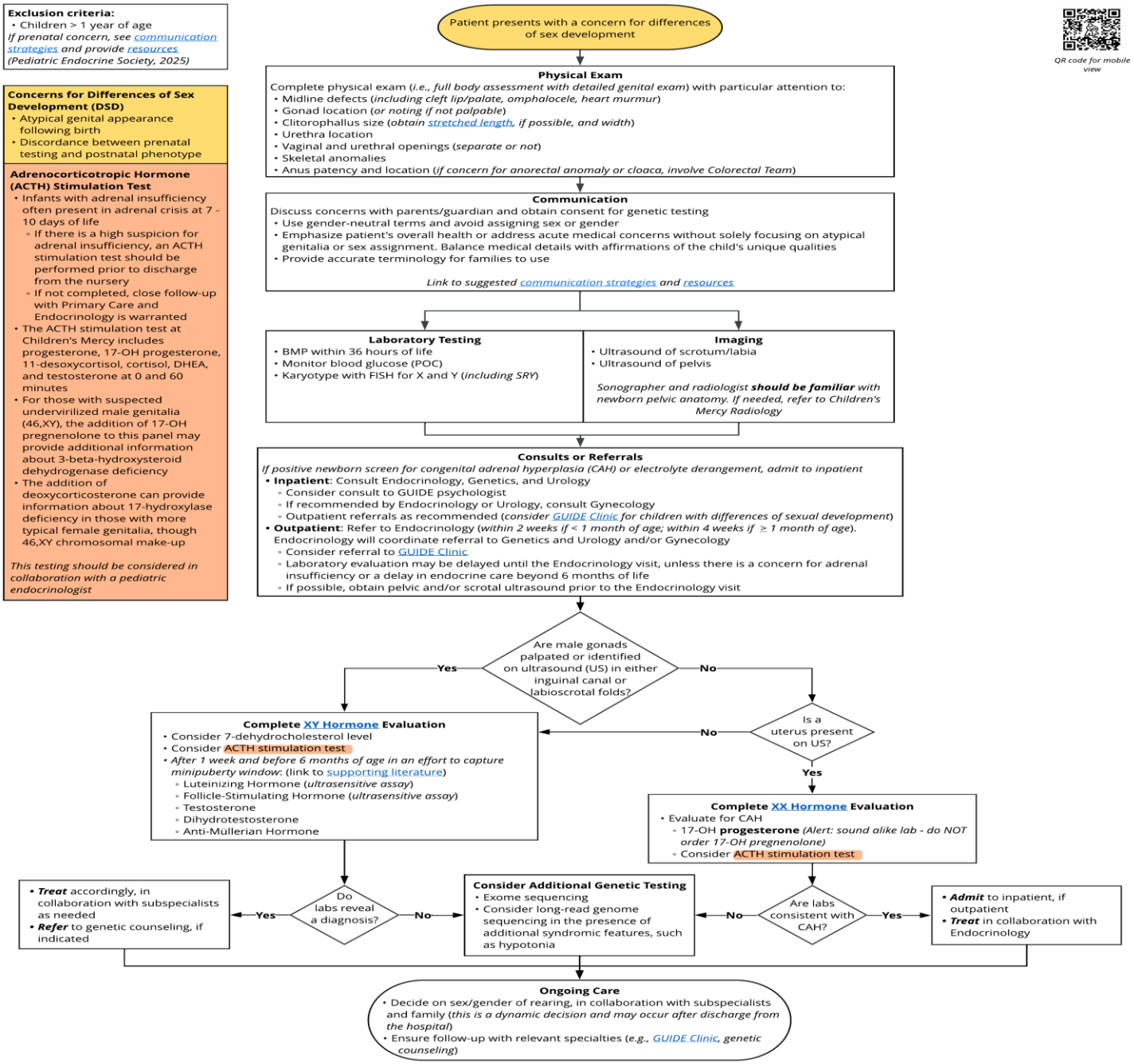
Differences of Sex Development
Clinical Pathway Synopsis

Differences of Sex Development Algorithm



These clinical pathways do not establish a standard of care to be followed in every case. It is recognized that each case is different, and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time. It is impossible to anticipate all possible situations that may exist and to prepare a clinical pathway for each. Accordingly, these clinical pathways should guide care with the understanding that departures from them may be required at times.

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Objective of Clinical Pathway

To provide care standards for the patient with a concern for differences of sex development. The Differences of Sex Development Clinical Pathway aims to provide guidance for the initial discussion and evaluation of infants with atypical genitalia or another concern for differences of sex development.

Background

Differences of sex development (DSD) are a group of congenital conditions in which the development of chromosomal, gonadal, and/or anatomical sex is atypical (Cools et al., 2018; Davies & Cheetham, 2017; Lee et al., 2016; Ochoa et al., 2024). These conditions may result in variations of external genitalia, internal reproductive organs, or sex chromosome patterns (Allen et al., 2022; Lee et al., 2021; Ochoa et al., 2024). For an infant born with a concern for DSD, an initial evaluation, including a thorough clinical assessment and hormonal laboratory workup, is essential to establish an accurate diagnosis and initiate appropriate management (Ahmed, 2021; Grinspon et al., 2021; León et al., 2019; Weidler et al., 2024).

The Differences of Sex Development Clinical Pathway Committee recognizes that guidance regarding the initial management of infants with suspected DSD is lacking. Therefore, the aim of this clinical pathway is to inform providers within and outside Children's Mercy about the recommended clinical and hormonal workup, necessary consultations or referrals, and best practices for family communication. This pathway does not provide comprehensive guidance on the management of a patient with suspected DSD. Instead, it offers initial guidance to ensure patients can be evaluated and triaged appropriately for multidisciplinary evaluation and care.

The Differences of Sex Development Clinical Pathway is designed for patients less than 1 year of age, as hormonal evaluation during this time is most likely to provide relevant information leading to a diagnosis. While some recommendations may apply to older children with suspected DSD, advanced testing may be required for diagnostic purposes, and conversations may differ about the impact of their underlying condition on their identity due to their already established sex assignment.

Target Users

- Physicians and Advanced Practice Providers (Neonatology, Endocrinology, Urology, Gynecology, Genetics, Hospital Medicine, General Pediatrics, Residents, Fellows)
- Clinical Genetics (genetic counselors, nurses)
- Psychologists
- Social Workers

Target Population

Inclusion Criteria

- Patient with concern for DSD (e.g., atypical genital appearance following birth, discordance between prenatal testing and postnatal phenotype)

Exclusion Criteria

- Children > 1 year of age
- If prenatal concern, see communication strategies (link) and provide resources (Pediatric Endocrine Society, 2025)

Practice Recommendations

In lieu of a clinical practice guideline fully addressing the management of infants with suspected DSD, guidance from pediatric DSD literature was used in conjunction with the expert consensus of the Differences of Sex Development Clinical Pathway Committee to inform the initial exam, laboratory and imaging workup, consults or referral guidance, and communication in this pathway.

Additional Questions Posed by the Clinical Pathway Committee

No additional clinical questions were posed for this review.

Updates from Previous Versions of the Clinical Pathway

- The Differences of Sex Development Clinical Pathway is a newly developed evidence-based pathway with no previous version for comparison

Measures
- Access of the Differences of Sex Development Clinical Pathway (website hits)
- Utilization of associated order sets

Value Implications

The following improvements may increase value by reducing healthcare costs and non-monetary costs (e.g., missed school/work, loss of wages, stress) for patients and families, and reducing costs and resource utilization for healthcare facilities.
- Decreased risk of inaccurate hormonal laboratory workup
- Decreased risk of missed life-threatening conditions or associated congenital anomalies (i.e., congenital adrenal hyperplasia, Turner syndrome)
- Decreased risk of incorrect or delayed diagnosis
- Decreased risk of an inaccurate sex assignment
- Decreased unwarranted variation in care

Organizational Barriers and Facilitators

Potential Barriers
- Variability in experience among clinicians
- Need for effective communication and coordination among clinicians and specialties
- Challenges with access to healthcare and health literacy faced by some families

Potential Facilitators
- Collaborative engagement across the continuum of clinical care settings and healthcare disciplines during clinical pathway development
- Consistent utilization of the clinical pathway when applicable

Bias Awareness

Bias awareness is our aim to recognize social determinants of health and minimize healthcare disparities, acknowledging that our unconscious biases can contribute to these inequities.

Order Sets
- ICN Ambiguous Genitalia

Associated Policies
- There are no relevant policies associated with this clinical pathway

Educational Materials
- Genetic Testing
  - Found in Cerner depart process
  - Available in English and Spanish

Clinical Pathway Preparation

This pathway was prepared by the EBP Department in collaboration with the Differences of Sex Development Clinical Pathway Committee, composed of content experts at Children's Mercy. If a conflict of interest is identified, the conflict will be disclosed next to the committee member's name.

Differences of Sex Development Clinical Pathway Committee Members and Representation
- Michelle Knoll, MD, MHPE | Endocrinology | Committee Chair
- Shannon Haines, MD, MPH, FAAP | Neonatology | Committee Member
- Kelli Ayars, MSN, RN, NNP-BC | Neonatology | Committee Member
- John Gatti, MD | Urology | Committee Member

- Joel Koenig, MD | Urology | Committee Member
- Anne-Marie Priebe, DO | Gynecology | Committee Member
- Jeanette Higgins, RN, MSN, CPNP | Gynecology | Committee Member
- Anna Egan, PhD, ABPP | Developmental and Behavioral Health | Committee Member
- Gail Robertson, PhD, ABPP | Developmental and Behavioral Health/Endocrinology | Committee Member
- Cassandra Barrett, PhD, MS, CGC | Clinical Genetics | Committee Member
- Holly Welsh | Clinical Genetics | Committee Member
- Sarah Dierking, MSN, RN, CPHQ | Clinical Practice and Quality | Committee Member

Patient/Family Committee Member

- Brianna Schmitz | Committee Member

EBP Committee Members

- Kathleen Berg, MD, FAAP | Evidence Based Practice
- Kelli Ott, OTD, OTR/L | Evidence Based Practice

Clinical Pathway Development Funding

The development of this clinical pathway was underwritten by the following departments/divisions: Endocrinology, Neonatology, Urology, Gynecology, Developmental and Behavioral Health, Clinical Genetics, Clinical Practice and Quality, and Evidence Based Practice.

Conflict of Interest

The contributors to the Differences of Sex Development Clinical Pathway have no conflicts of interest to disclose related to the subject matter or materials discussed.

Approval Process

- This pathway was reviewed and approved by the EBP Department and the Differences of Sex Development Committee after committee members garnered feedback from their respective divisions/departments. It was then approved by the Medical Executive Committee.

Review Requested

Department/Unit	Date Obtained
Endocrinology	January 2026
Neonatology	January 2026
Urology	January 2026
Gynecology	January 2026
Developmental and Behavioral Health	January 2026
Clinical Genetics	January 2026
Clinical Practice and Quality	January 2026
Patient and Family Engagement	January 2026
Evidence Based Practice	December 2025

Version History

Date	Comments
January 2026	Version one – (*developed algorithm and the associated synopsis, and revised educational materials*)

Date for Next Review

- January 2029

Implementation & Follow-Up

- Once approved, the pathway was implemented and presented to the appropriate care teams:
  - Announcements made to relevant departments
  - Additional institution-wide announcements were made via the hospital website and relevant huddles
  - Community clinics affiliated with Children's Mercy received announcements via "Progress Notes"

- Order sets consistent with recommendations were reviewed for the Neonatal Intensive Care Unit
- Care measurements may be assessed and shared with appropriate care teams to determine if changes need to occur.
- Pathways are reviewed every 3 years (or sooner) and updated as necessary within the EBP Department at Children's Mercy. Pathway committees are involved with every review and update.

Disclaimer

When evidence is lacking or inconclusive, options in care are provided in the supporting documents and the power plan(s) that accompany the clinical pathway.

These clinical pathways do not establish a standard of care to be followed in every case. It is recognized that each case is different, and those individuals involved in providing health care are expected to use their judgment to determine what is in the best interests of the patient based on the circumstances existing at the time.

It is impossible to anticipate all possible situations that may exist and to prepare clinical pathways for each. Accordingly, these clinical pathways should guide care with the understanding that departures from them may be required at times.

References

Ahmed, S. F., Achermann, J., Alderson, J., Crouch, N. S., Elford, S., Hughes, I. A., Krone, N., McGowan, R., Mushtaq, T., O'Toole, S., Perry, L., Rodie, M. E., Skae, M., & Turner, H. E. (2021). Society for Endocrinology UK guidance on the initial management of a suspected difference or disorder of sex development (Revised 2021). *Clinical Endocrinology*, 95(6), 818-840. https://doi.org/10.1111/cen.14528

Alimussina, M., Diver, L. A., McGowan, R., & Ahmed, S. F. (2018). Genetic testing of XY newborns with a suspected disorder of sex development. Current Opinion in Pediatrics, 30(4), 548-557. https://doi.org/10.1097/MOP.0000000000000644

Allen, N. G., Krishna, K. B., & Lee, P. A. (2022). Differences of sex development: What neonatologists need to know. *Clinics in Perinatology*, *49*(1), 207-218. https://doi.org/10.1016/j.clp.2021.11.013

Busch, A. S., Ljubicic, M. L., Upners, E. N., Fischer, M. B., Raket, L. L., Frederiksen, H., Albrethsen, J., Johannsen, T. H., Hagen, C. P. & Juul, A. (2022). Dynamic changes of reproductive hormones in male minipuberty: Temporal dissociation of Leydig and Sertoli cell activity. *The Journal of Clinical Endocrinology & Metabolism*, *107*(6), 1560-1568. https://doi.org/10.1210/clinem/dgac115

Cools, M., Nordenström, A., Robeva, R., Hall, J., Westerveld, P., Flück, C., Köhler, B., Berra, M., Springer, A., Schweizer, K., Pasterski, V., & COST Action BM1303 Working Group 1 (2018). Caring for individuals with a difference of sex development (DSD): A consensus statement. *Nature Reviews Endocrinology*, *14*(7), 415-429. https://doi.org/10.1038/s41574-018-0010-8

Davies, J. H., & Cheetham, T. (2017). Recognition and assessment of atypical and ambiguous genitalia in the newborn. Archives of Disease in Childhood, 102(10), 968-974. https://doi.org/10.1136/archdischild-2016-311270

Délot, E C., Papp, J. C., DSD-TRN Genetics Workgroup, Sandberg, D. E., & Vilain, E. (2017). Genetics of disorders of sex development: The DSD-TRN Experience. *Endocrinology and Metabolism Clinics of North America*, *46*(2), 519-537. https://doi.org/10.1016/j.ecl.2017.01.015

Grinspon, R. P., Castro, S., & Rey, R. A. (2023). Up-to-date clinical and biochemical workup of the child and the adolescent with a suspected disorder of sex development. *Hormone Research in Paediatrics*, *96*(2), 116-127. https://doi.org/10.1159/000519895

Jacobson, J. D., Willig, L. K., Gatti, J., Strickland, J., Egan, A., Saunders, C., Farrow, E., & Heckert, L. L. (2020). High molecular diagnosis rate in undermasculinized males with differences in sex development using a stepwise approach. *Endocrinology*, *161*(5), bqz015. https://doi.org/10.1210/endocr/bqz015

Lee, B. R., Strobel, K. M., & Chu, A. The neonate with ambiguous genitalia. *NeoReviews*, *22*(4), e241-e249. https://doi.org/10.1542/neo.22-4-e241

Lee, P. A., Nordenström, A., Houk, C. P., Ahmed, S. F., Auchus, R., Baratz, A., Baratz Dalke, K., Liao, L. M., Lin-Su, K., Looijenga, L. H., 3rd, Mazur, T., Meyer-Bahlburg, H. F., Mouriquand, P., Quigley, C. A., Sandberg, D. E., Vilain, E., Witchel, S., & Global DSD Update Consortium (2016). Global disorders of sex development updates since 2006: Perceptions, approach, and care. *Hormone Research in Paediatrics*, *85*(3), 158-180. https://doi.org/10.1159/000442975

León, N. Y., Reyes, A. P., & Harley, V. R. (2019). A clinical algorithm to diagnose differences of sex development. The Lancet Diabetes & Endocrinology, 7(7), 560-574. https://doi.org/10.1016/S2213-8587(18)30339-5

Ochoa, B., Weidler, E., Parks, M. A., Speck, K. E., & van Leeuwen, K. (2024). Novel approaches to patients with differences of sex development. *Advances in Pediatrics*, *71*(1), 151-167. https://doi.org/10.1016/j.yapd.2024.04.002

Soursa-Johnson, K. I., Gardner, M. D., Brinkman, W., Carely, M., Gruppen, L., Liang, N., Lightfoot, S., Pinkelman, K., Speiser, P. W., VanderBrink, B., Wisniewski, J., Sandberg, D. E., & Stacey, D. (2023). A survey of healthcare professionals' perceptions of the decisional needs of parents with an infant born with a disorder/difference of sex development. Journal of Pediatric Urology, 19(1), 39-49. https://doi.org/10.1016/j.jpurol.2022.09.015

Van der Straaten, S., Syryn, H., Dessens, A., Cools, M., & Tack, L. (2025). Role of the pediatrician in the initial management of a newborn with differences of sex development or hypospadias. *European Journal of Pediatrics*, *184*(5), 307. https://doi.org/10.1007/s00431-025-06140-6

Weidler, E. M., Ochoa, B., & van Leeuwen, K. (2024). Prenatal and postnatal evaluation of differences of sex development: A user's guide for clinicians and families. *Current Opinion in Pediatrics*, *36*(5), 547-553. https://doi.org/10.1097/MOP.0000000000001388