ULTRASOUND OF THE FETAL GENITOURINARY TRACT

Jude P. Crino, M.D.

RENAL DEVELOPMENT
Nephron formation
- Pronephros (3rd-5th week)
  - nonfunctional
- Mesonephros (5th-12th week)
  - able to form urine
  - renin production
- Metanephros
  - final stage
  - mature metanephric kidney

RENAL DEVELOPMENT
Metanephros
- Tubular function begins 9th-12th week
- Functional loop of Henle by 14th week
  - tubular reabsorption
- New nephron formation through 36 wks

AMNIOTIC FLUID DYNAMICS
Determinants of AFV

AMNIOTIC FLUID DYNAMICS
normal amniotic fluid volume
NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys

- Visualization - transvaginal
  - earliest 9 weeks
  - 100% by 13 weeks
- Visualization - transabdominal
  - earliest 13-14 weeks
  - most patients by 16-18 weeks

NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys

- Paraspinal
- Circular/elliptical shape
- Hypoechoic
- Echogenic rim more prominent with advancing GA

NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys

- Renal pelvis
  - slit-like, central, anechoic
- Medullae
  - hypoechoic
  - arranged in A-P orientation around pelvis
- Cortex
  - echogenicity similar to surrounding tissues

NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys – 13 weeks

NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys – 18 weeks

↑ gain, ↓ dynamic range
NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys – 18 weeks

- normal echogenicity transverse

Gynecology and Obstetrics

NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys – 18 weeks

- renal arteries

Gynecology and Obstetrics

NORMAL SONOGRAPHIC ANATOMY
Fetal Kidneys – 36 weeks

Gynecology and Obstetrics

NORMAL SONOGRAPHIC ANATOMY
Fetal Bladder

- Visualization
  - earliest 10-12 wks (TA or TV)
  - almost 100% by 16 wks (TA)
- Appearance
  - rectangular, anechoic
  - thin wall

Gynecology and Obstetrics

NORMAL SONOGRAPHIC ANATOMY
Fetal Bladder – 13 weeks

Gynecology and Obstetrics

- Level of iliac crest in transverse
- Int iliac arteries along lateral walls
  - can aid in identification
- Variation in volume
  - filling - emptying cycle 20-30 min
NORMAL SONOGRAPHIC ANATOMY
Fetal Bladder – 18 weeks

NORMAL SONOGRAPHIC ANATOMY
Fetal Bladder – 30 weeks

NORMAL SONOGRAPHIC ANATOMY
Fetal Genitalia

• Visualization GA, position dependent
• Must distinguish labia from scrotum
  – testes descend 28-34 weeks
  – testes in scrotum 100% reliable
• ID of penis provides further evidence
• Pitfalls: prominent clitoris, small penis, undescended testicles

FIRST TRIMESTER

Table 1: Gender identification according to crown-rump length (CRL)

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>CRL (mm)</th>
<th>Patients (n)</th>
<th>Females identified by ultrasound (%)</th>
<th>Male</th>
<th>Died at birth (%)</th>
<th>Lost to follow-up (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.0 &lt; 12.0 - 8.0</td>
<td>55.4 - 82.5</td>
<td>180</td>
<td>155 (85%)</td>
<td>135</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>12.0 - 9.0</td>
<td>62.0 - 68.0</td>
<td>218</td>
<td>209 (96%)</td>
<td>194</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>12.0 - 11.0</td>
<td>68.0 - 73.0</td>
<td>381</td>
<td>371 (97%)</td>
<td>376</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>654</td>
<td>613 (92.6%)</td>
<td>555</td>
<td>58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FIRST TRIMESTER
### Urinary Tract Abnormalities

**Classification**

- Severe hypoplasia/agenesis
- Ectopia
- Dilatation/obstructive uropathy
  - UPJ obstruction
  - UVJ obstruction
  - Bladder outlet obstruction
- Renal cystic disease
  - Cystic dysplasia
  - Multicystic dysplastic kidney disease
- Polycystic kidney disease
- Syndromes with cysts
- Tumors
- Abnormal genitalia

### Bilateral Renal Agenesis

**Gynecology and Obstetrics**

Potter, Pathology of the Fetus and the Newborn, 1952

### Pelvic Kidney

**Gynecology and Obstetrics**
Urinary Tract Dilation Consensus Meeting

• March 14-15 in Linthicum, MD (AUA Headquarters)
• Participants:
  – 1 director and 12 panelists
  – Audience consisting of clinicians and researchers from the various specialties
  – Webinar for those not able to attend
• Format:
  – 1st day: current literature was reviewed and discussed
  – Evening: Panelists drafted a consensus statement
  – 2nd day: Statement presented to audience and discussed until the entire group arrived at consensus
Participants

Prenatal
• Society for Maternal - Fetal Medicine
  – Anthony Odibo
  – Jude Chino
• American Institute of Ultrasound in Medicine
  – Bryann Bromley
• American College of Radiology
  – Beverly Coleman
• Society of Radiologists in Ultrasound
  – Carol Benson

Postnatal
• Society for Fetal Urology and Society for Pediatric Urology
  – Anthony Herndon
• Society for Pediatric Radiology
  – Jeannie Chow
  – Kasra Darghe
• American Society of Pediatric Nephrology
  – Michael Somers
  – Deborah Stein

Goals of the UTD Classification System

• To propose a unified description of UT dilation that can be applied pre- and postnatally.
  – Simple but detailed enough to be meaningful for both clinical use and future research endeavors.
  – Allow for communication of information between specialists, providing consistent terminology.
• To propose standardized schema for the perinatal evaluation of these patients based on sonographic criteria
  – Intended to be a starting point for observation and study
  – Will be modified over time based on the accumulated evidence.

Recommendation # 1: Terminology

• Discourage the use of non-specific terms in describing UT dilation (e.g. hydronephrosis, pyelectasis, pelviectasis, urephrosis, UT fullness or prominence, pelvic fullness)
• Suggest the consistent use of the term “UT dilation”
• Further determination of the severity of UT dilation is characterized by specific sonographic findings, delineated by the UTD Classification System

Recommendation #3: Defining Normal

<table>
<thead>
<tr>
<th>Ultrasound Findings</th>
<th>16-27w</th>
<th>≥ 28w Postnatal (&gt; 48h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior posterior diameter</td>
<td>&lt; 4mm</td>
<td>&lt; 7mm</td>
</tr>
<tr>
<td>Calyceal dilation</td>
<td>Central No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Peripheral No</td>
<td>No</td>
</tr>
<tr>
<td>Parenchymal thickness</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Parenchymal appearance</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Ureter(s)</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Bladder</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Recommendation #3: Stratification of Risk

• Risk of what ???
  – Defined as the presence of postnatal urological pathology
• Further research will be needed to correlate risk stratification to clinical outcomes (UTI, pain, stone, need surgery, renal function, urological pathologies)
• Propose follow up recommendation based on risk stratification
Central calyceal dilation with APRPD ≥ 7mm (≥16-17 wk) or ≥ 10 mm (≥28 wk)

Peripheral and central calyceal dilation with APRPD < 7mm (≥16-17 wk) or ≥ 10 mm (≥28 wk)

Abnormal renal parenchyma with APRPD < 7mm (≥16-17 wk) or < 10 mm (≥28 wk)

Dilated ureter with normal renal parenchyma and APRPD < 7mm (≥16-17 wk) or < 10 mm (≥28 wk)

### CAUSES OF URINE FLOW IMPAIRMENT

**Renal causes**
- UpJ anomaly
- UVJ anomaly
- Post urethral valves
- Duplex systems
- Ureterocele/ectopic ureter

**Extrarenal causes**
- Urethral atresia
- Cloacal anomaly
- Vesicoureteral reflux
- Megaureter
- Megacystis microcolon hypoperistalsis synd

**Splanic causes**
- Sacrococcygeal teratoma
- Hydrometralpos
- Other pelvic masses

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**Gynecology and Obstetrics**
OBSTRUCTIVE UROPATHY

Prognostic Factors

- Site of obstruction
- Degree of dilatation
- Cortical appearance
- Amniotic fluid volume
- Associated anomalies
- Urine biochemistry

Evaluation & Management

- Look for associated anomalies
- Offer karyotype
- Patient counseling
- Pediatric subspecialty consultation
- If urethral level obstruction (LUTO):
  - consider urine biochemistry
  - consider vesicoamniotic shunt

FETAL LOWER URINARY TRACT OBSTRUCTION (LUTO)

- Incidence 2.2 per 100,000 births
- Most common etiologies in males: posterior urethral valves, urethral stenosis or atresia, prune belly syndrome
- Most common cause in females: complex cloacal developmental anomalies
- High mortality and morbidity
- Most common cause of death: pulmonary hypoplasia

LUTO – SONOGRAPHIC FINDINGS

- Urinary tract dilation
  - renal pelves ≥ 10 mm
- Hydroureter
- Dilated bladder
  - thick wall
  - “keyhole sign”
- ± signs of renal dysplasia
LUTO – PATHOLOGIC FINDINGS

Potter, Pathology of the Fetus and the Newborn, 1952
Gynecology and Obstetrics

HYDROURETER

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LUTO – “KEYHOLE” BLADDER

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LUTO – RENAL FINDINGS

Nyberg, Diagnostic Imaging of Fetal Anomalies
Gynecology and Obstetrics

LUTO – RENAL FINDINGS
LUTO – URINE ASCITES WITH THICK-WALLED BLADDER

LUTO – EVALUATION

- Karyotype
  - amniotic fluid, fetal urine, fetal blood, chorionic villi
- Detailed sonography
- Serial urine testing
  - sodium, chloride, calcium, osmolality, total protein, β-2 microglobulin
  - at least 3 samplings 48-72 hrs apart

LUTO – BLADDER ASPIRATION

LUTO URINE VALUE THRESHOLDS

- Sodium: < 100 mmol/L
- Chloride: < 90 mmol/L
- Osmolality: < 200 mOsm/L
- Calcium: < 8 mg/dL
- β-2 microglobulin: < 6 mg/dL
- Total protein: < 20 mg/dL

RATIONALE FOR FETAL THERAPY

- Life threatening malformation
- Known pathophysiology
- Prevents fetal organ development
- Correction would allow development

OBSTRUCTIVE UROPATHY Criteria for in utero Rx

- Lower urinary tract obstruction (LUTO)
- Normal male karyotype
- Oligohydramnios or ↓ AFV
- No other significant anomaly
- Improving fetal urine values
LUTO – CRITERIA FOR IN UTERO Rx
NORMAL MALE KARYOTYPE

VESICOAMNIOTIC SHUNTING IN FETAL LUTO: RATIONALE

- Pathophysiology of LUTO
  - associated with abnormal renal development and function leading to oligohydramnios
  - oligohydramnios predisposes fetus to pulmonary hypoplasia and postural anomalies
- Percutaneous fetal bladder catheter:
  - bypass urethral obstruction
  - protect fetal kidneys from "backpressure" leading to parenchymal damage
  - restore amniotic fluid volume allowing optimal pulmonary development

VESICOAMNIOTIC SHUNTING IN FETAL LUTO: TECHNIQUE

• Percutaneous fetal bladder catheter:
  - bypass urethral obstruction
  - protect fetal kidneys from "backpressure" leading to parenchymal damage
  - restore amniotic fluid volume allowing optimal pulmonary development
VESICOAMNIOTIC SHUNTING IN FETAL LUTO: PROBLEM AREAS

- Natural history is highly variable
- Limited accuracy of antenatal assessment of prognostic factors:
  - etiology
  - renal function
- Procedure related complications
- Poor quality of available evidence of efficacy

LUTO: CLINICAL EXAMPLE

VESICOAMNIOTIC SHUNTING IN FETAL LUTO: OUTCOMES

- 75% postnatal survival
- 25% shunt displacement
- Posterior urethral valves dx in 50%
- 25% ESRD w/ renal transplants
- 25% “acceptable” renal function
- No long term pulmonary sequelae

COMPLICATIONS OF FETAL VESICOAMNIOTIC SHUNTING

- Shunt displacement 30-45%
- Fetal death up to 5%
- Vescicoperitoneal fistula
- Gastrochisis
- Abdominal wall hernia
- Chorioamnionitis
- Premature rupture of the membranes
- Preterm labor

VESICOAMNIOTIC SHUNTING IN FETAL LUTO: OUTCOMES

- PUV only, other dx excluded
- 9 stents, 1 cutaneous ureterostomy, 2 bladder marsupialization, 2 laser ablation of valves
- 57% postnatal survival
- 21% ESRD w/ renal transplants
- 4/5 no dysplasia on prenatal sono
Prenatally Shunted LUTO
Long Term Outcomes

- Pulmonary function
- Renal function
- Bladder function
- Growth and nutrition
- Musculoskeletal issues
- Neurological issues
- Quality of life

LUTO: Is a Stent Justified?

- YES, with the following caveats:
  - Antenatal assessment must be systematic and complete
  - Patients must be thoroughly counseled and informed of both short term and long term outcomes
  - Ideally should be included in a clinical trial or registry

Multicystic Dysplastic Kidney Disease

- Complete proximal obstruction or atresia before 10 weeks
- Sonographic appearance
  - Enlarged kidney, irregular contour
  - Multiple cysts, various sizes
  - No communication between cysts

Multicystic Dysplastic Kidney Disease

- Dysplastic kidney nonfunctional
- May diminish in size or disappear
- 40% contralateral abnormality
  - UPJ most common
- Prognosis
  - Good if unilat, other kidney nml
  - Fatal if bilateral

Multicystic Dysplastic Kidney Disease

Multicystic Dysplastic Kidney Disease

Multicystic Dysplastic Kidney Disease

Multicystic Dysplastic Kidney Disease
MULTICYSTIC DYSPLASTIC KIDNEY DISEASE

POLYCYSTIC KIDNEY DISEASE
• Autosomal recessive (infantile)
  – usually evident in utero
  – symmetrically enlarged, echogenic appearance
  – presentation depends on fraction of renal tubules affected
  – hepatic fibrosis inversely proportional to renal involvement

POLYCYSTIC KIDNEY DISEASE
• Autosomal dominant (adult onset)
  – commonly presents in young adults
  – occasionally seen in utero
  – enlarged, echogenic kidneys, ± cysts
  – family history crucial
AMBIGUOUS GENITALIA

- Genitalia not typical for male or female
  - Cannot differentiate penis from clitoris
  - Cannot differentiate scrotum from labia
    - Empty scrotum resembles labia
    - Fused labia resemble scrotum
- Secondary structures rarely seen in fetus
  - Uterus, ovaries, undescended testes

AMBIGUOUS GENITALIA MORPHOLOGY

- Male
  - Hypospadias / epispadias
  - Microphallus
  - Chordee (ventral curvature of penis)
  - Cryptorchidism (undescended testes)
- Female
  - Clitoromegaly
  - Prominent or fused labia

AMBIGUOUS GENITALIA ETIOLOGY

- Congenital adrenal hyperplasia (CAH)
  - Treatable
- Female pseudohermaphroditism
  - 46,XX, fetal or maternal androgen source
- Androgen insensitivity syndrome
  - 46,XY, ↓ end organ testosterone effect
  - Complete – female external genitalia
  - Incomplete – ambiguous genitalia
- Mixed gonadal dysgenesis
- Pure gonadal dysgenesis
  - 45,X/46,XY
- True hermaphroditism
- Aneuploidy
- Duplication and deletion syndromes

AMBIGUOUS GENITALIA EVALUATION

- Determine genetic sex
  - cfDNA, amniocentesis
- Evaluate for aneuploidy, duplication and deletion syndromes
  - Karyotype, microarray
- Evaluate for CAH if virilized female
  - Molecular genetics, amniotic fluid 17 OHP
  - Maternal dexamethasone if affected female

AMBIGUOUS GENITALIA

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AMBIGUOUS GENITALIA

HYPOSPADIAS

- Urethral orifice on ventral side of penis
  - 50% anterior near glans
  - 30% middle
  - 20% posterior
- Blunt ended or bulbous penis
- "Tulip" sign – small penis between scrotal folds
- Other urogenital anomalies in 40%

MEGAUURETHRA
MEGALOURETHRA

SCROTAL MASS
- Inguinal hernia
  - Indirect (bowel passes into scrotum through processus vaginalis)
  - Echogenic mass separate from testis
    - May see peristalsis – pathognomonic
- Testicular torsion
  - Variable echotexture, size, shape of testis
- Tumor (rare)

INGUINAL HERNIA

HYDROCOLPOS
- Vaginal obstruction
- Distension of vagina with secretions
- Unilocular retrovesicular cystic mass funneled to perineum
- Look for evidence of cloacal anomaly

HYDROCOLPOS

OVARIAN CYST
- Fetal ovarian response to maternal hormones
- Abdominal cyst in female fetus
  - Usually in lower abdomen / pelvis
  - Variable in size
  - May be simple, complex, septate
- GI and urinary tracts normal
- May resolve spontaneously
- Hemorrhage, torsion may occur
OVARIAN CYST

BLADDER EXSTROPHY

- Lower abdominal wall defect
- Exposed bladder
  - Soft tissue mass – posterior bladder wall
- Abdominal cord insertion at superior margin of exposed bladder
- Wide iliac wing angle, separated pubic symphysis
- Abnormal genitalia
  - Bifid penis, separated labia
BLADDER EXSTROPHY

CLOACAL MALFORMATION

- Complex malformation – failure of cloacal division
- Spectrum of abnormal anatomy
- Septated retrovesicular mass with fluid-fluid level
- Genitourinary, bowel, spine anomalies common

PROTOCOL FOR GENITOURINARY ANOMALIES

- Genitourinary system evaluation
  - measure renal pelves, renal lengths
  - assess renal appearance (contour, echogenicity, cysts)
  - demonstrate renal artery blood flow (color or power Doppler), consider pulsed Doppler study
  - image bladder in transverse and coronal/sagittal planes, measure bladder volume and/or wall thickness if appropriate

- Genitourinary system evaluation (cont’d)
  - look for ureteral dilatation
  - if kidneys or bladder are enlarged, measure fetal abdominal circumference at maximum level in addition to standard level
- Evaluate amniotic fluid volume
- Complete anatomic survey
- Fetal echocardiography
- Consultation as appropriate (genetic counseling, pediatric urology, neonatology)
THANK YOU!