Consultation - Multispecialty
NICU - 1 day old baby with ambiguous genitalia
- Born at 39 wks via normal vaginal delivery
- Uncomplicated pregnancy
- Prenatal Ultrasound:
  - Female fetus
  - No abnormalities detected,
  - Week of test performed unknown
- No history of fertility problems or spontaneous abortions in self or family
- No ingestion of drugs

- Labio-scrotal folds
- Intermediate size phallus
- No palpable gonad
- Single meatus at the base of the phallus

Gonads
- Non palpable:
  - No testicles
  - Undescended testicles
- Palpable (Unilateral)
  - Inguinal: Testicle, Dysgenetic Gonad, Ovo testis, Ovary
  - In labio-scrotal fold: Most likely a testicle
- Palpable (Bilateral)
  - Most likely testicles
Na : 135  Cl : 107  K : Hemolysed  
BUN : 17  Creat : 0.91  
Glucose : 67  
Temp : 36.6 F.  
Pulse : 124  RR : 24  BP : 68/39 mmHg  
O2 : 100% at room air  

Boy or girl ?  
Differential diagnosis :  
- 46, XX DSD (Hypervirilized female - Female pseudohemaphrodite)  
- 46, XY DSD (Hypovirilized male - Male pseudoheraphrodite)  
- 45, X/46, XY MGD DSD (Mixed gonadal dysgenesis)  
- 46, XX or 46, XY or 46, XX/46, XY Ovotesticular DSD (Hermaphrodite)  

DSD squad team  
- Neonatologist  
- Pediatric Endocrinology  
- Pediatric Urology  
- Psychology  
- Geneticist  

Investigation  
- Genetic  
- Biochemical  
- Hormonal  
- Radiologic  
- Endoscopic - Surgical  
- Psychologic  

Genetic  
Karyotype :  
XX, XY, Mosaicism  
Other chromosomal anomalies  
(translocations, etc) including SRY  
Other syndromes  

Biochemical / Hormonal  
Electrolytes  
Evaluation of the Cholesterol metabolites pathways  
Evaluation of the Hypothalamo-pituitary-gonadal axis  
Stimulation studies  
MIS  
Normal values varies with age!  
Insure proper hormonal balance (CAH)  
Induction of puberty, Adult follow-up
Radiologic

Ultrasonography: Renal + Pelvic
Radiologic: Sinusography - VCUG
MRI: Pelvic structures (rarely done)

Role of the Psychologist

- Coordinator of the DSD team
- Liaison between parents and medical team members
- Educate parents as to typical development and differentiation of the sexual/reproductive system.
- Educate parents as to how their infant/child's sexual/reproductive system differs from the typical
- Educate parents to understand the need for the various medical tests and procedures performed
- Answer all questions, address fears
- Provide synopsis of medical evaluation, diagnosis, treatment and a roadmap of future medical/psychologic issues
- Long term follow up.

Initial discussions

- Meetings with both parents
  - Psychology - Urology - Endocrinology
  - Proper terminology
  - "your child" - phallus - labio-scrotal swellings, gonads, etc...
- We have to wait for the tests results before making any recommendations.
- We are aware of the stressful situation and will do everything to promptly get the answers and to communicate with them the results of the investigation.
- It can take a long time to get the results of some of the tests. We work as a team.

Laboratory Values
Day 1.5
- K 5.4
- Normal 17 OH-progesterone
**46, XY DSD**

**Laboratory Values**

**Day 1.5**

- K 5.4
- Normal 17 OH-progesterone
- Testosterone 165
- DHT 54 (normal for males, high if female)
- FSH 1.3
- LH 0.3

**Endocrine studies**

- 2 windows of opportunity to measure Testosterone
  - Immediately after birth (100ng/dl)
  - LH surge - Beginning of the 4th week of life
  - Postnatal Testosterone surge at 2 months

**Laboratory Values**

**Day 1.5**

- K 5.4
- Normal 17 OH-progesterone
- Testosterone 165
- DHT 54 (normal for males, high if female)
- FSH 1.3
- LH 0.3

- A few days later (8-9) - Karyotype: 45 XO
Day 11
- Long discussion with the family - Urology/Psychology
- Review of external appearance - ambiguous
- Review of radiologic findings - Vagina + Uterus + Horseshoe kidney
- Review of Laboratory tests and karyotype
- Normal testosterone level with 45, XO sex chromosomes
- External genital ambiguity due to the presence of testosterone
- Need for SRY - Awaiting karyotype results on 100 cells +/- SRY probe
- Parents comfortable with Female sex of rearing
- did research on the topic
- Questions about sexuality, fertility, menstrual cycle, size of phallus
- Need for laparoscopy + gonadectomy explained
- To do soon: decrease Testosterone influence on phallic size
- Risk of gonadal tumor
- Possibility of preserving a normal ovary if present
  (Ovotesticular DSD — but this is not compatible with 45,XO)
- Discussion of unknown factors : Sexual orientation, gender identity

Day 18
- Meeting with the family - Endocrinology/Psychology
- Review of all up to date findings
- Clarification of any information that might confuse the parents
- Confirmation of surgery
- Answering all questions from Parents

26 days
- Mom called re : swelling in the groin
- Examination : left palpable Gonad with left inguinal herniae

Karyotype
- Majority of cells 45, XO
- 13/100 cells 46, XY (abnormal)

Evaluation under G.A. (day 36)
Cystoscopy - Laparoscopy

- Low confluence of the vagina
- Normal urethra and bladder
- Single vagina
- Single normal cervix
Genetic evaluation of the gonads

Right gonad: No growth - analysis not possible

Left gonad: 45,X/46,X, idic(Y)(pter->q11.2::q11.2>q11.2-->pter)

(Abnormal Y chromosome - Yq-terminus lost on both alleles)

Diagnostic

45, X/46, XY(abnormal) MGD DSD

What next?

- Long term psychologic follow-up for the child and family
- Clitoridal reduction?
- Induction of puberty/menstrual cycle
- Eventual vaginoplasty
- Egg donation

Work-up of ambiguous genitalia

CAH: Pre-natal Dx and Therapy.

- Autosomal Recessive mode of transmission
- Dexamethasone started before the 10th week of gestation can prevent female pseudohermaphroditism by CAH.
  - At 15 - 18 Weeks: Stop dexa. if male or un-affected female (only one/eight fetus needs it!)
  - Outcome:
    » 1/3: neonate with normal genitalia
    » 1/3: significantly virilized
    » 1/3: some virilization
Pre-Natal Therapies

Dexamethasone update:
- Start at 8 weeks - Diagnosis made at 12 weeks
Mysteries:
- How come dexamethasone is effective when ACTH cannot be demonstrated in the fetal pituitary?
- Treated babies are born with a responsive pituitary axis, no Cushingoid features and normal birth weight (Fetal resistance to dexamethasone!)
- What are the unwanted effects of prenatal dexamethasone on the affected and non affected children?

Preimplantation Genetic Diagnosis
- During In Vitro Fertilization
- For single gene Mendelian traits