ANTENATAL GENITOURINARY ANOMALIES
Evaluation and Management

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PRENATAL ULTRASOUND

Are we discovering the obvious?

Are we making a difference?
WHAT CAN WE DETECT IN THE GENITOURINARY TRACT PRENATALLY?

- Hydronephrosis
- Absence of kidney(s)
- Abnormally developed renal parenchyma
  - Renal cystic disease
- Abnormal bladder development
  - Obstructed
  - Exstrophied
  - Absence
- Genital anomalies
  - Inadequately developed male genitalia
  - Hydrocele

MCDK
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HYDRONEPHROSIS

- Description of appearance of upper urinary tract
  - Collecting system
    - Calyces and pelvis
    - Ureter

- Is NOT a disease / disorder = sign
  - Not always indicative of obstruction
  - Pattern may imply etiology
PRIMARY MEGAURETER
UVJ OBSTRUCTION
VESICOURETERAL REFLUX
HYDRONEPHROSIS

Etiologies

Obstruction

[Renal or bladder]

Vesicoureteral reflux

Obstruction and reflux

Nonobstructive and non-refluxing
(Physiologic)
PRENATAL GU MILESTONES

- Kidneys first detectable.............13 wks
  - Hydronephrosis..........................16 wks

- Internal renal structure distinct
  - Kidney surrounded by fat.............20 wks

- Fetal bladder
  - Filling/emptying cycles..................15 wks

- Ureters normally not visualized
PRENATAL HYDRO INCIDENCE

- Most common prenatal anomaly
  - 30 – 50% prenatal US anomalies

- Urinary tract dilation:
  - 1/100 pregnancies (1%): pelviectasis or greater
  - Significant uropathy: 1/500 (0.2%)
DEFINING PRENATAL HYDRONEPHROSIS

- AP diameter
  - Simplest and most sensitive parameter
    (Corteville JE et al., Am J Obstet Gynecol, 1991)
  - Dependent upon gestational age
  - More significant with calyceal / ureteral dilatation
WHAT ELSE TO LOOK FOR

**Kidney:**
- Degree of dilation
- Renal parenchyma echogenecity / thickness
- Calyceal-pelviectasis
- Unilateral vs bilateral
- Variation in hydro

**Other:**
- Amniotic fluid volume
- Extra renal fluid
- Other anomalies
- Gender
- Overall growth and development

**Ureter:**
- Ureteral dilation

**Bladder:**
- Size and cycling

**Urethra:**
- Urethral dilation
# Differential Diagnosis of Prenatal Hydronephrosis

## Unilateral:
- UPJ obstruction (39-64%)
- UVJ obstruction (9-14%)
- Vesicoureteral reflux (33%)
- MCDK (4-25%)
- Ureterocele/ectopic ureter
- Duplex system
- PCKD
- Physiologic
- Extra-renal pelvis

## Bilateral:
- Posterior urethral valves (2-9%)
- Vesicoureteral reflux
- Urethral aplasia
- Prune belly syndrome
- Megacystis-megaureter
- PCKD
PRENATALLY DIAGNOSED HYDRONEPHROSIS

- **Scope**
  - 1-5% all pregnancies
  - Wide spectrum of urologic conditions

- **Implication**
  - Ability to detect obstruction / reflux
  - Prevent UTIs / calculi / renal dysfunction or failure
HOW GOOD IS ULTRASOUND?
GENITOURINARY SYSTEM

- Sensitivity for GU anomalies: 89%
  - Grandjean H et al, AJObGyn 1999
  - Stefor T et al, J Mat Fet Med, 1999

- Very high sensitivity → excellent screening test
# FETAL UROLOGY

## The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydrenephrosis

Hiep T. Nguyen\textsuperscript{a,*}, C.D. Anthony Herndon\textsuperscript{b}, Christopher Cooper\textsuperscript{c}, John Gatti\textsuperscript{d}, Andrew Kirsch\textsuperscript{e}, Paul Kokorowski\textsuperscript{a}, Richard Lee\textsuperscript{a}, Marcos Perez-Brayfield\textsuperscript{f}, Peter Metcalfe\textsuperscript{g}, Elizabeth Yerkes\textsuperscript{h}, Marc Cendron\textsuperscript{a}, Jeffrey B. Campbell\textsuperscript{i}

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient hydrenephrosis</td>
<td>41–88%</td>
</tr>
<tr>
<td>UPJ obstruction</td>
<td>10–30%</td>
</tr>
<tr>
<td>VUR</td>
<td>10–20%</td>
</tr>
<tr>
<td>UVJ obstruction/megaureters</td>
<td>5–10%</td>
</tr>
<tr>
<td>Multicystic dysplastic kidney</td>
<td>4–6%</td>
</tr>
<tr>
<td>PUV/urethral atresia</td>
<td>1–2%</td>
</tr>
<tr>
<td>Ureterocele/ectopic ureter/duplex system</td>
<td>5–7%</td>
</tr>
<tr>
<td>Others: prune belly syndrome, cystic kidney disease, congenital ureteric strictures and megalourethra</td>
<td>Uncommon</td>
</tr>
</tbody>
</table>
HOW GOOD IS ULTRASOUND?
HYDRONEPHROSIS

- Very high sensitivity → excellent screening test
- Hydronephrosis requiring monitoring: 25 – 50%
  - Surgical intervention: < 10%
- Relatively low specificity - ? outcome measure?
  - Significant pathology
WHAT DOES IT MATTER?

- Benign screening test
  - High sensitivity and low specificity

- No risk!

- BUT.............
WORK-UP NEEDED TO EVALUATE PRENATALLY DETECTED HYDRO?

MRI

Postnatal US

IVP

VCUG

Diuretic Renogram
PARENTAL ANXIETY
Diagnosis of US sign ➔ acute distress

- Anxiety surrounds abnormal fetal ultrasound
- Mood / anxiety scores = major depressive episode
  - Not only those with fetal malformation / genetic disorder / intrauterine fetal death
- Underestimated by health care providers
HOW GOOD IS PRENATAL ULTRASOUND FOR HYDRONEPHROSIS?

MUCH TOO GOOD!
WHEN LIFE WAS EASIER

Urinary Tract Anomaly
- Reflux
- Obstruction

Symptoms
- UTI
- Mass
- Hematuria
- FTT

Work-up
- US/IVP
- VCUG
- Renogram
- Antegrade

INTERVENTION
PRENATAL ULTRASOUND

While it is the ideal imaging study for fetuses and children...........

It has forced us to ask new questions
What is the Fate of Prenatal Hydronephrosis?

Prenatal US  
Postnatal US
Natural History of Prenatal Hydro Second Trimester

11465 scan at 18-23 wks

N= 268 (2.3%)

4-7 mm (81%)
- 80% Resolved Antenatally
- 20% Persisted @ birth
- 82% Resolved @ 1 mos.
- 18% Persisted @ 1 mos.

> 7 mm (19%)
- 0% Resolved Antenatally
- 100% Persisted @ birth
- 44% Resolved @ 1 mos.
- 31% had surgery (>10 mm)
- 14% Abx.
- 11% Death

All resolved > 1 yr.

MAGIC NUMBER: 7mm

(Sairam et al., Ultrasound Obstet Gynecol 2001)
Natural History of Prenatal Hydro Third Trimester

- 20,049 cases: 1.9% with hydro
- 5-8 mm (88%); 9-15 mm (10%); > 15 mm (2%)

100% Resolved
12% Worsened
15% Resolved
25% Improved
48% Unchanged
33% Worsened
67% Improved

MAGIC NUMBER: 9mm

Feldman et al. (J Ultrasound Med, 2001)
ETIOLOGY OF HYDRO RESOLUTION

- Fetal urine flow
  - 4 - 6 X > postnatal

- Change in collecting system and ureteral compliance
  - Increased collagen

- Fetal ureteral folds
  - Longer ureter than needed early in gestation
CONSEQUENCES OF HYDRONEPHROSIS

- Urinary tract infection
  - Pyelonephritis → 10% renal scarring

- Upper tract pressure
  - Renal parenchymal atrophy

- Hypertension
- Loss of Renal Function
- End Stage Renal Disease
IMPLICATION OF PRENATAL DIAGNOSIS HYDRONEPHROSIS

- Reduction of postnatal UTI
- Preservation of renal function
- Prevention of acquired renal damage
- ? Reduction in frequency of postnata presentation
IMPACT OF PRENATAL DIAGNOSIS

- Does prenatal ultrasound afford preservation of renal function?

- **UPJ** (upper tract hydronephrosis)
  - No evidence

- **Ureteroccele/duplicated systems**
  - Tackett, et al  AAP 1997
  - Bolduc J Urol 2002
    - No effect on upper pole function

- **PUV**
    - No effect - same degree renal failure (30%)
  - Kousidis G et al  BJUInt 2008
    - Modest improvement renal function long-term
UPPER TRACT HYDRONEPHROSIS OUTCOME

- SFU consensus statement

- Prenatal hydronephrosis resolves in majority
  - “mild” – 12% UT pathology
  - “severe” – 88% UT pathology
  - < 5% require surgery

- No studies concluding outcomes benefit: renal function

Nguyen HT et al JPU 2010
Does prenatal ultrasound change the pathology that we see?

Upper tract obstruction
Vesicoureteral reflux
Posterior urethral valves
DOES PRENATAL US CHANGE THE PATHOLOGY?

- Vesicoureteral reflux

Normal | Reflux
Prenatal VUR- multicenter study

- 56 males / 15 females
- Initial postnatal US normal 25%
  - 50% Grade 3-5
  - 20% Grade 3-5 VUR resolved
- 0.9 yrs boys / 2.1 yrs girls

Conclusion: Prenatal VUR high grade / males / bilateral / renal dysplasia / high resolution rate
### VUR PRESENTATION COMPARISON

<table>
<thead>
<tr>
<th></th>
<th>Prenatal Detection</th>
<th>Postnatal Detection</th>
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</thead>
<tbody>
<tr>
<td>Male :: Female</td>
<td>5:1</td>
<td>1:5</td>
</tr>
<tr>
<td>Normal Renal / Bladder US</td>
<td>20 – 40%</td>
<td>80 – 90%</td>
</tr>
<tr>
<td>Normal DMSA</td>
<td>50%</td>
<td>85%</td>
</tr>
<tr>
<td>Resolution Rate Grade for Grade</td>
<td>Much Higher</td>
<td>Lower</td>
</tr>
</tbody>
</table>
BENEFIT OF PRENATAL DIAGNOSIS

- Presymptomatic diagnosis
  - Ureterocele / megaureter

- Increased diagnosis of abnormalities
  - UPJ / MCDK

- Avoid pyelonephritis
  - High incidence renal scarring in infants
  - High incidence of bacteremia and sepsis

- Treating a different disease?

- Preservation of renal function
  - No evidence
OUTCOME PREDICTION?

Bilateral Hydronephrosis

Bladder Outlet Obstruction
POSTERIOR URETHRAL VALVES

Normal VCUG

BLADDER

POSTERIOR URETHRA

30% end stage renal disease

PUV
HYDRONEPHROSIS: FACTORS PREDICTIVE OF OUTCOME

- Amniotic fluid volume
- Parenchymal echogenicity
- Degree of hydronephrosis
- Renal function
- Other anomalies
  - Chromosomes (8-10% abnormal)
OLIGOHYDRAMNIOS

Postnatal Renal Function
AMNIOTIC FLUID

1. Fetal swallowing and reabsorption by intestine
2. Secretion from respiratory tract

Exchange across fetal skin possible only for small lipid-soluble gases

Net water movement between mother and fetus across chorion frondosum

Fetal urine

AMNIOTIC FLUID

Mid 2nd Tri = 90% AF
OLIGOHYDRAMNIONS

- 4 - 5% pregnancies
- Amniotic fluid leak
- Amnion nodosum
- Urinary tract anomalies

Consequences
- Pressure anomalies
- Potter’s characteristics
- Pulmonary hypoplasia
AMNIOTIC FLUID

- Pulmonary development
  - 23 – 26 wk
  - Prevents extensive compression
  - Stenting of tubules
  - Tubules developed by 24 weeks

- Prevents compression deformities
  - Head
  - Thorax
  - Extremities
Amniotic Fluid
Swallowing
Urine Production
PROGNOSTIC FACTORS IN PRENATAL HYDRO

- Multivariant analysis 148 children
  - Oligohydramnios
  - Prematurity
  - Initial GFR <20ml/min

Increased perinatal demise
Poor postnatal renal function

Oliviera et al Ped Neph 1999
PROGNOSTIC FACTORS IN PRENATAL HYDRO

Echogenicity

Parenchymal Thinning
PARENCHYMAL ECHOGENICITY

Postnatal Renal Function
PRENATAL ULTRASOUND: PREDICTIVE FACTORS

◆ Echogenicity

<table>
<thead>
<tr>
<th>Renal Function</th>
<th>Markedly Increased</th>
<th>Slightly Increased</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 10%</td>
<td>10 (50)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10%–19%</td>
<td>0</td>
<td>1 (14)</td>
<td>0</td>
</tr>
<tr>
<td>20%–39%</td>
<td>2 (10)</td>
<td>4 (57)</td>
<td>13 (9)</td>
</tr>
<tr>
<td>40% or Greater</td>
<td>7 (35)</td>
<td>1 (14)</td>
<td>136 (90)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>1 (5)</td>
<td>1 (14)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

Chi et al J Urol 2006
Prenatal Ultrasound: Predictive Factors

- Renal parenchymal thinning

<table>
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<tr>
<th>Renal Function</th>
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<tr>
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<td>2 (9)</td>
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<td>0</td>
<td>0</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>20%–39%</td>
<td>3 (14)</td>
<td>3 (43)</td>
<td>13 (9)</td>
</tr>
<tr>
<td>40% or Greater</td>
<td>17 (77)</td>
<td>4 (57)</td>
<td>126 (85)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>0</td>
<td>0</td>
<td>5 (3)</td>
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Chi et al J Urol 2006
FACTORS PREDICTIVE OF OUTCOME

- Amniotic fluid volume
- Parenchymal echogenicity
- Degree of hydronephrosis
  - Poor predictor of postnatal renal function
  - Indicative of surgical intervention – at extremes
- Renal function
- Other anomalies
  - Chromosomes (8-10% abnormal)
FACTORS PREDICTIVE OF OUTCOME

- Amniotic fluid volume
- Parenchymal echogenicity
- Degree of hydronephrosis
- Renal function
- Other anomalies
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FETAL RENAL FUNCTION ASSESSMENT

- Indirect
  - Watch bladder fill and empty over time
  - Diuretic stimulation

- Direct
  - Urinary biochemistries
BLadder TAP
FETAL URINARY BIOCHEMISTRIES

- Urine production @ 13 weeks
  - Ultrafiltrate of fetal serum
  - Hypotonic - selective resorption Na/Cl

- Poor prognosis
  - Isotonic urine (“salt wasting”)
    - Loss of ability to resorb Na/Cl
  - Glomerular leakage of small proteins
PROGNOSTIC CRITERIA
NORMAL VALUES

- **Na** <100 mEq/L
- **Cl** <90 mEq/L
- **Osm** <210 mOsm/L
- **Ca** <2 mmol/L
- **PO_{4}** <2 mmol/L
- **B_{2}-microglobulin** <2 mg/L

- No cortical cysts / Normal echogenicity
Urinary Chemistries

Oligohydramnios Timing

Urinary Chemistries

Renal Parenchymal Status

POSTNATAL RENAL FUNCTION

Good Prognosis

Poor Prognosis
GENERIC PRENATAL INTERVENTION ISSUES

- Accuracy of diagnosis
- Indications for intervention
- Contraindications for intervention
- Risks of intervention
- Consequences of nonintervention
- Ethical considerations
PRENATALLY HYDRO INTERVENTION

- Ureteropelvic junction obstruction
- Ureterovesical junction obstruction
- Bladder outlet obstruction
  - Posterior urethral valves
  - Sacrococcygeal teratoma
  - Intestinal duplication
  - Ureterocele
  - Neuropathic bladder
- Urethral atresia
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Solitary kidney
SIGNS OF BLADDER OUTLET OBSTRUCTION

- Bilateral hydroureteronephrosis
- Persistent bladder distention
  - Incomplete emptying
- Bladder wall thickening
- Perinephric urinoma
- Ascites
- Oligohydramnios
- Dilated posterior urethra
BLADDER OUTLET OBSTRUCTION

- Differential diagnosis
  - Posterior urethral valves
  - Prune Belly Syndrome
  - Urethral atresia
  - VUR
  - Megacystis - Megaureter
  - Ureterocele
POSTERIOR URETHRAL VALVES
SPECTRUM OF PUV

VUR

Renal Dysplasia
CONSEQUENCES OF NONINTERVENTION

- Newborn mortality: 5 – 10%
  - Pulmonary hypoplasia
- Chronic renal failure: 30 – 35%
GOALS OF INTERVENTION

- Preserve renal function
  - Never demonstrated clinically / experimentally

- Prevent pulmonary hypoplasia
  - Mechanical restriction lung growth / chest expansion
  - Insufficient AF inhibits lung branching
RENAL EMBRYOLOGY

- 5th week gestation
  - Ureteral bud induces metanephros
  - Blastema → nephron development

- Nephrogenesis
  - 80% nephrons mid 2nd trimester
  - 100% nephrons 36 weeks

- Ultrasound sensitivity dx hydro
  - Mid second trimester
VARIABLES AFFECTING POSTNATAL RENAL FUNCTION

- **Renal dysplasia**
  - Predetermined non-reversible at any stage of detection or intervention
  - Begins at 5 – 8 weeks

- **Obstructive nephropathy**
  - Variable
    - Etiology of obstruction
    - Degree of obstruction / compliance of collecting system
    - Reversibility???????????????????
INDICATIONS FOR PRENATAL INTERVENTION
Which Patients Will Benefit?

- Obstructive hydronephrosis
  - Progressive
- Bilateral / solitary kidney
- Progressive oligohydramnios
- Favorable renal function
- Minimal / no renal dysplasia
- No other severe anatomic / chromosomal anomalies
ANTENATAL INTERVENTION

Unfavorable Prognosis

- Early / sustained oligohydramnios < 20 wks
- Renal cortical cysts / marked renal echogenicity
- Urinary electrolytes “poor urine”
  - Na > 100 m Eq / L
  - Cl > 90 m Eq / L
  - Osm > 210 mOsm / L
  - B-microglobulin > 2 mg / L
  - Calcium > 8 mg / dl
- Reduced lung / thoracic area
TIMING OF PRENATAL INTERVENTION

- **< 20 weeks** / bilateral hydronephrosis / severe oligohydramnios (??????????)
  - Irreversible renal dysplasia likely
  - No intervention

- **> 32 weeks** (? >26 weeks)
  - Consider early delivery
  - Assess pulmonary maturity
  - Normal AF → term delivery
PULMONARY HYPOPLASIA
OLIGOHYDRAMNION

- Mechanical relationship

- Restoration of fluid
  - Urinary diversion
  - Artificial fluid replacement

- Timing critical to prevent pulmonary hypoplasia
  - Pulmonary development 22-26 weeks
Prenatal Intervention

Ethical / Legal Issues

- Invasive therapy → experimental [not evidence-based]

- Conflict of interest
  - First - mother’s health
  - Second – fetus

- Must select only fetuses that can benefit from treatment

- Most abnormalities best managed postnatally
PRENATAL INTERVENTION

MATERNAL RISK

- Operative risk of general anesthesia and midgestational hysterotomy / intervention

- Risk for premature labor following hysterotomy / intervention

- Risk for compromising future reproductive potential

- 50% complication rate
PRENATAL INTERVENTION FOR BLADDER OUTLET OBSTRUCTION

- Vesicoamniotic shunt

- Complication rate - 50% (<)
  - Shunt migration / poor drainage
  - Premature labor
  - Urinary ascites
  - Infection
OTHER INTERVENTIONS FOR BOO

- Reduce bladder pressure
  - Vesicocentesis - bladder aspiration – diagnostic / therapeutic
    - Multiple sequential

- Improve pulmonary development
  - Restoration amniotic fluid
    - Sequential amniotic infusions
Systematic review of the effectiveness of antenatal intervention for the treatment of congenital lower urinary tract obstruction

RK Morris, a GL Malin, b KS Khan, a MD Kilby a,b

a School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK b Department of Fetal Medicine, Birmingham Women’s Foundation Trust, Birmingham, UK

Correspondence: Prof. MD Kilby, Department of Fetal Medicine, Birmingham Women’s Foundation Trust, Metchley Park Road, Edgbaston, Birmingham B15 2TG, UK. Email m.d.kilby@bham.ac.uk

◆ Review of 20 series / 369 fetuses
◆ STROBE analysis
◆ Contact authors

<table>
<thead>
<tr>
<th></th>
<th>Good Prognosis</th>
<th>Poor Prognosis</th>
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<tbody>
<tr>
<td>Survival</td>
<td>Unchanged</td>
<td>Improved</td>
</tr>
<tr>
<td>Renal Function</td>
<td>Improved (NS)</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>

Int J Ob Gyn 2010
PRENATAL INTERVENTION

SUMMARY

- Impact on survival directly related to improvement in pulmonary function
- Little impact upon long-term renal function
Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial

Rachel K Morris, Gemma L Malin, Elisabeth Quinlan-Jones, Lee J Middleton, Karla Hemming, Danielle Burke, Jane P Daniels, Khalid S Khan, Jon Deeks, Mark D Kilby, for the Percutaneous vesicoamniotic shunting in Lower Urinary Tract Obstruction (PLUTO) Collaborative Group

- **RCT**
  - Vesicoamniotic shunt
  - No shunt

- **Primary outcome measures at 28 days and 2 years**
  - Perinatal survival
  - Serum creatinine
PLUTO TRIAL: RCT

Fetal medicine sub specialist uncertain whether to shunt

31

Fetus randomised

16

Shunt

15

Conservative management

Follow up until 5 years

45

Fetus enters registry

Follow up until 5 years

69 termination of pregnancy: 47%
PLUTO TRIAL
RCT

◆ **Survival**

<table>
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<tr>
<th></th>
<th>VA Shunt (%)</th>
<th>No Shunt (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 Days</td>
<td>50</td>
<td>26</td>
</tr>
<tr>
<td>2 Years</td>
<td>28</td>
<td>12</td>
</tr>
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</table>

◆ **Renal function**

◆ Abnormal in 8 / 10 survivors at 2 years

◆ **Conclusions**

◆ Survival improved

◆ Renal function abnormal in both – numbers insufficient
PRENATAL HYDRONEPHROSIS SCORECARD

- Is ultrasound beneficial in hydro detection?

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Improved survival</td>
<td>Yes</td>
</tr>
<tr>
<td>Improved renal function</td>
<td>No evidence – ? longer f/u</td>
</tr>
<tr>
<td>Parental counseling - outcomes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**PRICE: Parental distress and anxiety**
## Prenatal Hydronephrosis Scorecard

- **Is prenatal intervention beneficial?**

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Result</th>
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<tbody>
<tr>
<td>Improved survival</td>
<td>Yes</td>
</tr>
<tr>
<td>[Pulmonary]</td>
<td></td>
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<tr>
<td>Improved renal function</td>
<td>No evidence</td>
</tr>
<tr>
<td>Parental counseling - outcomes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
THE NEW DENOMINATOR

Pre - Prenatal US Era:

\[
\frac{\# \text{ cases symptomatic hydronephrosis}}{\# \text{ cases hydronephrosis}} = \sim 1
\]

Prenatal US Era:

\[
\frac{\# \text{ cases symptomatic hydronephrosis}}{\# \text{ cases hydronephrosis (↑↑↑↑↑)}} = \llllll 1
\]
FUTURE OF PRENATAL US

- Improve specificity
  - Refine parameters for postnatal evaluation

- Re-define beginning and endpoints
  - Detection and intervention
    - Renal function
    - Survival
    - Quality of life