Evidence Based Management of Pediatric Stones

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Epidemiology

The New York Times

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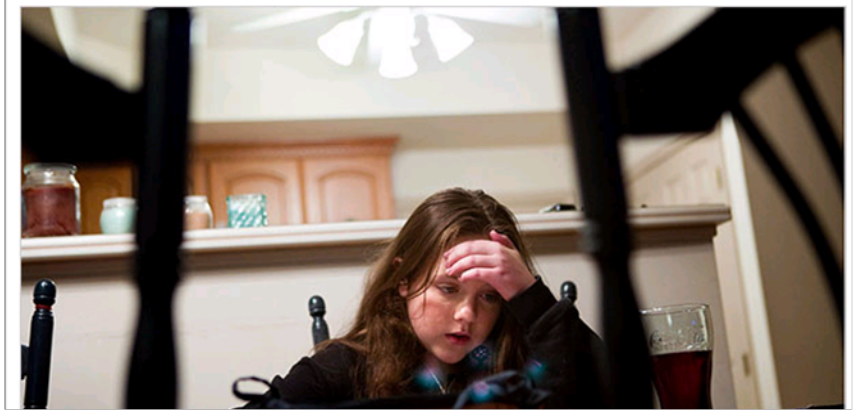
A Rise in Kidney Stones Is Seen in U.S. Children



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Kidney Stones and Kids: A Painful Combo

On the Rise in Young People, These Tiny Stones Can Cause Excruciating Pain

By CARI NIERENBERG
ABC News Medical Unit
Nov. 14, 2008

abc NEWS
1 comment

Scott Nellis is barely old enough to get a driver's license but the 16-year-old from Lake City, Minn., has already had something most grown-ups have not -- three episodes of kidney stones.

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Docs report increase in kidney stones among children

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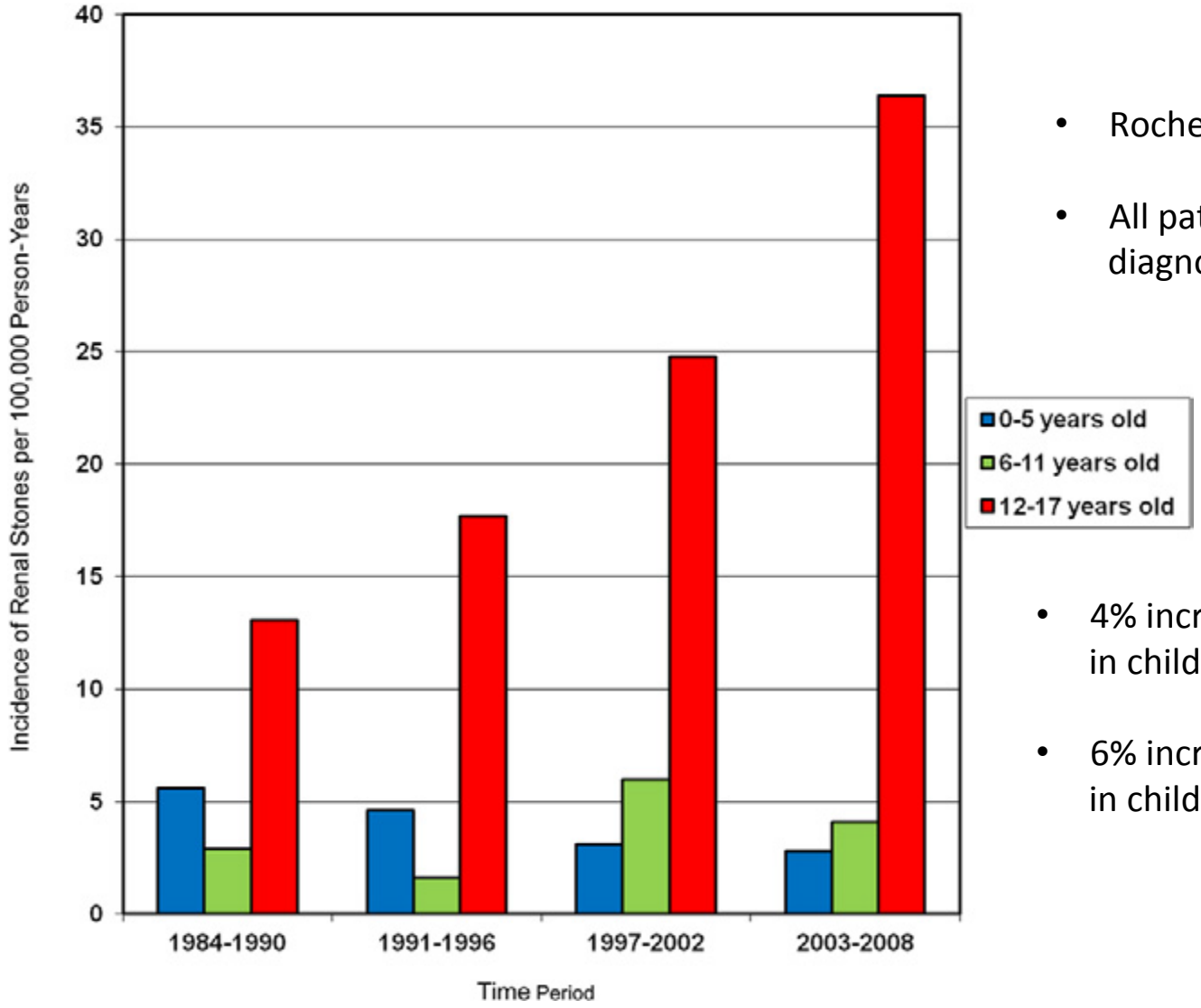
Doctors are reporting a "steep rise" in the number of young children with kidney stones, according anecdotal data cited by

Urolithiasis in children is on the rise

Epidemiology



- Rochester Epidemiology Project
- All patients 18 years or younger diagnosed with kidney stones

- 4% increase in the incidence of stones in children/year
- 6% increase in the incidence of stones in children/year ages 12-17

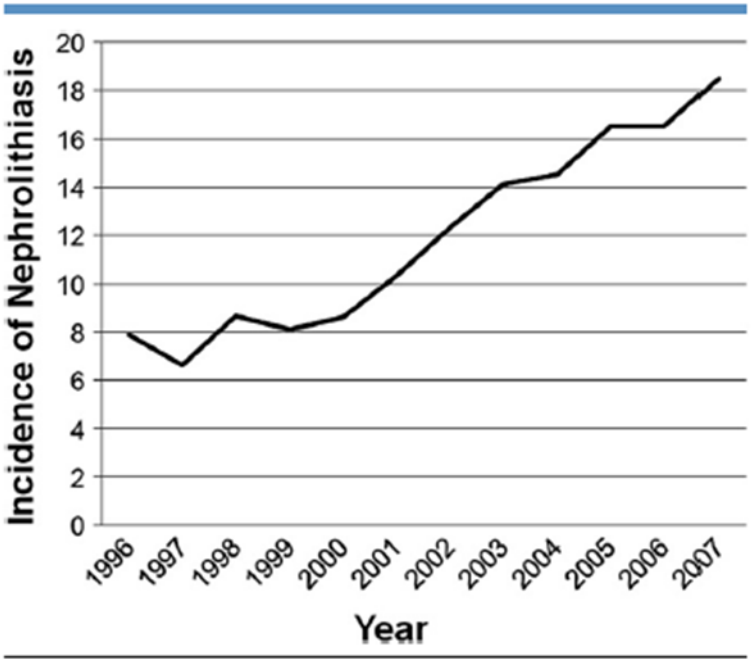
Dwyer et al 2012

Epidemiology

Emergency Room Visits

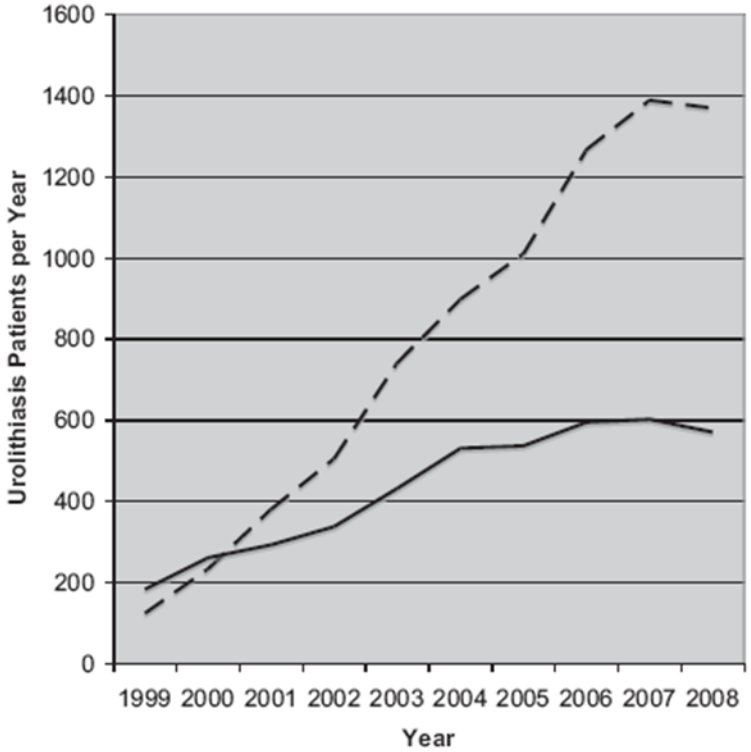
	Incidence rate
1996	7.9 /100 000
2007	18.5/100 000

($p < .0001$)



[2] Sas et al 2010

Hospital Admissions



Number of pediatric urolithiasis patients annually before (broken line) and after (solid line) correcting for hospital volume.

[3] Routh et al 2009

Epidemiology: Sex and Race

Table 1 Age and gender distribution among pediatric stone formers

Age quartile (years)	1997		2000		2003	
	Male *n* (%)	Female *n* (%)	Male *n* (%)	Female *n* (%)	Male *n* (%)	Female *n* (%)
0–5	98 (60)	66 (40)	111 (54)	95 (46)	168 (55)	111 (45)
6–10	136 (57)	101 (43)	208 (53)	186 (47)	269 (57)	256 (43)
11–15	213 (44)	275 (56)	327 (45)	401 (55)	452 (49)	589 (51)
16–20	299 (26)	852 (74)	954 (27)	2645 (73)	1153 (23)	3766 (77)
Total	746 (37)	1294 (63)	1600 (32)	3327 (68)	2042 (30)	4722 (70)
p value	<0.0001		<0.0001		<0.0001	

The numbers in parentheses represent the percentages of male and female stone patients in each age group. The *p* value represents the difference in age distribution between males and females for the given year

Ages 0-10 Males > Females

Ages 11-20 Females > Males

Age > 16 Females 3X > Males

Race: White (88%) > Hispanic (15%) > Black (6%) > Asian (1%)

Bush et al 2010

Matlaga et al. 2010

Economic Impact: Pediatric Stones

- KID Database : 7,348 Hospital admissions
- NEDS Database: 33,038 ED encounters
  - Median charges/admission: $13,922 for a total of $229 million/yr
  - Median charges/ ED encounter: $3,991/ for a total of 146 million/yr

Total Cost for Pediatric Stone admissions and ED evaluation ~ $375 million per year

Wang et al. 2015

Clinical Presentation: Age Dependent

- **Premature/Very Low Birth Weight Infants**
  - 102 very low birth weight infants
    - 6% had renal calcification
      - 100% incidentally found

Change et al 2011

- **Infants (<1 year)**
  - **UTI**
    - Males (34%) Females (21%)
  - **Restlessness**
    - Males (17%) Females (17%)
  - **Hematuria**
    - Males (10%) Females (14%)
  - **Incidental discovery**
    - Males (22%) Females (29%)

Alpay et al 2013

Clinical Presentation: Age Dependent

Younger Children and Adolescents

	< 10 years	> 10 years
Pain	**63%**	**82%**
Hematuria	**13%**	**11%**
UTI	**23%**	**8%**

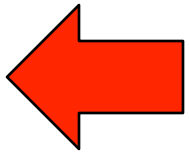
Valentini et al. 2011, Kalorin et al 2009

Diagnosis: Symptomatic Patient

Labs

- Urinalysis
  - Microscopic hematuria
  - Sterile Pyuria
- Urine culture
- CBC
- BMP

Radiological Imaging



- **CT**
- **KUB**
- **Sonography**
- **MRI**

Radiological Imaging: CT

All comers, not just stone patients

- **Migliorei et al. 2013**
  - Use of CT scanning in children between 1996 and 2010.
    - **Doubled** in children < 5 years of age
    - **Tripled** in children >5 years and < 14 years
    - Radiation effective dose for abdominopelvic CT
      - ~ 10.6 mSV
      - 14% > 20 mSv

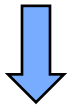
TABLE 7
Estimated Lifetime Risk of Radiation-Associated Solid Cancer Deaths in the LSS after Exposure to 0.1 Sv

Age at exposure	Sex	Lifetime risk (%)	Years of life lost per excess death	Background risk (%)
10	M	2.1	13.0	30
	F	2.2	13.3	20
30	M	0.9	12.7	25
	F	1.1	14.4	19
50	M	0.3	10.2	20
	F	0.4	11.2	16

Preston et al 2003

Radiological Imaging: CT

Projected lifetime risk of solid cancer



30 cases of radiation induced solid cancer/10,000 CT scans in girls
15 cases of radiation induced solid cancer/10,000 CT scans in boys

4.25 million CT scans in children/year

4870 Future Radiation Induced Cancers/year in Children

Migliorei et al. 2013

Radiological Imaging: CT

1999-2008

6318 children

1999		2008
26% CT	→	45 % CT

79%

2 or more CTs

med 2 per child

range 1-8

Routh et al 2010

Radiology Imaging: CT

Do we need CT imaging in Children with Symptomatic Stones?

Johnson et al. 2011

- **42 children treated for stones**
  - **~11 years**
  - **All had an US and/or KUB**
    - **90% had a stone seen on KUB and/or US**
    - **76% (32) had a CT scan**
      - » **All stones missed on US were distal stones**
        - **May have been seen if KUB was obtained**
      - » **No change in management even with CT**

90% of pediatric patients treated for symptomatic urolithiasis could have completed their evaluation and treatment without a CT scan.

Johnson et al. 2011

Radiological Imaging

Boston Children's 2009

US vs CT

50 consecutive patients

CT and US

	Sensitivity	Specificity
CT ⇨	94-99%	95-98%
US ⇨	76%	100%

Table 5. *Stone characteristics not seen on US but seen on CT with blinded radiology review*

Pt No.	Size (mm)	Location	Hydronephrosis
1	3	Distal ureter	No
6*	6	Kidney	No
14	5	Proximal ureter	Yes
15	2	Kidney	No
17	1	Kidney	No
18	2	Kidney	No
20	2	Kidney	No
	3	Bladder	—
30	2	Kidney	No
	2	Distal ureter	No
36	2	Kidney	No
54	2	Kidney	No
55	1	Kidney	No

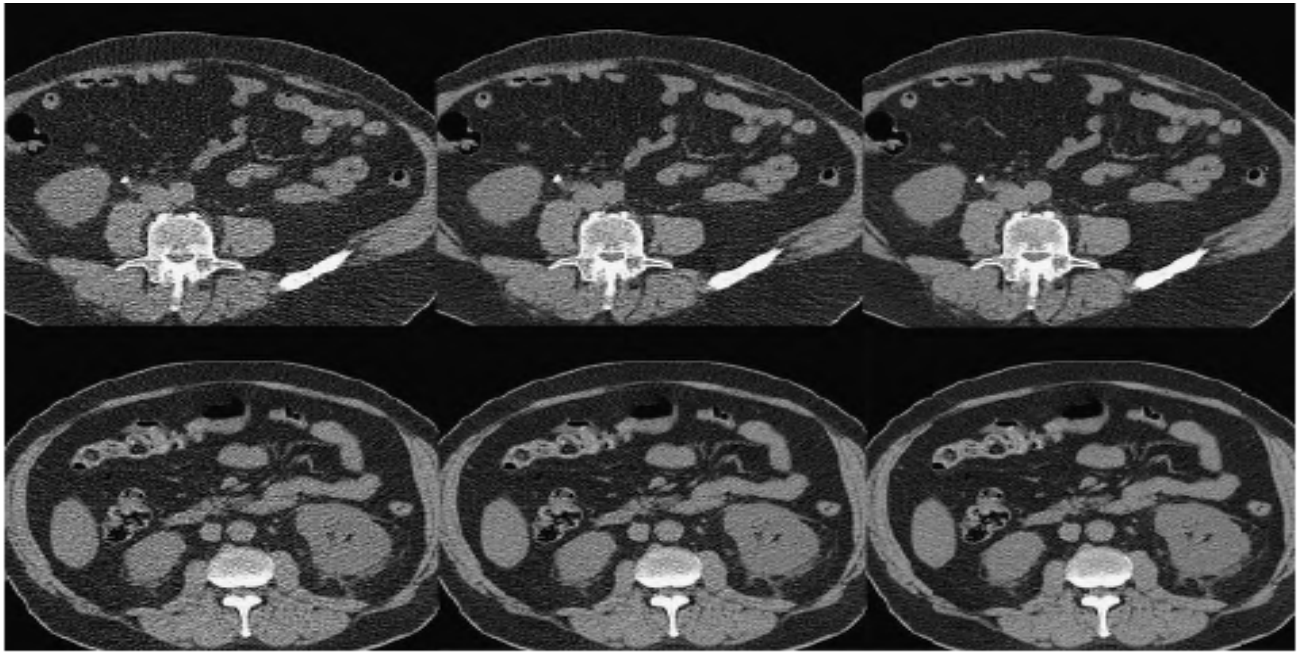
* Stone was echogenic with no shadowing.

16 discrepancies between CT and US.
3 cases long term management changes were recommended
All others management was not altered

Missed stones were small, no changes in immediate management of the stone.

Passerotti et al 2009

CT Imaging: Decreasing Radiation



Tube Current	25%	50%	100%
Effective Dose	1.9mSv	3.8mSv	7.3mSv

Niemann et al. 2008

Radiological Imaging: KUB

Radiological Imaging

KUB + US

	Sensitivity	Specificity	PPV	NPV	Accuracy
US + KUB	71-97%	85-92.7%	95%	46-68%	87.5%
CT	92-93%	96%	98%	86%	93.7%

Stones missed by Ultrasound and KUB passed spontaneously without complications

Conclusion: US + KUB adequately identified clinically significant stones with minimal loss of diagnostic accuracy

Ripolles, et al.2002, Catalano et al. 2004, Haddad et al. 1992, Deyoe et al. 1995

Radiological Imaging: Urolithiasis

- KUB and US first line evaluation in children with suspected urolithiasis
- Low dose CT scanning protocols should be requested when evaluation of children with CT is deemed necessary.
- KUB and or ultrasound should be the imaging modality of choice for post-operative follow-up

Expectant Management of Pediatric Nephrolithiasis

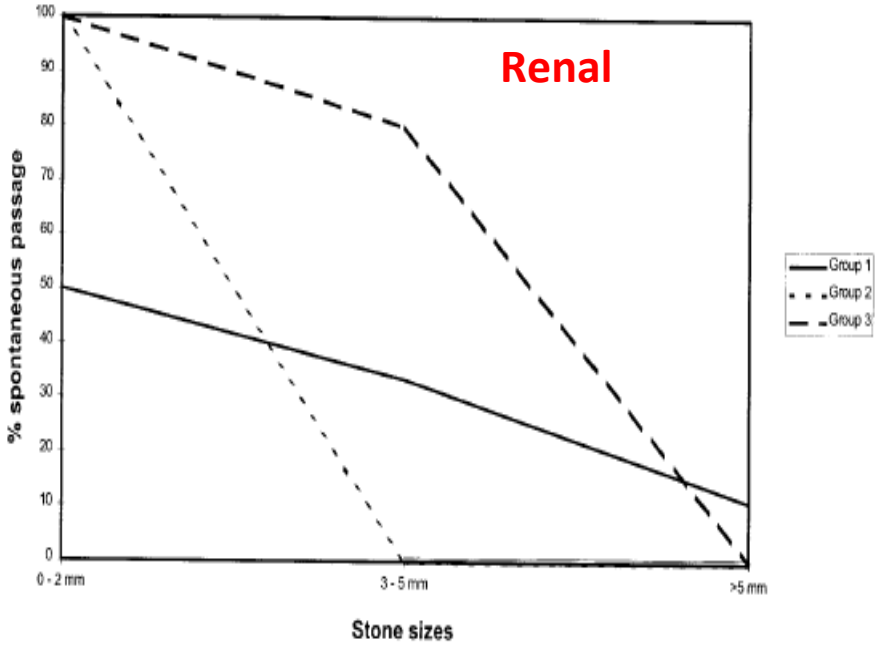


FIG. 1. Passage of renal stones plotted against stone size in 3 patient groups

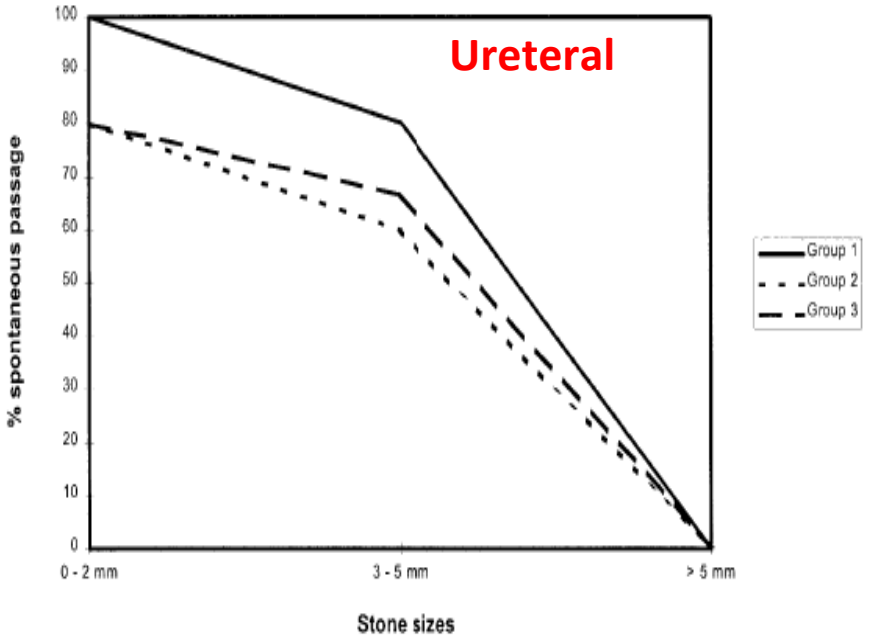


FIG. 2. Passage of ureteral stones plotted against stone size in 3 patient groups

Group 1	0-5 yrs
Group 2	6-10yr
Group 3	11-18yr

Pietrow et al. 2002

Medical Expulsion Therapy

Table 1. Patient demographics and clinical data

	Group 1	Group 2	*P* Value
Patients (n)	21	24	
Age (y)	7.2 ± 3.5	6.0 ± 3.5	.31
Weight (kg)	23.3 ± 9.7	23.5 ± 13.3	.55
Sex			.47
Boys	10	14	
Girls	11	10	
Stone size (mm)	4.45 ± 1.5	4.58 ± 1.7	.61

Data presented as mean ± standard deviation or n.

Table 2. Follow-up results

	Group 1 (n = 21)	Group 2 (n = 24)	*P* Value
Overall expulsion rate	6 (28.6)	17 (70.8)	.005
Expulsion rate by stone size (mm)			
<5 (n = 21)	5/12	9/9	.007
5-10 (n = 24)	1/9	8/15	.008
Expulsion rate by age (y)			
3-6 (n= 23)	4/11	11/12	.009
≥7 (n = 22)	2/10	6/12	.204
Interval to expulsion (d)			.001
Median	8	6	
Interquartile range	7.75-8.25	5.5-6	
Interval by stone size (mm)			
<5			.001
Median	8	6	
Interquartile range	7.5-8	5-6	
5-10			NA
Median	9 [9-9]	6	
Interquartile range		6-7	
Daily pain episodes (n)			
Median	1	1	.023
Interquartile range	1-2	1-1	

NA, not available.

Lower Ureteral Stones

Group 1
- Ibuprofen 10mg/kg BID

Group 2
- Ibuprofen 10 mg/kg/d
- Doxazosin 0.03 mg/kg/d

4 weeks F/U

Erturhan et al 2013

Medical Expulsive Therapy

Table 2 Overall results in both groups.

	Group I	Group II	P value
Expulsion rate	87.8%	64.2%	<0.01
Days to expulsion (mean ± SD)	8.2 ± 3.4	14.5 ± 4.5	<0.001
Pain episodes (mean ± SD)	1.4 ± 1.2	2.2 ± 1.4	<0.02
Need for analgesia (mean ± SD)	0.7 ± 0.9	1.4 ± 1.1	<0.02
Side effects (n)			
• postural hypotension	0	0	
• syncope	0	0	
• palpitations	0	0	
• somnolence	3	2	
• headache	1	1	
• nasal congestion	5	3	
Total	9	6	

Group 1
- Tamsulosin 0.2mg/day< 4 years old
- Tamsulosin 0.4mg/day> 4 years old
- Ibuprofen 10 mg/kg BID

Group 2
- Placebo
- Ibuprofen 10 mg/kg BID

All stones < 12 mm

Follow-up = 4 weeks

Stone Free Rate
- Tamsulosin 88%
- Placebo 64%

Mokhless et at 2011

Surgical Intervention

- **Failure of stone passage**
  - 2-4 week trial +/- α_1-antagonist
- **Uncontrolled pain**
- **Vomiting**
  - Inability to tolerate oral intake
- **Development of urinary tract infection**
  - Drainage of obstructed system
    - JJ Stent or PCN
  - Appropriate antibiotic treatment
    - 2 weeks (?)

Pre-Operative Considerations

- Urine Culture prior to intervention
- Antibiotics
  - Ureteroscopy
    - Cefazolin
  - PCN
    - Ampicillin and Gentamycin
    - Fluoroquinolone
  - Indwelling stent or PCN
    - Ampicillin and Gentamycin
    - Fluoroquinolone

Surgical Intervention

1999-2008

7921 children with urolithiasis

1712 (22%) Surgical intervention

Ureteroscopy	
1999	6.4%
2008	7.5 %

Stent Placement	
1999	12%
2008	11 %

PCNL	
1999	4.8%
2008	2.5 %

SWL	
1999	9.4%
2008	4.4%

We are doing more ureteroscopy, less SWL and PCN

Routh et al 2010

Shockwave Lithotripisy

- **Introduced in 1986 as treatment for pediatric stones**

- **(EAU)/ (AUA) Nephrolithiasis Guideline Panel:**

2007 Guideline for the Management of Ureteral Calculi

  - Treatment choice
    - Child's size
    - Urinary tract anatomy
    - Small pediatric ureter and urethra favor SWL
    - SWL first-line treatment option for most upper tract stones

Preminger et al. 2007

Shockwave Lithotripisy

- 500 children treated with SWL
  - Age:~ 8 yrs
    - (9 months-17 years)
  - Stone size:
    - 4-20 mm (kidney)
    - 4-10 mm (ureter)
  - Location:
    - 90% Kidney
    - 10% Ureter
  - Technique
    - ~2500 shocks
    - 16-19 kvolts
    - 60-80 shocks/minute
  - Follow –up
    - 3 months
    - Stone free
      - No stone
      - No fragment

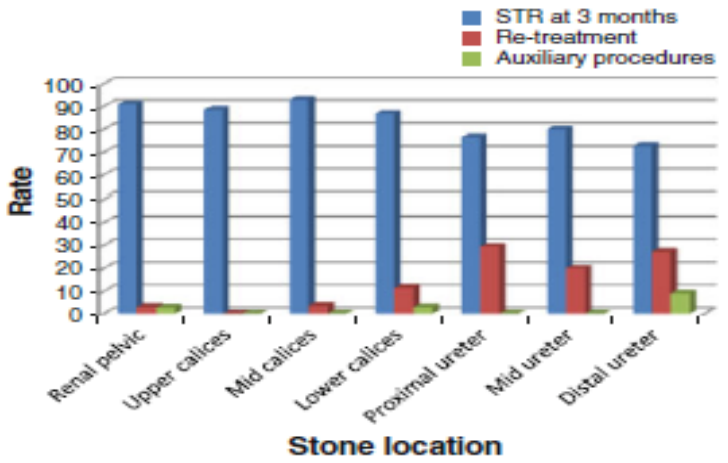


Fig. 1 Stone-free rate and re-treatment rate based on stone location

<u>Stone Free Rate at 3 months</u>:

90% Renal stones

77% Ureteral stones

Badawy et al 2012

Factors effecting the success of SWL

- Stone Location
  - **Kidney Lower pole**
    - Mandal et al 2012: SWL Children vs Adults for LP stones < 2.0 cm
      - Children: Higher success rate and fewer complications
  - **Ureteral**
    - Pirincci et al 2012: SWL for Children with Ureteral Stones
      - 62 children (50% proximal, 16% mid, 34% distal)
      - 93% stone free at 3 months with no differences in stone size/location
- Stone Composition
    - Brushite, Cystine and Calcium Oxalate monohydrate
- Skin to stone distance
    - McAdams et al 2010
      - SSD was not a significant predictor of successful SWL treatment

Factors effecting the success of SWL

- Stone Attenuation
  - McAdams et al 2010
    - < 1000 HU 77% stone free
    - >1000 HU 33% stone free
- Rate of shock wave delivery
  - Salem et al 2013
    - 60 children randomized to 80 s/min. or 120 s/min.
    - 80s/min. 90% stone free 120s/min. 74% stone free
- Stone Size and Number of stones
  - **Stone Size**
    - Landau et al 2009: SWL in Children with Renal Stones 6-24 mm
      - 80% stone free at 3 months with stone size most important factor
      - Best results at ≤ 11 mm
    - McAdams et al 2010
      - Only Stone diameter predicted SWL success

Complication of SWL in Pediatrics

- **Pain (18%)**
- **Bleeding (5%)**
- **Sepsis (4%)**
- **Urinary Retention (2%)**
- **Ureteral obstrucion (2%)**
- **UTI (2%)**
- **Stricture (1%)**

Granberg et al. 2012

Long-term Concerns after SWL

- Rinkmann et al 2001
  - 64 children
    - 80% stone free rate at 3 months
    - No:
      - Renal scarring
      - Change in renal function
      - Change in blood pressure
      - Growth difference in treated vs untreated kidney
    - Hematuria and proteinuria resolved in all stone free children

Ureteroscopy in Pediatrics

- 1st case of pediatric ureteroscopy: 1988
- SWL vs Ureteroscopy
  - 2000 to 2002
    - **24% ureteroscopy**
    - 78% SWL
  - 2006 to 2008
    - **50% ureteroscopy**
    - 50% SWL

Richey et al 1988, Wang et al. 2012

Ureteroscopy in Pediatrics

- Ureteral Access
  - Primary ureteroscopic access
  - Semi-rigid ureteroscopy >>> flexible ureteroscopy
  - Hand Irrigation Pump
  - Ureteral dilation:
    - Passive dilation:
      - Ureteral stent
    - Active dilation
      - Ureteral dilation
        - » 8 or 10 F ureteral coaxial dilator
        - » Balloon dilation

Ureteral Dilation: Passive

- Ureteral stent
  - ➢ Kim et al. 2008
    - 57% of ureters could not be accessed via primarily
      - 83% were in children <10 years
    - 100% of stented ureters were accessible
  - ➢ Corcoran et al 2008
    - 40% required ureteral stenting
      - Age, height, weight and BMI do not predict need for stent
    - 100% of stented ureters were accessible

No Significant Complications Long Term

Kim et al. 2008, Corcoran et al 2008,

Ureteral Dilation: Active

- Ureteral Coaxial Dilator
  - 100 children with stones
    - 70% ureteral dilation (8 or 10F ureteral coaxial dilators)
    - Mean follow up 10 months (median 2.6)
    - No major intraoperative complications
      - 5 post op stent for ureteral perforation
      - 1 post operative stricture
- Ureteral Balloon Dilator
  - 16 children (ages <7 years)
    - 30% ureteral balloon dilation
    - Mean follow up 10.3 months
    - No major complications
      - 1 case of perforation
      - No long term complications

Smaldone et al 2008, Unsal et al. 2011

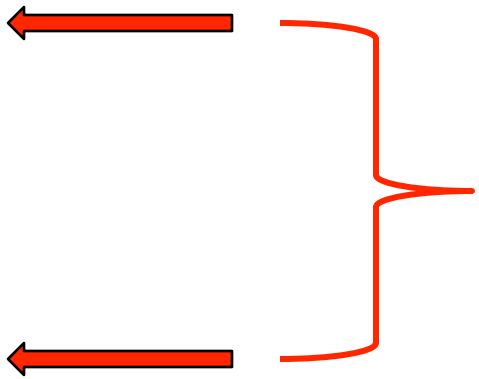
Ureteral Access Sheath

- 96 children with stones
  - Stone size ~ 9.6 mm
  - Follow up ~ 11 months
  - 42% required ureteral access sheath
    - 7 intraoperative complications
      - 4 perforations
      - 2 submucosal wires
      - 1 stent migration
      - More common with sheath use (p=0.02)
    - No ureteral strictures

Wang et al 2011

Ureteroscopy in Pediatrics

- Stone Free Rates
  - Age:
    - < 7 years of age 93%
    - > 7 years of age 90%
  - Location
    - Kidney 81%
    - Ureter 100%
  - Size
    - < 10 mm 91%
    - > 10 mm 79%



Lower if stone in the kidney and/or larger than 1 cm

Uygm et al 2012

Ureteroscopy in Pediatrics

- Complications:
  - 0 to 8%
    - Renal colic
    - Gross hematuria
    - Febrile UTI
    - Ureteral stricture
    - Ureteral perforation

Predictive Factor for Complications
>> Increased operative time

Dogan et al. 2011

PCN in Pediatrics

- **First reported use in Children:**
  - Woodside et al. 1985
- **Use has decreased with time**
  - Indications for PCN
    - Anatomic abnormalities
    - Known stone composition resistance to SWL
      - Brushite, Cystine, Calcium oxalate monohydrate
    - Struvite Infectious stone
    - Large Stone burden

PCN in Pediatrics

- PCN in infants:
  - 19 infants (7-36 months)
    - All Staghorn calculus
      - 100% ureteral catheter pre-op
      - 100% post op Nephrostomy tube
    - Stone Free:
      - 95%
    - Complications
      - 16% post operative fever
    - ~ 27 months
      - No long term complications noted.

Zang et al 2012

PCN in Pediatrics

- 10 years of pediatric PCNs
  - 95 patients
    - ~ age 12 years (3-17)
  - Indications
    - Stones > 2cm
  - Stone Free
    - 83% after 1 treatment
    - 91% after 2 treatments
  - Complications:
    - 16% post op fever (2 sepsis)
    - 9% transfusion
    - 3% hydrothorax (2 chest tubes)

Bhageria et al. 2013

PCN in Pediatrics: What's Hot?

Mini-PCN (15-17F Nephroscope with ~ 20F sheath)

Ultra Mini PCN (9.5-11F Nephroscope with ~ 12F sheath)

Micro PCN: (16-guage "all-seeing needle")

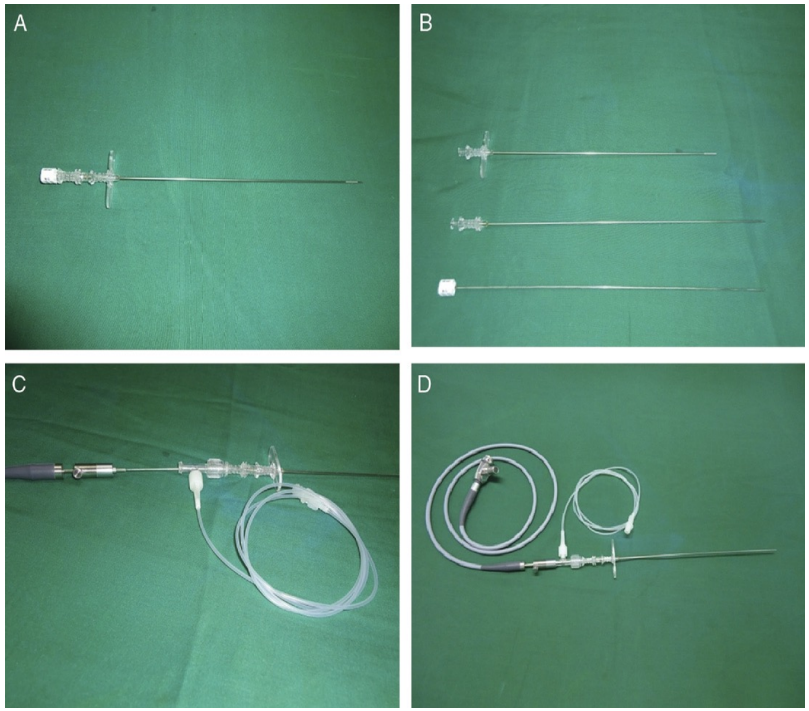
- Not approved in the US

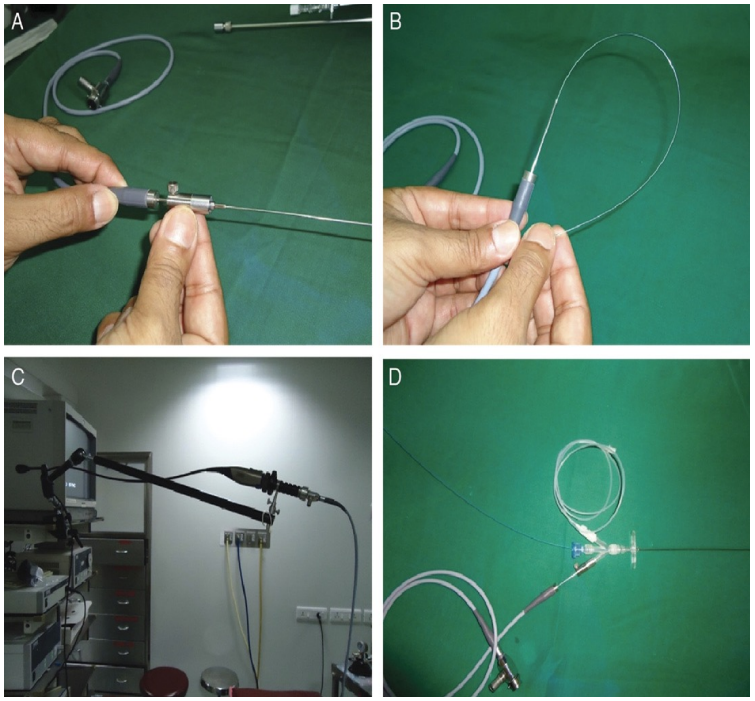
PCN in Pediatrics

- Mini-PCN vs Ureteroscopy
  - 201 children
    - 106 Mini-PCN
    - 95 Ureteroscopy
  - Stone burden 10-30mm
    - Smaller in Ureteroscopy (~14mm vs 12 mm)
  - Outcomes
    - Ureteroscopy:
      - Less Floroscopy use
      - Shorter OR time
      - Shorter Hospitalization
    - Mini PCN
      - More Blood Loss

Resorlu e al. 2012

PCN in Pediatrics: Micro PCN





- **140 Procedures**
  - **6-32 mm stones**
  - **Stone free 82%**
  - **12 conversations to mini-PCN**

Desai et al 2011 Haipoqlu et al. 2013

PCN in Pediatrics

- **Mini PCN vs Micro PCN:**
  - < 18 years of age
  - Stone size: 10-20 ~ 13 mm
- **Outcomes:**
  - **No difference between groups:**
    - Operative Time
    - Stone Free Rates
    - Success Rates
    - Complications
  - **Micro Group:**
    - Shorter:
      - Floroscopy time
      - Length of Hospitalization
    - Less Blood loss in Mini PCN Group

Karataget al 2015

Pediatric Nephrolithiasis

Asymptomatic Stones

- Kang et al. 2012 JUrol
  - 347 patients
    - ~ 4.4 mm (1-10mm)
    - All located in the kidney
  - 46% no stone related event
  - 54% had stone related event
    - 24% required intervention
      - 5% surgery

Residual Fragments

- Dincel et al. 2013
  - 85 children
    - SWL, URS or PCN
    - ~ 22 months (6-50 mths)
    - < 4mm

Table 2 Outcomes of residual fragments.

		p value
Spontaneous passage (%)	22/85 (25.8%)	
According to stone location		<0.05 *
Renal pelvis	4/7 (57.1%)	
Mid/upper pole	9/26 (34.6%)	
Lower pole	5/31 (16.1%)	
Multi-caliceal	4/21 (19.1%)	
IPA		<0.05 *
≥45°	7/15 (46.7%)	
<45°	0/11 (0%)	
According to no. fragments		<0.05 *
Single (%)	15/50 (30%)	
Multiple (% [median, range])	7/35 (20% [3, 2 – 4])	
Growth in size (%)	18 (21.2%)	
Stone related events (%)	34 (40%)	
Renal colic	21 (24.7%)	
Hematuria	14 (16.4%)	
Urinary tract infection	5 (5.8%)	

Recurrence Rates

- Retrospective Review 1999-2007
  - 60 children < 18 years
    - Stone surgery and stone free
    - ~ age at surgery 5 years
  - Follow up 5 years
- Overall recurrence rate 55%
  - Abnormal anatomy 65%
- 24 hour urine
  - Hypercalciuria and/or Hypocitraturia
- Conclusion
  - High recurrence rate in children with stones requiring surgical intervention
  - Aggressive evaluation and management

Lao et. al. 2014

Post Intervention: Follow up

- **Radiographic imaging:**
  - Document clearance of stone/fragments
  - Resolution of hydronephrosis
  - Evaluate for possible stricture
    - Ultrasound +/- KUB
- **24 hour urine**
  - 50% have an abnormality noted on 24 hour urine
  - Recurrence rates > 50%
- **Serum Labs**
  - Chem 7, PO3, Mg, UA, AlkPO4

Preminger et al 2007

Conclusion

- Pediatric Stone Disease is on the Rise
- Clinical presentation varies age
- US and KUB is the imaging choice for children
- Conservative management with medical expulsive therapy is beneficial
- Surgical Intervention requires special considerations
- Medical Evaluation and follow up is necessary

Thank You!

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