Belfast Health and Social Care Trust

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Title:	Disorders of sexual development in neonates - Guidelines for the investigation and management of				
Author(s)	Dr. David Sweet Consultant Neonatologist david.sweet@belfasttrust.hscni.net [redacted] Paediatric Specialty Registrar [redacted] Additional authors Dr. Noina Abid Consultant paediatric Endocrinologist Mr David Marshall, Consultant Paediatric Surgeon/ Urologist; Dr Fergus Harnden, Paediatric Registrar				
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Version control for drafts:

Date	**Version**	**Author**	**Comments**
3/11/09	0.1	[redacted]	Initial draft
17/12/09	0.2		Amendments
13/5/13	1.1	[redacted]/Sweet	Review
2/7/13	1.2	Dr. Sweet/[redacted]	Minor changes made and widely circulated amongst Excellence and Clinical Governance Committee, Supervisors of Midwives and all key workers. End date for comments 17/7/2013.

17/7/2013	1.3	Dr. Sweet/[redacted]	Comments made by [redacted] S&G Committee have been addressed by Dr. Sweet. Guideline returned to S&G for approval by the Policy Committee.
7/5/2014	V2	Dr. Marshall and Dr. N. Abid	Suggestions made and guideline amended accordingly. Sent to [redacted] for uploading onto the intranet.
1/8/2019	V3	Dr D Sweet/Dr N Abid/Mr D Marshall/Dr F Harnden	Initial investigations revised in keeping with UK Society for Endocrinology guidance Recommendation regarding use of external masculinsation score added Detail regarding interpretation of hCG test removed New information leaflet reference added

1.1.1 DEFINITION/BACKGROUND

Any doubt around sex of rearing of a child is a stressful and unsettling time for families. These guidelines are to provide a succinct investigation and management plan for all such babies to allow a working diagnosis to be made as soon as possible after birth with advice for the counselling of parents during this time.

1.2 Purpose

To provide guidance for staff involved in the management of babies born with disorders of sexual development and in the counselling of their parents.

1.3 Objectives

To provide a multi-professional guideline to help with management of babies born with disorders of sexual development and the counselling of their parents.

2.0 SCOPE OF THE POLICY

Neonatal medical staff (consultants, registrars, specialty trainees), midwifery and neonatal nursing staff, paediatric surgical team, paediatric endocrine team.

3.0 ROLES/RESPONSIBILITIES

Responsibility of all staff involved in management of babies with disorders of sexual development to read guideline.

4.0 KEY POLICY PRINCIPLES

Key Policy Statement

Any doubt around sex of rearing of a child is a stressful and unsettling time for families. These guidelines are to provide a succinct investigation and management plan for all such babies to allow a working diagnosis to be made as soon as possible after birth with advice for the counselling of parents during this time.

4.1 Policy Principles

Genital malformations are thought to occur in 4-5 per 1000 live births. The prevalence of complex genital anomalies where gender assignment is not possible at birth is thought to occur in 1/4500 live births. If there is any doubt around sex of rearing then gender should **not** be assigned until the baby is discussed with and reviewed by senior paediatrician/ endocrinologist. This means that no-one should hazard a well-meaning guess before the relevant investigations have been performed.

This is a stressful and unsettling time for families and there should be sensitive and open communication with them at all times. It may be necessary to involve the paediatric surgical team, clinical psychology as well as paediatric endocrinology **early** on in the diagnostic process.

Parents should be advised not to name or register their baby until gender is formally assigned. It may be useful for the family to assign someone as spokesman for them to tell friends/family that "the baby" is unwell and that immediate family cannot take calls for the next few days and would appreciate it if people could respect their privacy.

Pages 5-6 of the DSD Families parent advice leaflet referenced below give some excellent advice on a range of ways various families might wish to discuss these difficult issues, especially in the traumatic early days.

Neutral terminology should be used by everyone until gender is assigned:
"baby‟ instead of he/she
"phallus‟ instead of penis/clitoris
"gonads‟ instead of testes/ovaries
"labio-scrotal folds‟ instead of labia/scrotum
"disorder of sexual differentiation‟ (DSD) instead of ambiguous genitalia or intersex

Investigations should be performed in the following circumstances:
Overt genital ambiguity (sex of rearing uncertain)
Isolated perineal hypospadias
Bilateral cryptorchidism (impalpable undescended testes)
Micropenis (stretched penile length <2.5cm)
Females with inguinal/labial mass (apparent inguinal hernia)
Isolated clitoromegaly +/- labial fusion

Clinical assessment:

- full **history** should be taken including family history, previous miscarriages, maternal health and potential fetal androgen exposure
- full **clinical examination** including:
- phallic length (pubic symphysis to tip of phallus)
- number and site of perineal external orifices/urogenital sinus
- development of labio-scrotal folds
- presence and position of gonads
- degree of virilisation
- signs of adrenal insufficiency (skin pigmentation, hypotension, hypoglycaemia)
- signs of underlying congenital malformation/syndrome

Consider calculating External Masculinisation Score (EMS). UK Society for Endocrinology guidance recommends investigating infants who have a combination of genital anomalies with an EMS of <11.

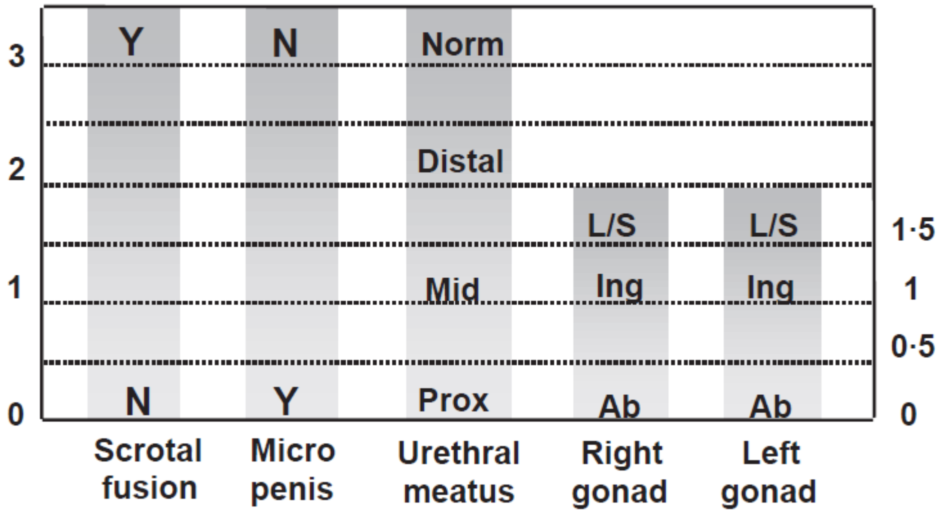

Fig. 1 Calculating the External Masculinisation Score provides an objective aggregate score of the extent of masculinization of the external genitalia. Each individual feature of the genitalia (phallus size, labioscrotal fusion, site of the gonads and location of urethral meatus) can be individually scored to provide a score out of 12. [1]Microphallus refers to a phallus below the male reference range. [2]L/S, labioscrotal; Ing, inguinal; Ab, abdominal or absent on examination.

Investigations
- **genetics: FISH for X/Y chromosomes, formal karyotype and DNA for storage**
- **abdominal/pelvic USS** for internal genitalia/presence of uterus
- **U&E (can be unreliable before 48 hrs of life), urinalysis and capillary glucose**
- **17-hydroxyprogesterone (17-OHP) (send at >48 hrs of life; phone Endocrine lab on ext 34043/33230 to arrange), androstenedione**

The results of the above investigations should be available in 48 hours to allow a working diagnosis to be made. Further investigations after this time period should be discussed with the regional paediatric endocrinology team.

Additional investigations after discussion with Endocrine Consultant
- urinary steroid profile (>5ml urine required)
- baseline testosterone, LH, FSH
- short synacthen test, plus additional tests 17-OHP, testosterone and androstenedione at 0 and 60 minutes
- human chorionic gonadotrophin (hCG) test
- Anti-Mullerian Hormone (Mullerian Inhibitory Substance)
- LHRH test

In a 46XX infant with DSD, an elevated 17-OHP and a uterus visible on pelvic ultrasound, the diagnosis is congenital adrenal hyperplasia.
In a XY or XO/XY infant with ambiguous genitalia, investigations are aimed at establishing the presence and function of testicular tissue. The hCG test is used for this:

1500 units of hCG should be given IM for 3 consecutive days and pre- (D1) and post- (D4) stimulation samples should be taken for testosterone, dihydrotestosterone and androstenedione

Results should be interpreted with guidance from the paediatric endocrine team.

Once the gender has been confirmed and the underlying problem diagnosed, a management plan will be made with involvement of the paediatric endocrine and urological teams.

Multilingual parent advice leaflets can be found on the DSD Families website: https://www.dsdfamilies.org/resources

5.0 IMPLEMENTATION OF POLICY

To be read by all neonatal staff and used as a guideline in NICU for investigation and management of babies with disorders of sexual development

5.1 Dissemination

Following ratification by the Standards and Guidelines Committee and approval by the Policy Committee this guideline will be published on the Belfast Trust Intranet Site and staff will be informed. The policy and guidelines section is regularly accessed by staff.

6.0 MONITORING

This guideline contains the current evidenced based thinking on this topic, however data and statistics are routinely collected and correlated and should the need arise the guideline will be updated.

7.0 EVIDENCE BASE / REFERENCES

This guideline has been produced after review of current literature (see references below):

Ahmed SF, Achermann JC, Arlt W, et al. Society for Endocrinology UK guidance on the initial evaluation of an infant or an adolescent with a suspected disorder of sex development (Revised 2015). *Clin Endocrinol (Oxf)*. 2016;84(5):771–788. doi:10.1111/cen.12857

Hughes IA, Houk C, Ahmed SF, et al. Consensus statement on management of intersex disorders Arch Dis Child 2006; **91**: 554-63

Hughes IA. The clinical management of ambiguous genitalia. In *Clinical Paediatric Endocrinology*, fifth edition, Ed. Brook, Clayton, Brown. Blackwell p192-212

Ogilvy-Stuart A, Midgley P. *Practical Neonatal Endocrinology*. 1st edition Cambridge Clinical Guidelines

Raine JE, Donaldson MDC, et al. Intersex and other disorders of sexual differentiation. In *Practical Endocrinology and Diabetes in Children*, second edition. Blackwell p109-126

Sax L. How common is intersex? A response to Anne Fausto-Sterling *J Sex Res* 2002; **39**:174-8

8.0 CONSULTATION PROCESS

Guideline has been written by [redacted] after consultation with neonatal, endocrine and paediatric surgical consultants.

9.0 APPENDICES / ATTACHMENTS

None

10.0 EQUALITY STATEMENT

Major impact ☐

Minor impact ☐

No impact. ☒

SIGNATORIES:

[redacted]	[redacted]
Clinical Director	**Head of Midwifery/ Maternity Services Manager**

Name [redacted]
Title Lead Clinician
Regional Neonatal Unit

Date

Author

Date