

Intelligence in Medicine

Reaching Consensus on Treatment of
Disorders of Sexual Development
based on Levels of Evidence

Levels of Evidence

- The goal of evidence-based medicine is for all doctors to make decisions about the care of individual patients based on "conscientious, explicit, and judicious use of current best evidence.
- To evaluate the strength of different types of clinical evidence, studies or clinical trials are ranked from those with **the least amount of bias to those with the potential for the greatest amount of bias**

Levels I

- Evidence is obtained from meta-analysis of multiple, well-designed, controlled studies. Randomized trials have with low false-positive and low false-negative errors (high power)

Level II

- Evidence is obtained from at least one well-designed experimental study
- Randomized trials have high false-positive and/or – negative errors (low power)

Level III

- Evidence is obtained from well-designed, quasi-experimental studies such as nonrandomized, controlled, single-group, pre-post, cohort, time, or matched case-control series

Level IV

- Evidence is from well-designed, nonexperimental studies, such as comparative and correlational descriptive and case studies

Level V

- Evidence is from case reports and clinical examples

Hierarchy of Evidence

- 1. meta-analysis (quantitative systematic review) using comprehensive search
- strategies
- 2. high-quality randomized controlled trial (RCT)
 - a. double blind
 - b. single blind
 - c. non-blinded
- 3. cohort study
- 4. case control studies
- 5. case series and case reports

The Evidence Pyramid



Methodology

- Established working groups
- Membership drawn from international experts
- Prepared prior written responses to a defined set of questions
- Questions generated from evidence based review of published reports
- Framework for a consensus document agreed upon

Nomenclature and Definitions

- Terminology is sensitive
- Ideal nomenclature is sufficiently flexible to incorporate new information
- Yet robust enough to maintain a consistent framework
- Terms descriptive and reflect etiology
- Terms can still accommodate a spectrum of variance
- Users must value term use
- Terms must be understandable

The last 5 years have generated a virtual storm of investigations into the field of intersexuality.

Questions remain:

- Diagnosis
- Gender identity
- Prevalence of intersexual diagnosis
- Time and success of surgery
- Cancer risks
- Quality of life
- Evolving ethics
- Legal implications

Outcomes Determined By:

1. Genetic sex - determined at fertilization by sex chromosome constitution.
2. Gonadal sex - differentiation to testes or ovary - genetic information determines the differentiation of the undifferentiated gonad.
3. Sex phenotype - male differentiation is an active process resulting from testicular secretions. Antimüllerian hormone (AMH) produced by sertoli cells inhibits Müllerian ducts, testosterone produced by Leydig cells is responsible for stabilization of the Wolffian ducts via transformation into DHT. This is responsible for virilization of external genitalia. In absence of testes, genital primordia are irreversibly committed to femaleness.

Optimal Gender Policy Goals

- Assign gender that gives best prognosis for future function
- Overall gender-appropriate appearance
- Stable gender identity
- Sexual function
- Minimal medical procedures
- Reasonably happy life

Goals of Intersex Management

- Good overall quality of life
- Stable unconflicted gender identity
- Attainment level of education commensurate with intellectual potential
- Appropriate functioning in work
- Capacity for long-term partnering
- Satisfying sexual functioning
- Reasonable social life
- Freedom from significant psychopathology

Psychosexuality

1. Gender role behavior and gender identity

2. Sexual life

- sexual orientation
- courtship
- partner bonding
- genital sexuality

3. Reproduction and parenting

Optimal Gender Policy

- “Will this child have a better chance for a reasonable life as a male or female.”

Meyer-Bahlburg 2002

Surgery

Long-term Outcomes

“Surgical techniques have changed radically in the last 20 years, and I hope that the results of the next generation of surgery are going to be an awful lot better. But in some cases you can never put it right. Nature got it wrong.”

Philip Ransley,
Pediatric Urologist
New Scientist (2001)

The Dilemma of Genital Surgery

Timing

Risks

Necessity

SURGICAL GOALS

SURGICAL GOALS ARE UNCHANGED

- Genital appearance compatible with gender of rearing
- Unobstructed urinary emptying without incontinence or infections
- Good adult sexual sensitivity and function
- Preservation of fertility if possible

Quality of Life

- Determine the impact of medical intervention on function, adjustment, and psychosocial well-being.
- Attempt to measure and ensure optimal outcomes of health care services.
- Subjective assessment of patient perception, appraisal, and satisfaction with current level function compared with their perception of ideal function.

The Outcomes of Consensus



General Concepts of Care

- Gender assignment must be avoided before expert evaluation in newborns
- Evaluation and long term management must be carried out at a center with an experienced multidisciplinary team
- All individuals must receive a gender assignment

General Concepts of Care

- Open communication with patients and families is essential and participation in decision making is encouraged
- Patient and family concerns should be respected and addressed in strict confidence

Gender Assignment

- Initial gender uncertainty is stressful for families
- Decision is required
- Evidence supports the raising markedly masculinized 46XX females with CAH as females
- 5 α RD2 and 17 β HSD3 deficiencies evidence supports male assignment as the majority live as males and have male fertility
- PAIS 25% unsatisfied with either assignment
- Evidence supports male rearing in micropenis

Surgical Management

- Surgeon has a responsibility to outline possible surgical management and consequent risks from birth to maturity
- Surgical feminization should only be recommended for severe virilization
- Emphasis on function rather than cosmesis
- Vaginal surgical reconstruction done in infancy will likely need refinement in adolescence
- Hypospadiac repair in infancy
- Surgical repair in DSD should consider options that facilitate fertility



Psychosocial Management

- Should be an integral part of care to promote positive adaptation
- Atypical gender role behavior is more common in children with DSD
- Gender dysphoria should be evaluated
- If desire to change gender persists the patient's wish should be supported
- Disclosure concerning karyotype, gonadal status and fertility should be a collaborative ongoing process
- Medical interventions and negative sexual experiences may foster post traumatic stress disorder

Future Studies

- Major shortfall in info about long term outcomes
- Use appropriate instruments that access outcomes in a standard manner
- Registry
- Prospective
- Representative sampling
- Avoid bias