Brigham and Women's Hospital
Founding Member, Mass General Brigham

PEDIATRIC NEPHROLOGY

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CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

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- University of Vermont College of Medicine
- Pediatric Residency: Mayo Clinic
- Pediatric Nephrology Fellowship:
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  - Clinical interests: glomerular diseases in children; pediatric dialysis
  - Research interests: nephrotic syndrome; quality metrics in pediatric nephrology

Disclosures

I have no disclosures relevant to this presentation.

Objectives

Use case vignettes to:

- Provide overviews of two conditions in children – nephrotic syndrome and hypertension -- where adult nephrologists are often consulted
- Emphasize differences in diagnosis and management for these conditions in children compared to typical care in adults

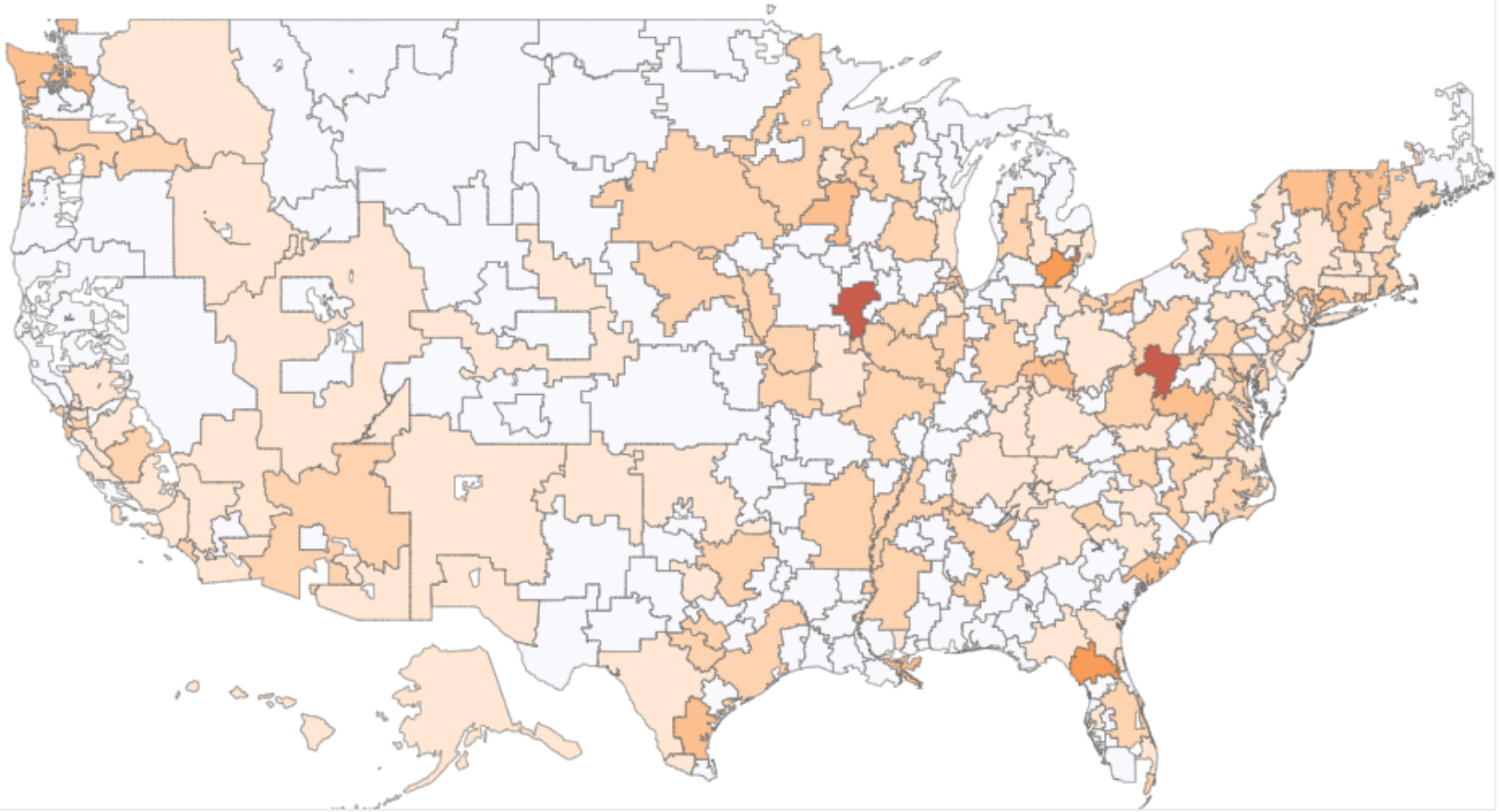
Overview

Childhood kidney disease is rare,
but pediatric nephrologists are few

Adult nephrologists are often called on to assess children and adolescents

US-Based Pediatricians Currently Certified in Pediatric Nephrology	Average # per HRR	Average # per 100,000 Children by HRR
651	**2.121**	**0.60**

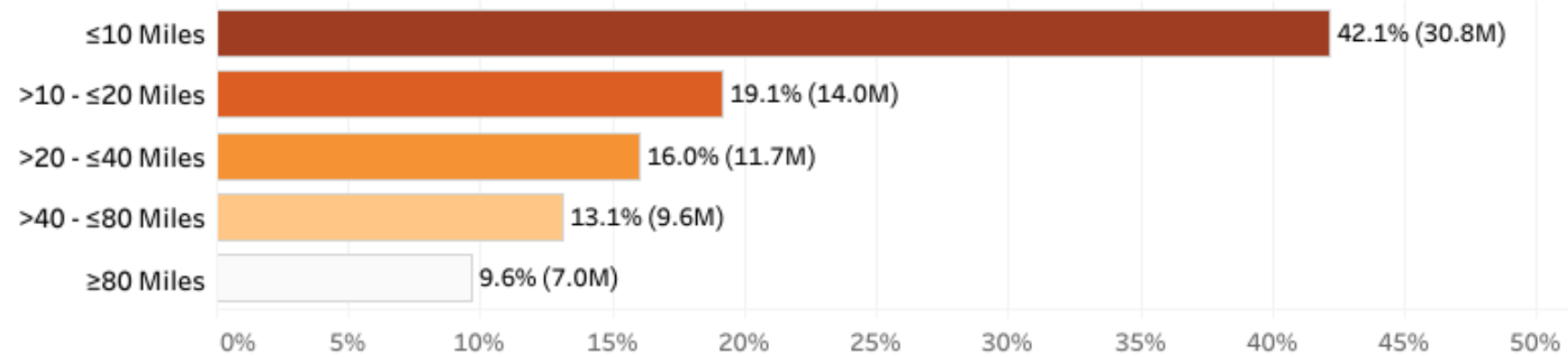
Those Certified in Pediatric Nephrology by Hospital Referral Region, per 100,000 children



Color Legend

- 0 Providers to 100,000 Children
- 0.01-1 Providers to 100,000 Children
- 1.01-2 Providers to 100,000 Children
- 2.01-3 Providers to 100,000 Children
- 3.01-4 Providers to 100,000 Children
- 4.01-5 Providers to 100,000 Children
- >5 Providers to 100,000 Children

Percent (%) of Children and Millions of Children in the US by Distance



	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	203
East North Central	0.615	0.601	0.614	0.619	0.631	0.638	0.657	0.662	0.666	0.673	0.676	0.682	0.674	0.685	0.690	0.693	0.6
East South Central	0.360	0.386	0.383	0.412	0.428	0.456	0.470	0.473	0.498	0.519	0.533	0.545	0.569	0.578	0.600	0.604	0.6
Middle Atlantic	0.547	0.531	0.564	0.570	0.571	0.584	0.596	0.599	0.598	0.603	0.587	0.584	0.576	0.583	0.582	0.583	0.5
Mountain	0.354	0.369	0.394	0.416	0.438	0.463	0.471	0.469	0.473	0.497	0.512	0.529	0.544	0.550	0.566	0.574	0.5
New England	0.722	0.712	0.701	0.683	0.689	0.676	0.687	0.695	0.705	0.702	0.708	0.712	0.711	0.699	0.697	0.690	0.6
Pacific	0.483	0.486	0.490	0.488	0.486	0.491	0.492	0.486	0.492	0.498	0.504	0.502	0.502	0.508	0.509	0.502	0.5
South Atlantic	0.506	0.514	0.540	0.553	0.559	0.567	0.582	0.588	0.600	0.604	0.614	0.615	0.626	0.636	0.642	0.646	0.6
West North Central	0.592	0.630	0.662	0.694	0.734	0.773	0.806	0.834	0.845	0.869	0.892	0.901	0.919	0.944	0.968	0.963	0.9
West South Central	0.421	0.422	0.425	0.431	0.435	0.437	0.440	0.434	0.437	0.441	0.440	0.438	0.433	0.437	0.437	0.438	0.4

Projection of Workforce Supply for Pediatric Nephrology

Model Parameters: Census Division, CWE, Subspecialists per 100,000 Children, Baseline

Case One

- A previously healthy 2-year-old girl is brought to her pediatrician for rhinorrhea and periorbital swelling.
- She is diagnosed with a viral syndrome and prescribed diphenhydramine.
- Her symptoms wax and wane for a week, and then over the course of 24 hours, she becomes markedly edematous.

Case One

On physical examination:

- Blood pressure is normal.
- Her weight has increased 3 kg from her visit last week.
- She has periorbital edema, abdominal fullness with a palpable fluid wave, and labial and lower extremity edema.

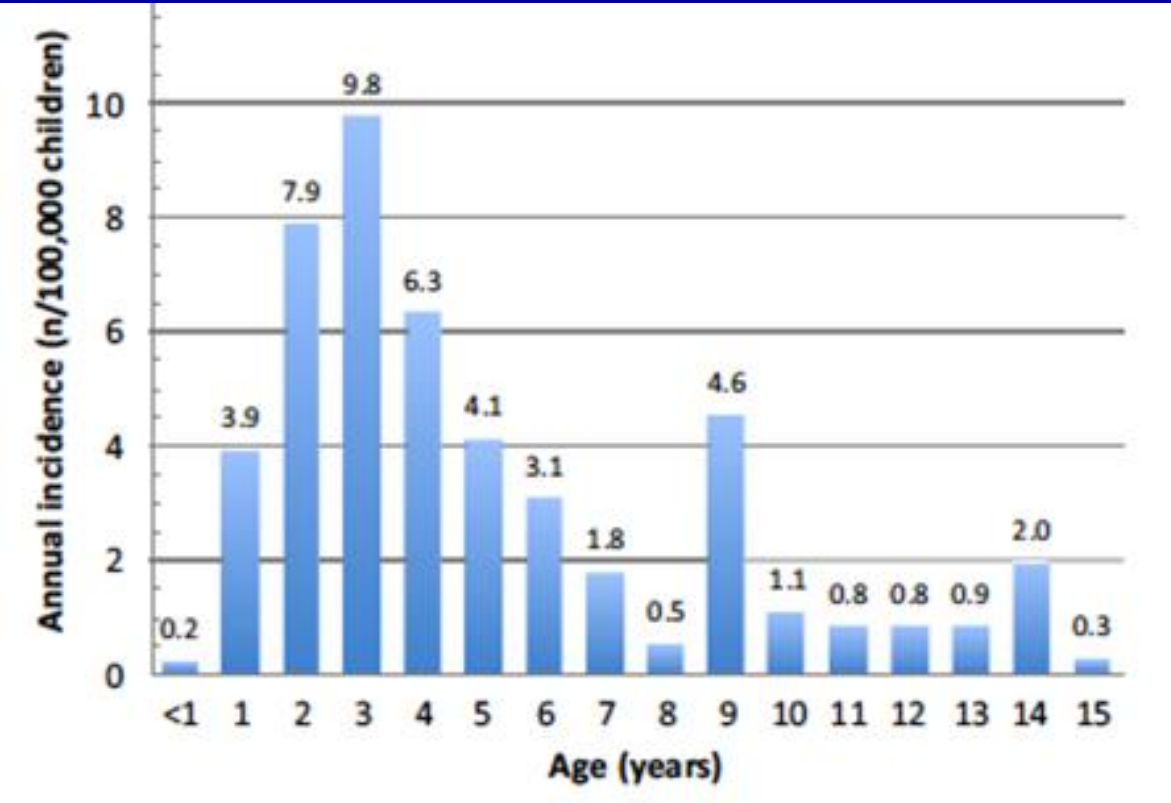
Case One

- Her serum creatinine is 0.2 mg/dl with a serum albumin of 1.2 g/dl.
- Her urinalysis has 3+ protein and 1+ heme, with 3-5 rbc/hpf, occasional hyaline casts, lipid droplets, and oval fat bodies.
- A random urinary protein:creatinine ratio (mg:mg) is 9.

Pediatric Definition

- Proteinuria
  - > 40 mg/M^2/hr
  - ≥ 50 mg/kg/day
- Hypoalbuminemia
  - Serum albumin ≤ 2.5 g/dl
- Hyperlipidemia
  - Cholesterol > 180 mg/dl
- Edema

Epidemiology: Incidence by Age

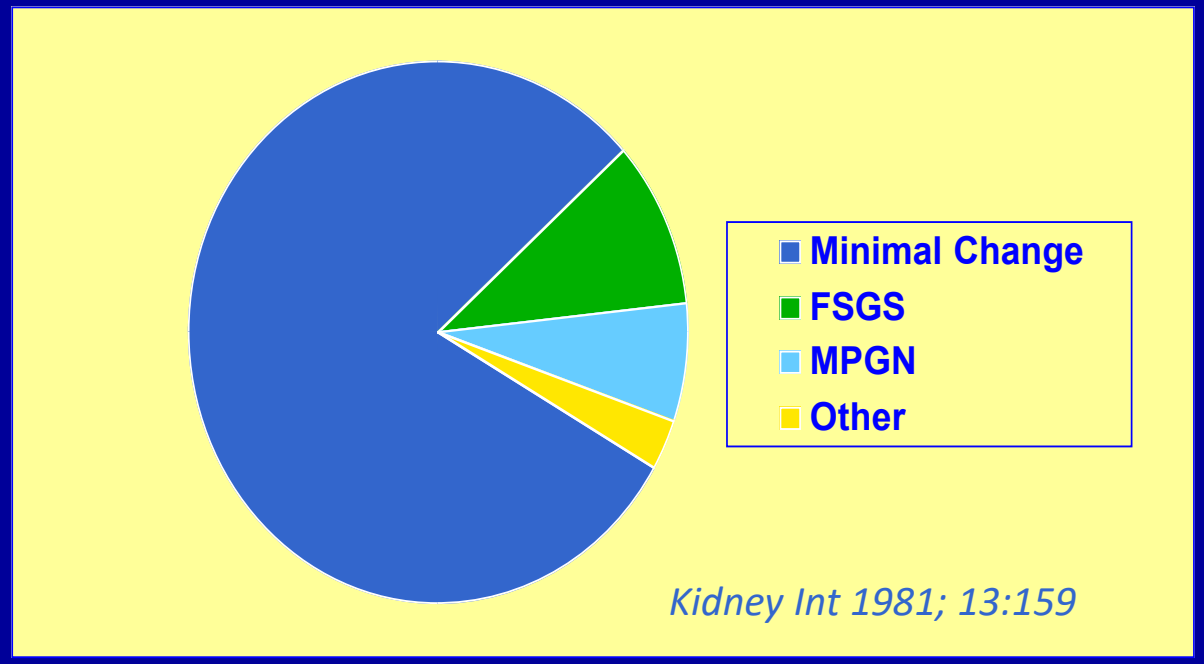


- Childhood nephrotic syndrome is rare at any age
- Incidence rates are highest in children of pre-school age
- Rates in later childhood are lower
- Pre-adolescence, boys outnumber girls 2:1; post-puberty similar incidence

Dossier C et al. Pediatr Nephrol 2019; 34: 671-678

Kidney Histology

International Study of Kidney Disease in Children



- Results used as worldwide benchmark
- All children biopsied at presentation
- 80% with Minimal Change; 10% with FSGS

Clinical Characteristics at Presentation:
Minimal Change vs FSGS

CHARACTERISTIC	MINIMAL CHANGE	FOCAL SCLEROSIS
Age ≤ 6 years old	80%	50%
Boys	60%	70%
Hypertension	20%	50%
Microhematuria	25%	50%
Elevated creatinine	30%	40%

CRITERIA FOR EMPIRIC STEROID THERAPY IN CHILDREN WITH NEPHROTIC SYNDROME

Age

- >80% of pre-pubertal children have steroid sensitive minimal change disease
- By adolescence, proportion with other diagnoses increases, but >50% still with minimal change

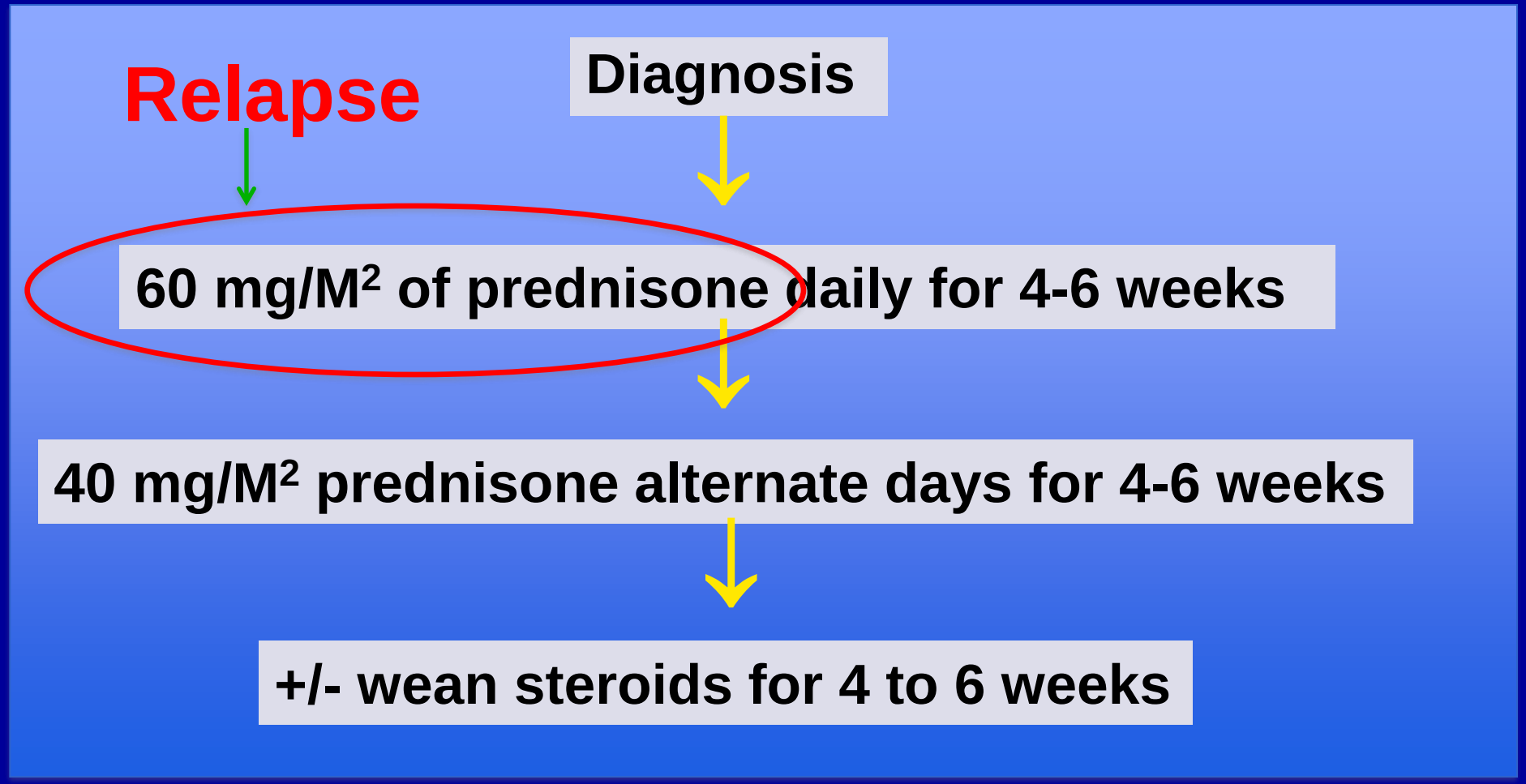
Normal blood pressure

Non-nephritic urinary sediment

Normal kidney function

Steroid Therapy:

Substantial in Dose and Lengthy



Pediatric Nephrology (2023) 38:877–919
https://doi.org/10.1007/s00467-022-05739-3

GUIDELINES

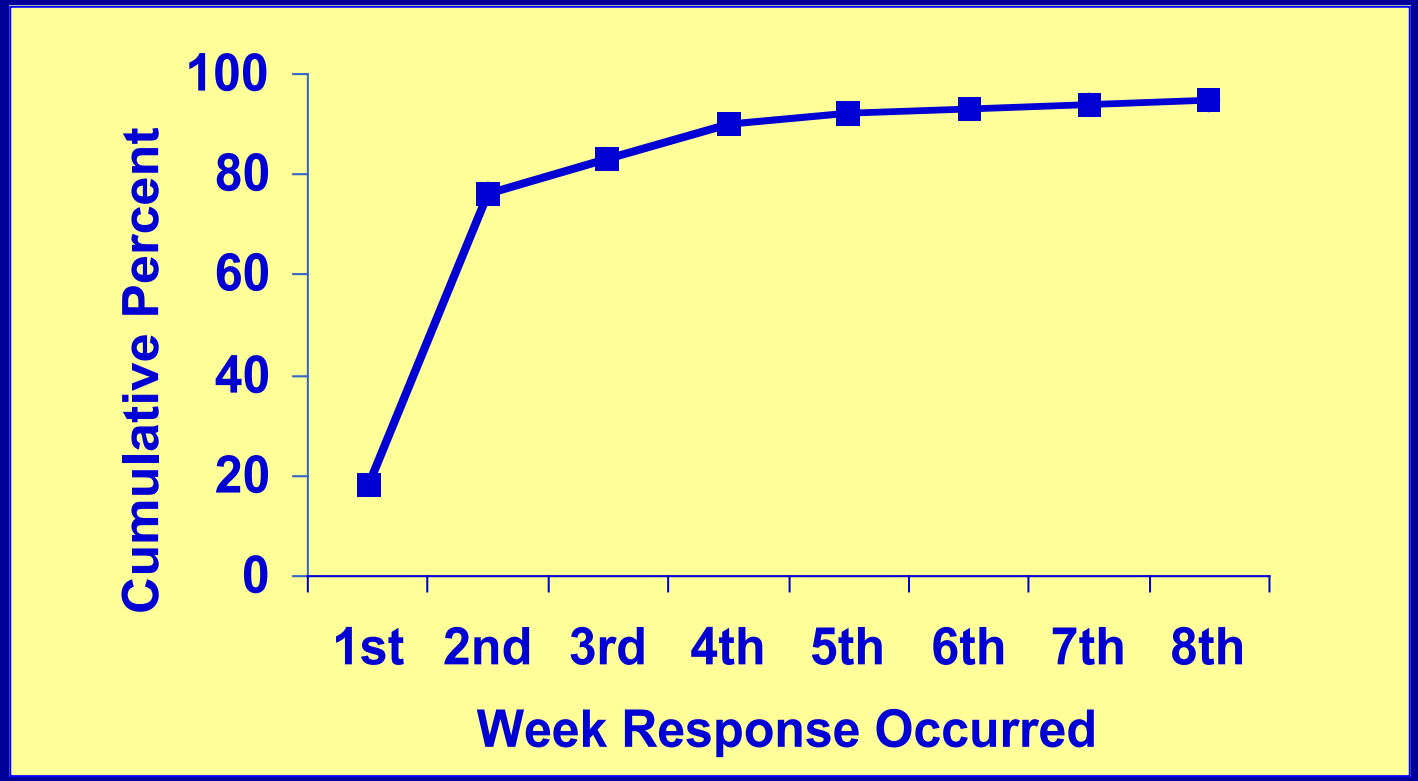
IPNA clinical practice recommendations for the diagnosis and management of children with steroid-sensitive nephrotic syndrome

Agnes Trautmann[1] · Olivia Boyer[2] · Elisabeth Hodson[3] · Arvind Bagga[4] · Debbie S. Gipson[5] · Susan Samuel[6] · Jack Wetzels[7] · Khalid Alhasan[8] · Sushmita Banerjee[9] · Rajendra Bhimma[10] · Melvin Bonilla-Felix[11] · Francisco Cano[12] · Martin Christian[13] · Deirdre Hahn[14] · Hee Gyung Kang[15] · Koichi Nakanishi[16] · Hesham Safouh[17] · Howard Trachtman[18] · Hong Xu[19] · Wendy Cook[20] · Marina Vivarelli[21] · Dieter Haffner[22] · on behalf of the International Pediatric Nephrology Association

Aggregate evidence quality	Benefit or harm predominates	Benefit and harm balanced
Level A • Intervention: well-designed and conducted trials, meta-analyses on applicable populations • Diagnosis: independent gold-standard studies of applicable populations	Strong recommendation	Weak recommendation (based on balance of benefit and harm)
Level B Trials or diagnostic studies with minor limitations; consistent findings from multiple observational studies	Moderate recommendation	
Level C Single or few observational studies or multiple studies with inconsistent findings or major limitations		
Level D Expert opinion, case reports, reasoning from first principles	Weak recommendation (based on low-quality evidence)	No recommendation may be made
Level X Exceptional situations where validating studies cannot be performed and benefit or harm clearly predominates	Strong recommendation Moderate recommendation	

Time to Response

ISKDC *Kidney Int 1981; 13:159*



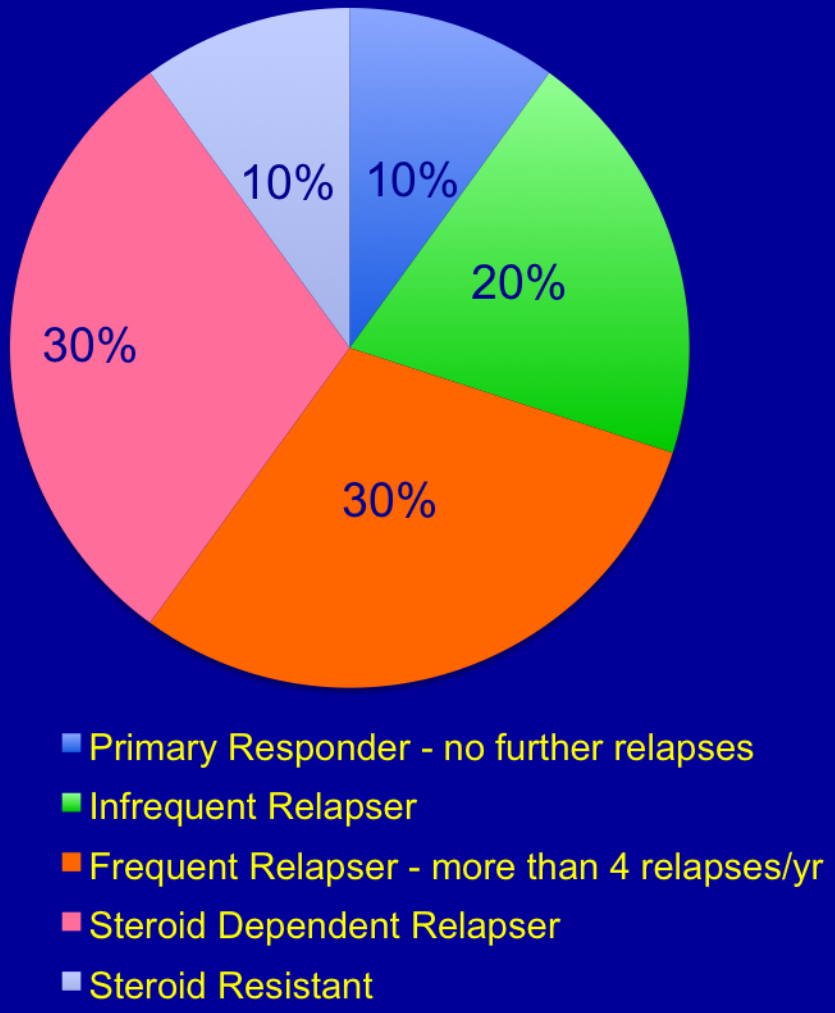
- Average time to response = 10 days
- >90% of responders respond by 4 weeks

SUPPORTIVE THERAPY FOR CHILDREN WITH NEPHROTIC SYNDROME

No added salt diet
Restrict fluids to estimated insensible losses (300 ml/M^2/day) plus output
Limited use of diuretics
No efficacy to prophylactic antibiotics
25% albumin infusions accompanied by IV diuretics for significant edema

Patterns of Response:

Boston Experience Since 1990



- Experiencing no relapses of nephrotic syndrome after diagnosis is very rare for any affected child
- About two-thirds of children have lots of relapses or cannot be weaned off steroids
- Ongoing need for steroid exposure increases risk for steroid-related sequelae and consideration of a steroid-sparing therapy

CHRONIC MANAGEMENT FOR CHILDREN WITH NEPHROTIC SYNDROME

Home urine dip (first morning void)

Anticipate flares (infections and allergic triggers)

Influenza and pneumococcal vaccines

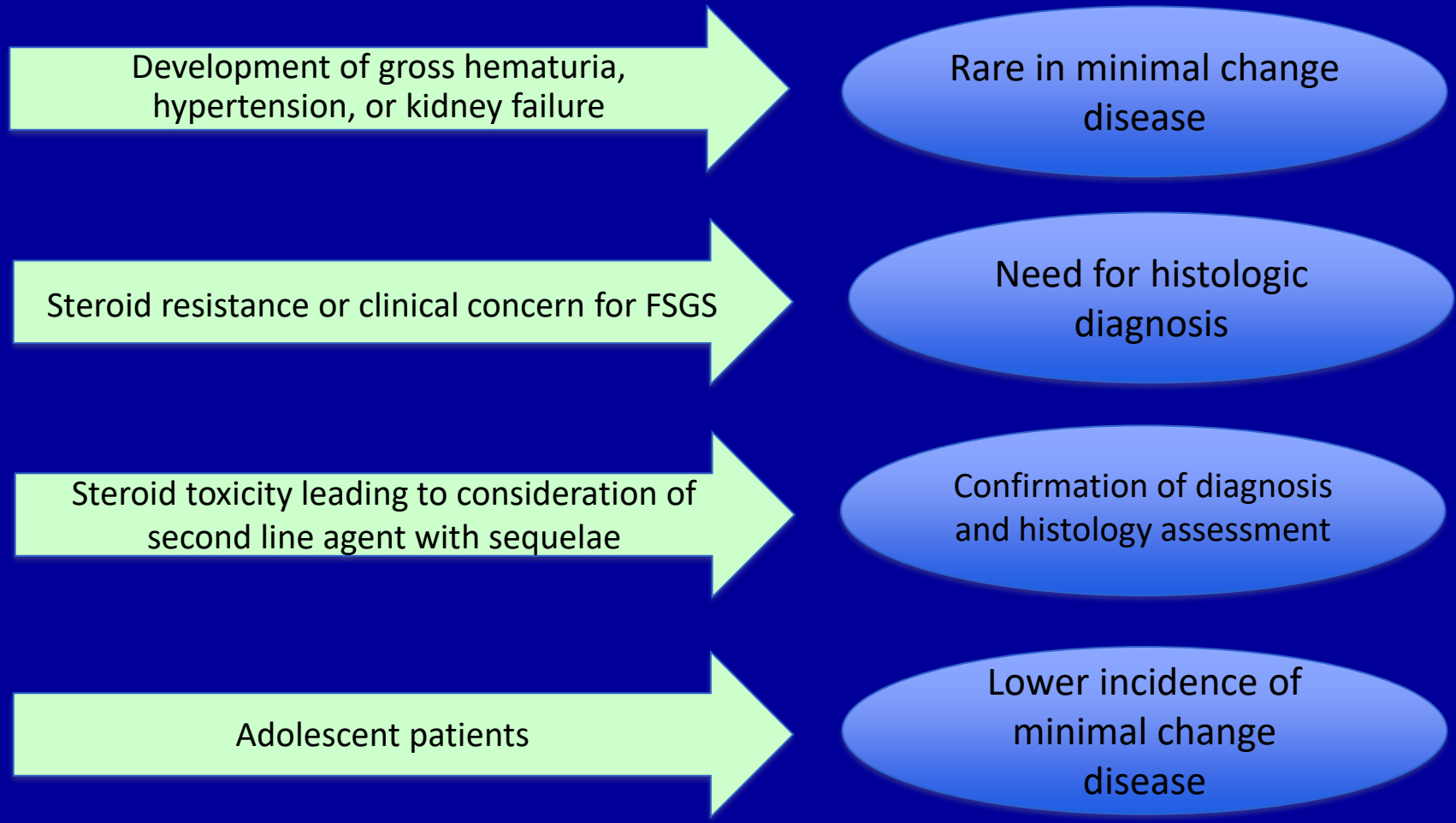
Follow growth closely

Follow bone health

Annual eye exam

Assess for serious steroid sequelae

Kidney Biopsy:
Considerations in Nephrotic Syndrome



Steroid Sparing Therapies

- Historically, both cyclophosphamide and chlorambucil were mainstays of therapy, but their use in North America for childhood nephrotic syndrome is now extremely uncommon
- Current most common steroid-sparing therapies:

  MMF

  Rituximab

  Calcineurin inhibitors

Choices often patient, provider, and center-specific

MMF for MCNS in Children

French Experience *Pediatr Nephrol (2016) 31: 2095-2101.*

	1 year before starting mycophenolate	1 year after starting mycophenolate	*p* value
Relapse rate (*n*/year)	3.00	0.86	<0.0001
Cumulative dose of prednisone (mg/m^2/month)	521 (317–863)	313 (244–402)	<0.001
Threshold dose of prednisone (mg/m^2/day)	13.0 (7.1–24.4)	3.2 (0.0–6.8)	<0.0001

Values are given as median (interquartile)

Comprehensive Review

Pediatric Nephrology
https://doi.org/10.1007/s00467-018-3970-y

EDUCATIONAL REVIEW

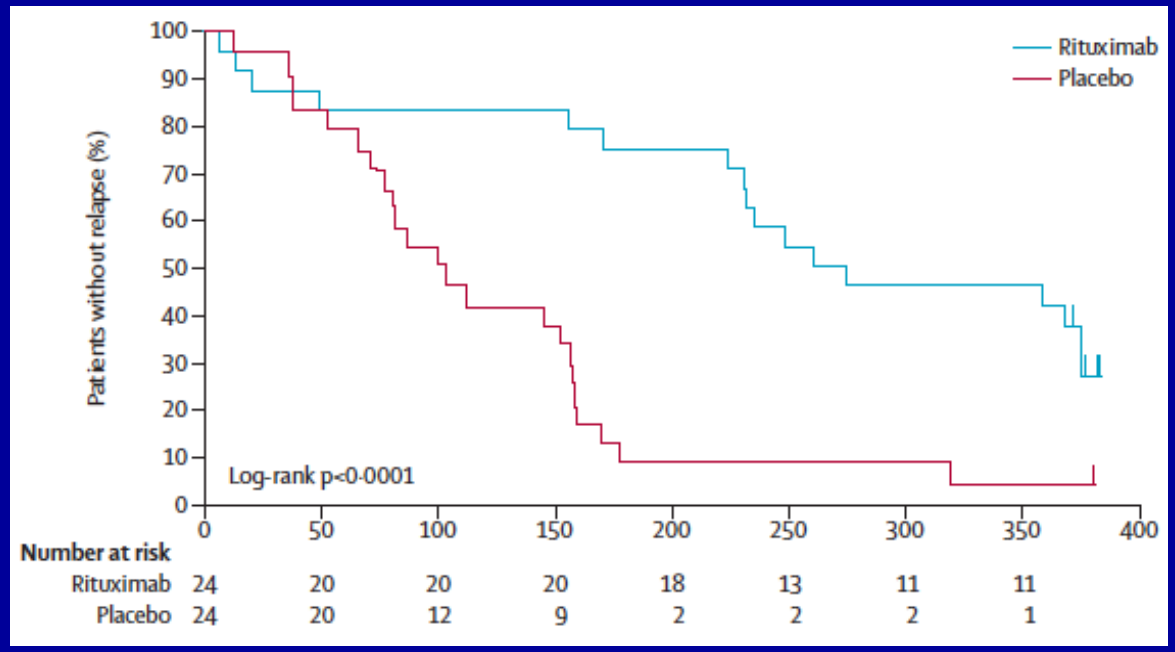
CrossMark

Mycophenolate mofetil for sustained remission in nephrotic syndrome

Uwe Querfeld[1] · Lutz T. Weber[2]

Rituximab for MCNS in Children

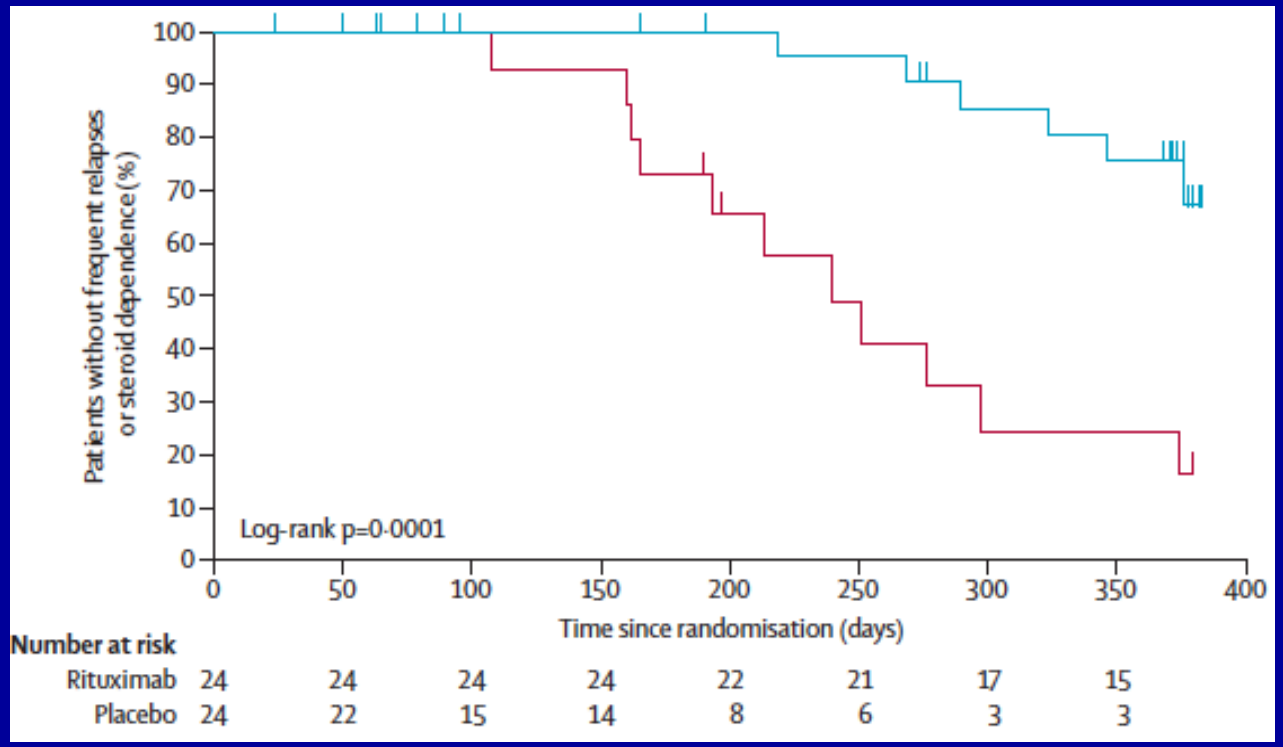
Japanese Experience ***Lancet 2014; 384: 1273–81.***



- Rituximab therapy led to longer interval remission than placebo
- Median duration of remission:
  267 days vs 101 days
- Hazard Ratio for relapse after rituximab 0.27, p<0.0001

Rituximab for MCNS in Children

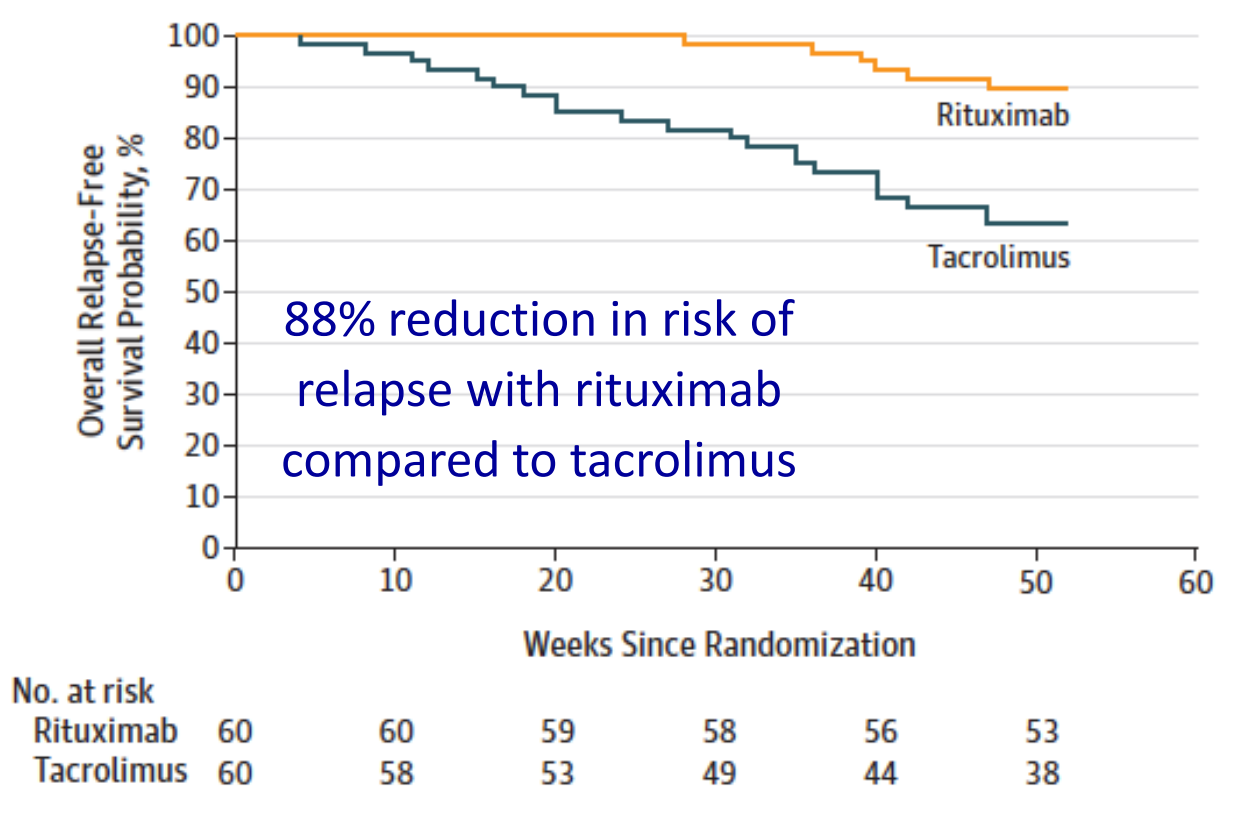
Japanese Experience ***Lancet 2014; 384: 1273–81.***



- The rituximab-treated children were much less likely to revert back to becoming frequently relapsing or steroid dependent
- Hazard ratio 0.17, p=0.0001

Rituximab vs Tacrolimus

Indian Experience *JAMA Pediatrics 2018; 172: 757–64.*



- Compared therapy with rituximab (375 mg/M^2 x 2 doses one week apart) to therapy with tacrolimus (0.2 mg/kg/day, trough 5-7 ng/ml)
- All children steroid sensitive, frequently relapsing, and no prior exposure to steroid sparing therapy

Rituximab followed by MMF

78 children with frequently relapsing, steroid dependent nephrosis

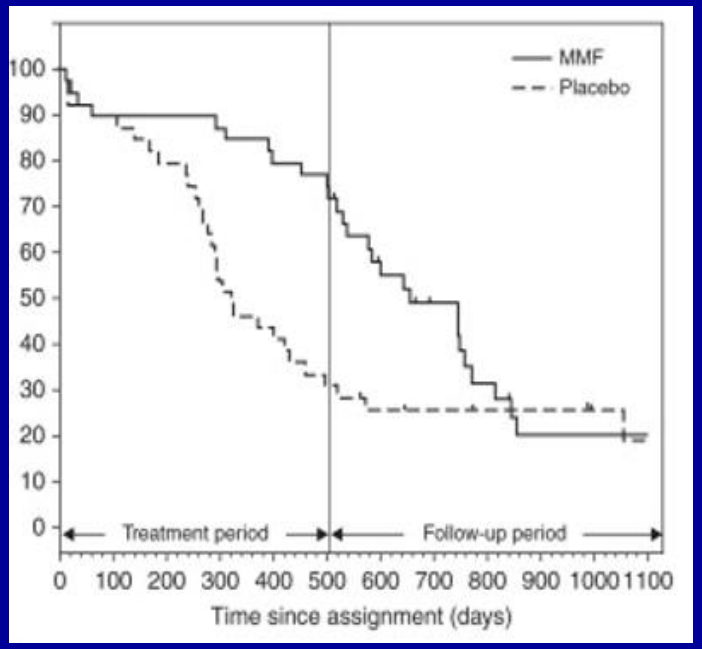
Rituximab
(375 mg/M^2)
days 1, 8, 15, 22

MMF x 17 months
(1200 mg/M^2/day)

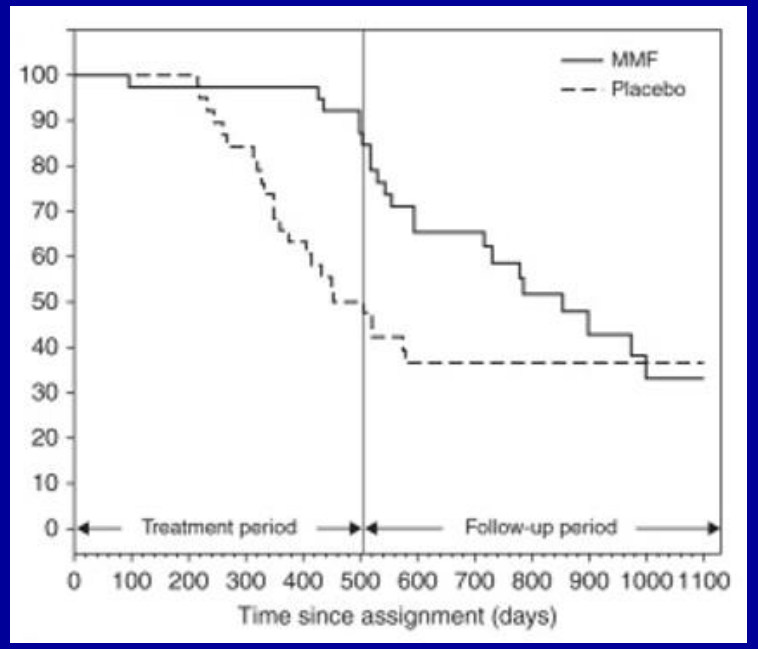
Placebo x 17 months

J Am Soc Nephrol (2022) 33: 401-419

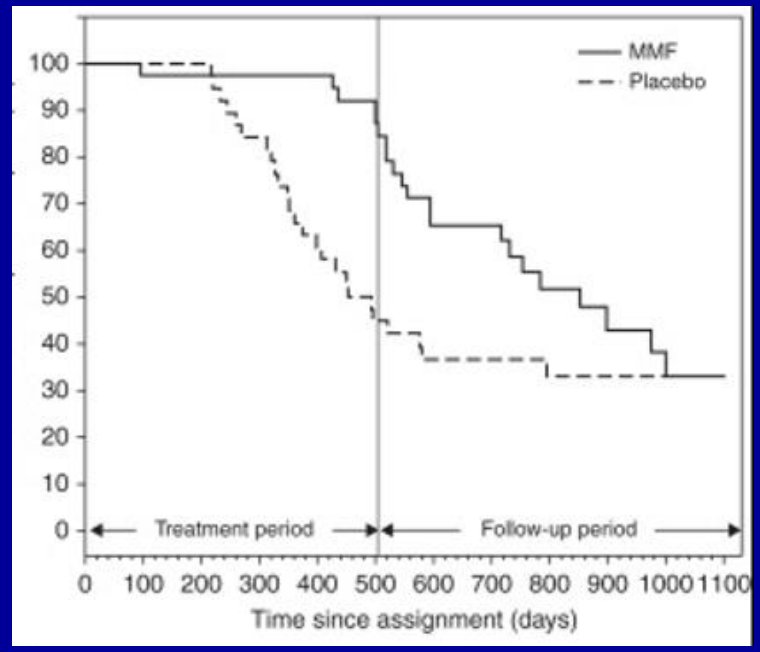
Rituximab followed by MMF



Any Relapses



Frequent Relapses



Steroid Dependency

J Am Soc Nephrol (2022) 33: 401-419

Rituximab followed by MMF

- Children receiving MMF after rituximab showed advantageous findings over children receiving placebo after MMF
  - Relapse free interval was prolonged 80%
    - MMF group with median days to relapse of 784
    - Placebo group with median days to relapse 472
  - Relapse rate reduced by 74%
  - Average daily steroid dose reduced by 57%

J Am Soc Nephrol (2022) 33: 401-419

Long-term Outcome MCNS

- About 90% children with steroid sensitive nephrosis enter a long-term remission by late adolescence or early adulthood
- Two separate single center studies have shown that 30% to 40% of patients will have at least one relapse as an adult, although these patients tend to continue to respond to steroids
- Steroid responsiveness almost always portends good long-term GFR

Am J Kidney Dis 2003; 41:550

J Pediatr 2005; 147:202

FSGS – Clinical Overview

- Found in 40% of children with initial steroid resistance
- Most common glomerular disease in children leading to ESKD
  - Number one ESKD cause in black children in North America
- Failure to respond to steroids, massive proteinuria, and hypertension are all poor prognostic signs
- ESKD within 5 years of onset in 50% of children who do not achieve complete or partial remission

Pediatric Nephrology (2020) 35:1529–1561
https://doi.org/10.1007/s00467-020-04519-1

GUIDELINES

IPNA clinical practice recommendations for the diagnosis and management of children with steroid-resistant nephrotic syndrome

Agnes Trautmann[1] · Marina Vivarelli[2] · Susan Samuel[3] · Debbie Gipson[4] · Aditi Sinha[5] · Franz Schaefer[1] · Ng Kar Hui[6] · Olivia Boyer[7,8] · Moin A Saleem[9] · Luciana Feltran[10] · Janina Müller-Deile[11] · Jan Ulrich Becker[12] · Francisco Cano[13] · Hong Xu[14] · Yam Ngo Lim[15] · William Smoyer[16] · Ifeoma Anochie[17] · Koichi Nakanishi[18] · Elisabeth Hodson[19] · Dieter Haffner[20,21,22] · on behalf of the International Pediatric Nephrology Association

Pediatric FSGS and Standard Therapies

- FSGS is generally resistant to conventional therapy for pediatric nephrotic syndrome
- Only 1/3 of children with FSGS initially respond to steroids; most quickly become resistant
- No clear benefit to oral cytotoxics
  - ISKDC, 1983: Compared qod steroids to qod steroids and cyclophosphamide
  - Remission rate in both groups near 25%

Pediatric FSGS and Calcineurin Inhibitors

- Small case series going back 30 years demonstrate benefit of CNI therapy with pediatric FSGS
  - Reports of up to 70% efficacy of some sort
  - Partial remissions 2 to 3 times more likely than complete remissions – quality of life effect can be profound
  - Relapse rates exceeding 75% reported with removal of CNI, sometimes with loss of efficacy with subsequent re-exposure to the same CNI

KDIGO and IPNA recommend CNI as initial post-steroid therapy with pediatric steroid-resistant nephrotic syndrome

WHEN TO CONSIDER GENETIC TESTING IN PEDIATRIC NEPHROTIC SYNDROME?

- Congenital disease or onset in first year of life
- Family history of nephrotic syndrome
- No response to immunosuppressive therapy
- Biopsy with FSGS, especially in young child
- Nephrotic syndrome with decreased GFR or ESKD
- Concern for some accompanying syndrome

adapted from S Joshi et al. Acta Paediatrica 2013; 102:844–856

Question One

A previously healthy 4-year-old boy presents with periorbital and abdominal swelling. He has normal blood pressure. His serum creatinine is 0.3 mg/dL, his serum albumin is 1.5 g/dL, and his urinalysis has 4+ protein and trace hematuria. Which of the following would be your best next step:

a. Kidney biopsy to define histology
b. Genetic studies for nephrin and WT1
c. Start prednisone at 2 mg/kg/day
d. Start furosemide at 1 mg/kg twice daily

Question One

Answer: *c. Start prednisone at 2 mg/kg/day*

This child has presented in a fashion typical for minimal change disease. He has normal blood pressure and normal kidney function and given that most children with minimal change disease will be steroid sensitive, steroids should be given empirically, without a preceding kidney biopsy.

Both WT1 and nephrin gene mutations are more likely to be found with congenital nephrotic syndrome, and this child is too old to consider that diagnosis.

Loop diuretics by themselves would not be part of initial therapy.

Question Two

You have been asked to evaluate a very swollen 3-year-old girl with nephrotic syndrome diagnosed 2 months ago. She has completed 8 weeks of high dose oral steroids without improvement. A kidney biopsy shows FSGS. The best next management step would be:

a. Pulse intravenous steroids
b. Genetic testing for podocyte mutations
c. Initiation of plasmapheresis
d. Initiation of an oral cytotoxic agent

Question Two

Answer: *b. Genetic testing for podocyte mutations*

There is a higher likelihood of finding a genetic mutation underlying nephrotic syndrome in young children with steroid resistant FSGS. Knowing that there is a mutation may influence clinical consideration of other immunomodulatory therapies and also affect counseling and planning for transplantation

In children, failing to respond to 8 weeks of steroids defines steroid resistance, and intensification of steroid therapy in this setting is not warranted. Although high dose intravenous steroids and cyclophosphamide have been given in some multidrug protocols for therapy resistant FSGS, an oral calcineurin inhibitor is now the preferred immunosuppressant. Plasmapheresis is often used with FSGS recurrence post-transplant but there is limited data as to its efficacy in a child such as described in this scenario.

Case Two

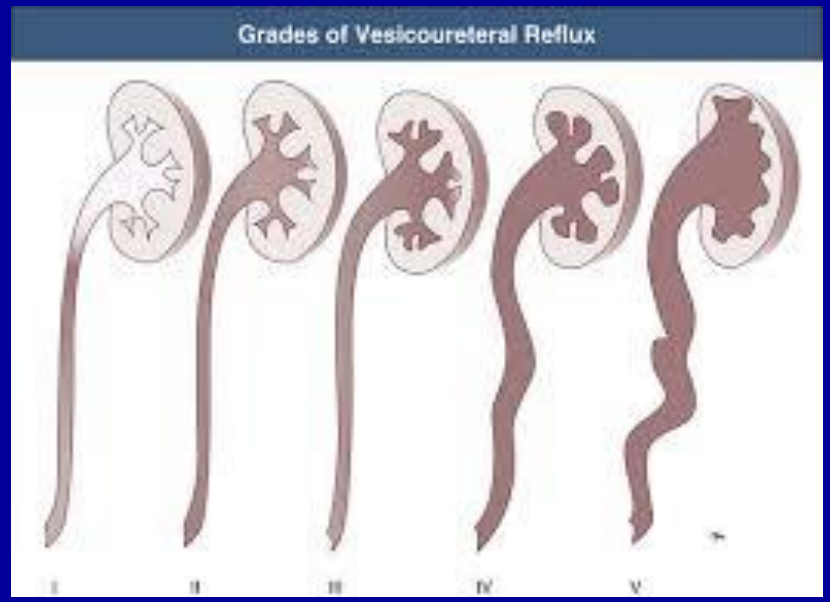
- A 10-year-old boy has recently moved with his family to the area and is being seen for an initial well child visit.
- Past medical history is remarkable for birth at 28 weeks gestation with a week of ventilatory support.
- He had sporadic emergency room visits during his first few years of life for febrile illnesses all diagnosed as ear infections.
- He has had little routine well child medical care over the last five years.

Case Two

- On physical examination, he is in the 25%ile for height and the 50%ile for weight.
- His blood pressure is 130/82 on several measurements by auscultation.
- His physical exam is otherwise non-focal, including good femoral and peripheral pulses.
- He comes back for blood pressure checks twice in the next month, and he has BP readings of 134-140/80 in his upper extremities.

Case Two

- Lab evaluation includes a serum creatinine of 0.6 mg/dl and normal electrolytes.
- His urinalysis is benign.
- A kidney ultrasound demonstrates a normal left kidney and a right kidney 2 cm smaller with focal upper pole scarring.
- VCUG with grade 3 right-sided reflux.



What is Hypertension?

For children < 13 yo:
Repeated casual measurement compared to a statistical BP range from children of same sex, age, and height

- Normal: BP < 90%
- Elevated Blood Pressure: BP ≥ 90% but < 95%
- Stage I Hypertension: up to 12 mm Hg ≥ 95%
- Stage II Hypertension: BP ≥ 95% + 12 mm Hg

What is Hypertension?

For adolescents at least 13 yo:
Hypertension is defined the same way as it is defined with adults

- Normal: BP < 120/<80
- Elevated Blood Pressure: BP 120/<80 to 129/<80
- Stage I Hypertension: BP 130/80 to 139/89
- Stage II Hypertension: BP $\geq$ 140/90

AAP Clinical Practice Guideline:
Hypertension in Children and Adolescents

Flynn et al. Pediatrics. 2017; 140(3):e20171904

- Updated the 2004 Fourth Task Force Report
- Aligned classification more with AHA and ACC
- Streamlined recommendations for initial evaluation and management
- Increased reliance on ABPM

AAP Clinical Practice Guideline:
Hypertension in Children and Adolescents

- Series of 30 Key Action Statements (KAS) and 27 additional recommendations based on expert opinion
- Evidence quality and strength of recommendation graded for each KAS
- Increased focus on chronic conditions in childhood predisposing to hypertension: obesity, prematurity, CKD, and sleep disordered breathing

AAP Clinical Practice Guideline:
Hypertension in Children and Adolescents

- New normative BP tables based on the auscultation of BP in 50,000 children of ***normal weight***
- Standardized for sex, age, and height
- Use of adult cut offs rather than statistical range for adolescents

AAP Clinical Practice Guideline:
Hypertension in Children and Adolescents

Tables are relatively detailed:

50%, >90%, ≥95%, and ≥95% + 12 mm Hg

Actual height in cm and inches provided

Age (y)	BP Percentile	SBP (mm Hg)						
		Height Percentile or Measured Height						
		5%	10%	25%	50%	75%	90%	95%
8	Height (in)	47.8	48.6	50	51.6	53.2	54.6	55.5
	Height (cm)	121.4	123.5	127	131	135.1	138.8	141
	50th	95	96	97	98	99	99	100
	90th	107	108	109	110	111	112	112
	95th	111	112	112	114	115	116	117
	95th + 12 mm Hg	123	124	124	126	127	128	129

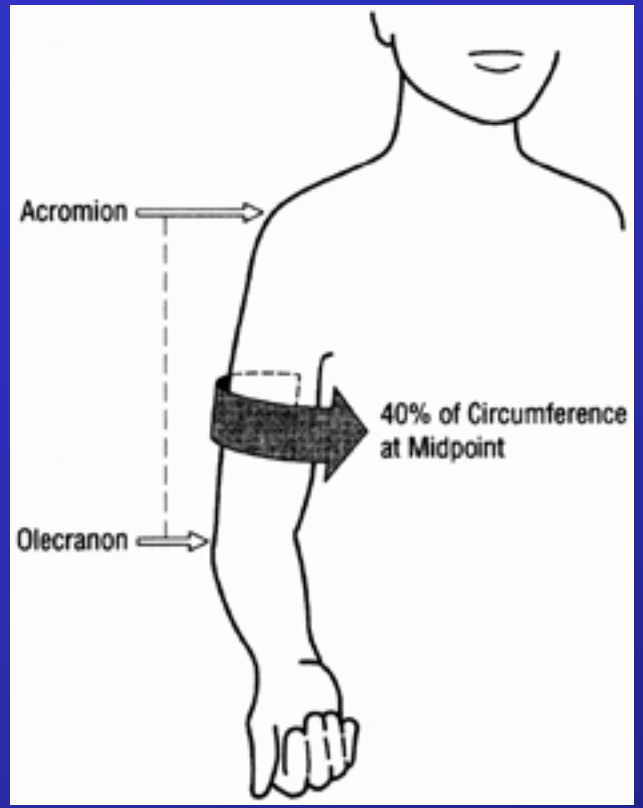
AAP Clinical Practice Guideline:
Hypertension in Children and Adolescents

- Useful simplified screening table based on 90%ile BP for age and sex and 5%ile for height
- Negative predictive value of >99%
- Quick assessment tool to determine if need for repeat BP measurement

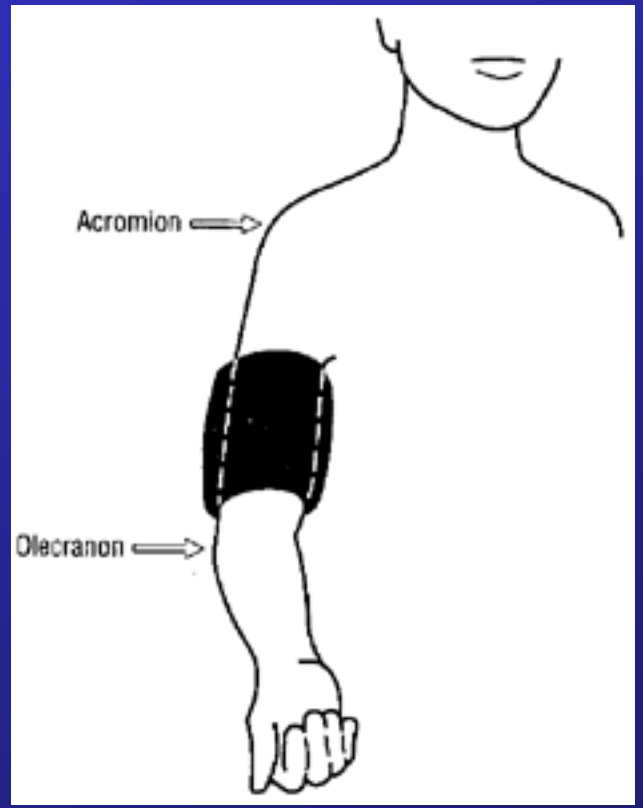
Age, y	BP, mm Hg			
	Boys		Girls	
	Systolic	DBP	Systolic	DBP
1	98	52	98	54
2	100	55	101	58
3	101	58	102	60
4	102	60	103	62
5	103	63	104	64
6	105	66	105	67
7	106	68	106	68
8	107	69	107	69
9	107	70	108	71
10	108	72	109	72
11	110	74	111	74
12	113	75	114	75
≥13	120	80	120	80

Sizing Blood Pressure Cuffs

Sizing Blood Pressure Cuffs



Cuff Width:
> 40% of arm
circumference



Cuff Length:
bladder length > 80%
of arm circumference

Oscillometry vs. Manual BPs

Oscillometry vs. Manual BPs

BPs differ by modality of measurement

- School based BP screen in Tampa
- 7,000 children aged 5 to 17 years
- BPs by both techniques
- Oscillometric readings higher:

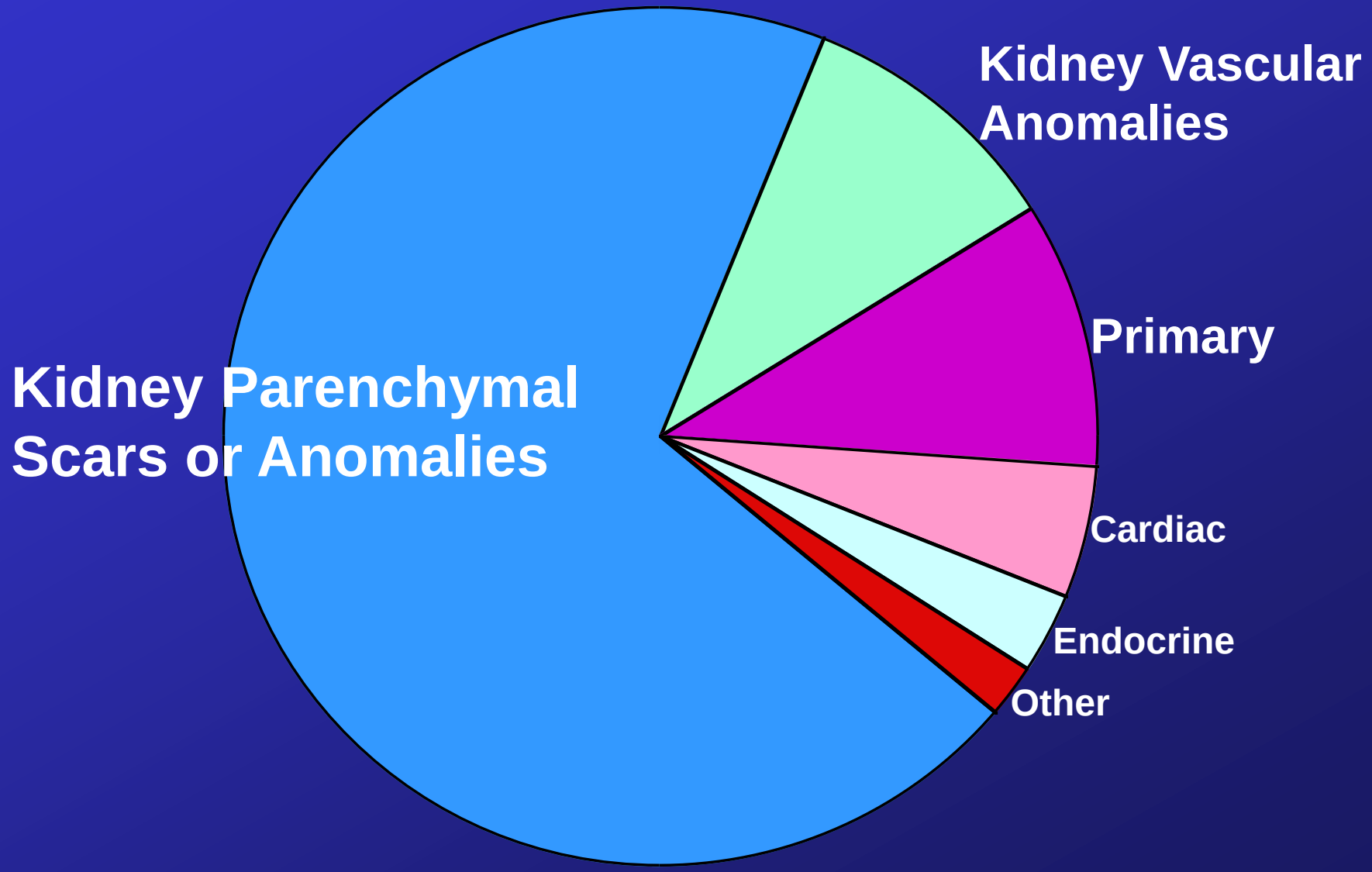
    Systolic readings 10 mm Hg higher

    Diastolic readings 5 mm Hg higher

Park et al. Arch Pediatr Adolesc Med 2001; 155:50-53.

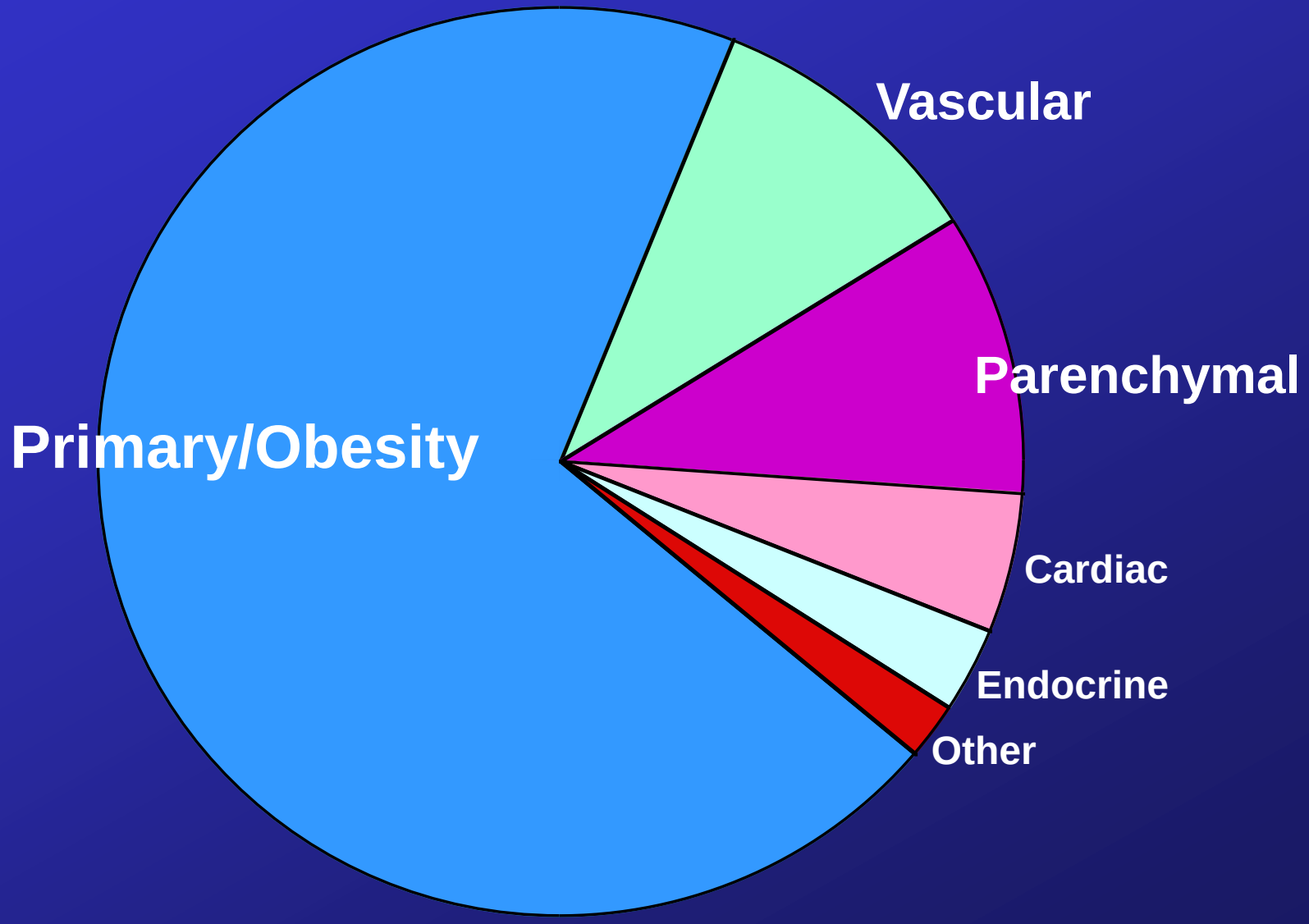
Hypertension by Etiology

Historical Pediatric Perspective

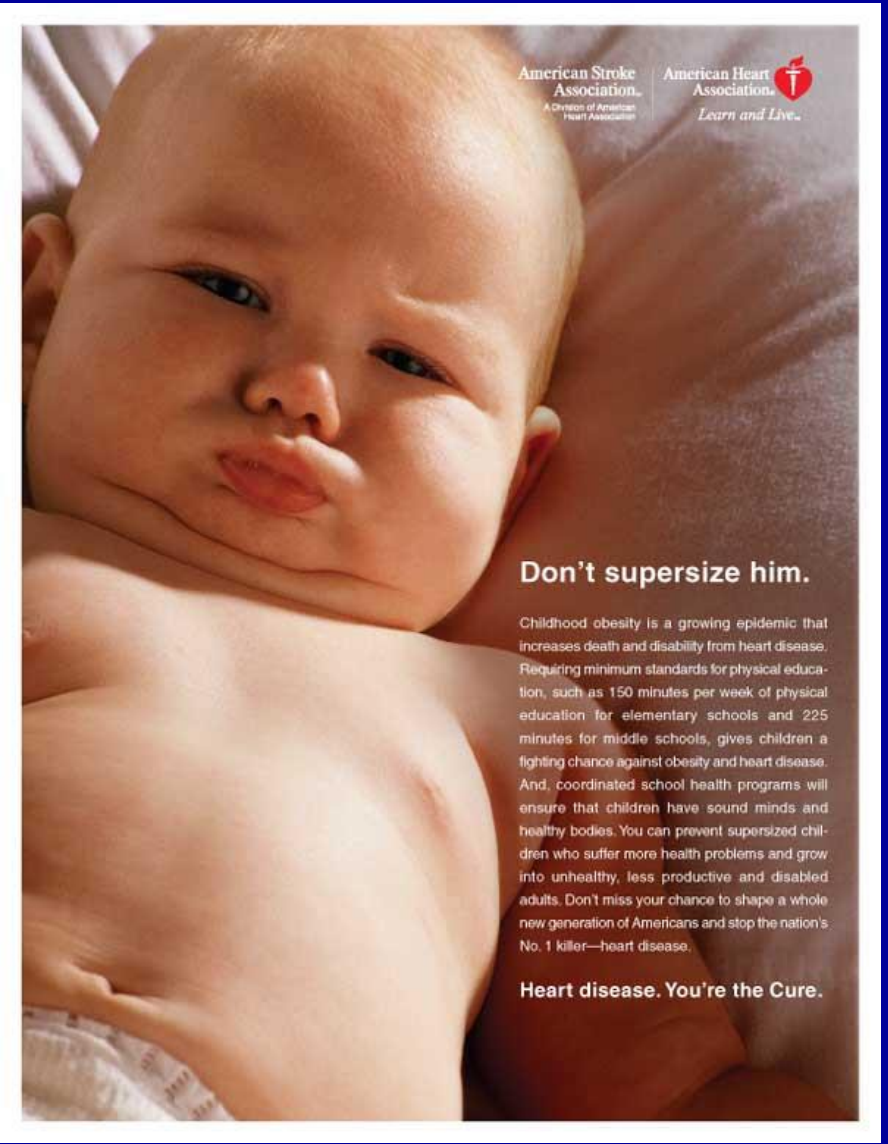


Hypertension by Etiology

Contemporary Perspective



Obesity and Hypertension



Obesity and Hypertension

- Prevalence of obesity has increased three-fold since 1970s and now is > 20%
- Latino, Black, and Native American children have even higher rates
- Obese children are at substantially higher risk for developing hypertension

Bogalusa Heart Study:

9,167 children 5-17yo followed longitudinally

Obese children manifest:

2.4x diastolic HTN

4.5x systolic HTN

Diagnostic Evaluation of HTN

History

Current Illness: kidney hypoperfusion or hypoxia

Birth History: prematurity, ventilation, umbilical lines

Illnesses: UTIs, fevers, changes in appearance of urine

Family History: HTN, MI, kidney disease

Medications: decongestants, OCPs, stimulants

ROS: headaches, palpitations, flushing, sweating

Diagnostic Evaluation of HTN

Physical Examination

Growth Curve

Unifying Syndrome

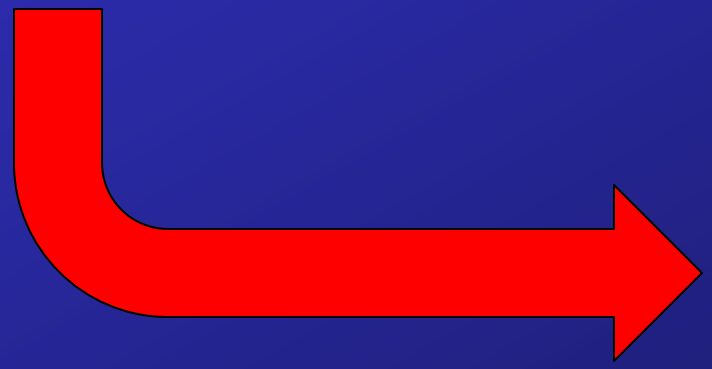
Four Extremity BPs

Focused Exam

Who Needs Immediate Care?

Focused on children with high risk of immediate target organ damage

- BP stage 2 HTN level *and* child symptomatic
- BP > 30 mm Hg above the 95%ile in child
- BP > 180/120 in an adolescent



Emergency Department

Hypertension Evaluation

Baseline Screening Tests – in all

- Urine dip -- micro if macro positive
- Electrolytes -- focus on K and HCO3
- Creatinine
- Lipid profile
- Kidney Ultrasound if < 6 yo or anyone with abnormal urinalysis or creatinine

Hypertension Evaluation

Additional Screening Tests

Obese children

- HbA1c (diabetes screen)
- AST and ALT (fatty liver screen)
- Fasting lipid profile

Select children (based on history and physical)

- CBC, TSH, renin, aldosterone, drug screen, metanephrines, sleep study

Hypertension Evaluation

Ambulatory Blood Pressure Monitoring

Consider if:

- BP has been in the elevated BP category ≥ 1 yr
- Consider if Stage One hypertension has been confirmed over three clinic visits
- Consider in children and adolescents with high-risk conditions
  - Assess hypertension severity and if abnormal circadian pattern present

Condition	Rationale for ambulatory blood pressure monitoring
Clinic hypertension	Confirmation of diagnosis
Secondary hypertension	Identify masked hypertension including nocturnal hypertension, abnormal dipping
Chronic kidney disease	Identify masked hypertension including nocturnal hypertension; assess mean arterial pressure and blood pressure targets to optimize therapy, slow disease progression, and reverse total organ damage
Coarctation of the aorta	Detect recurrent/masked hypertension years after primary repair
Types 1 and 2 diabetes	Identify abnormal circadian variation; optimize therapy to prevent/treat microalbuminuria and vascular changes
Obesity	Identify masked hypertension including nocturnal hypertension (which may signal comorbid obstructive sleep apnea) and abnormal dipping; optimize therapy to reverse total organ damage
Obstructive sleep apnea	Characterize hypertension severity, identify nocturnal hypertension or abnormal dipping
Genetic syndromes	Identify abnormal blood pressure patterns suggesting secondary cause of hypertension, such as renal artery stenosis and aortic coarctation
Neurofibromatosis type 1	
Turner syndrome	
Williams syndrome	
Antihypertensive drug treatment	Assess adequacy of blood pressure control and apparent treatment resistance, evaluate hypotensive symptoms
Research	Reduce sample size requirements for clinical trials; identify specific ambulatory blood pressure monitoring patterns associated with elevated cardiovascular risk

Pediatric Primary Hypertension: An Underrecognized Condition: A Scientific Statement From the American Heart Association. Hypertension. 2023 Jun;80(6):e101-e111.

Hypertension Evaluation

Follow-Up Tests

- Further evaluation guided by history, physical findings, and baseline laboratories
- Differentiate between:
  1) Suspected primary (essential) hypertension
  2) Suspected kidney parenchymal disease
  3) Unclear etiology
- Use of specialized kidney imaging, echo-cardiography and retinal exams to assess for end organ damage

Pharmacologic Therapy

Non-Urgent Hypertension

Several basic approaches to drug therapy:

- Choose an agent based on pathophysiology
- Begin with less than a full dose of an agent
- Remember pediatric dosing
- Titrate up to maximal dose as needed
- Aim for BP < 90% or < 130/80 – whichever is lower
- Add agents sequentially

CCBs and ACE/ARBs often best tolerated

Other Management Issues

- Echocardiography is recommended if there is consideration of pharmacologic treatment
  - *Repeat echo q 6-12 months to monitor for improvement or progression if abnormality found*
  - *Also consider repeating echo if stage 2 hypertension persists and no LVH initially seen on echo*
- Use non-pharmacologic adjuncts including diet, physical activity, optimization of weight, stress reduction

Question Three

You are seeing a 10-year-old girl with a benign past medical profile. Your clinical assistant gets several blood pressure readings of 130/80 in the girl's upper extremities using an automated blood pressure machine. Which of the following would be the best next step in your evaluation:

a. Elicit perinatal and family histories
b. Get 4 extremity blood pressures
c. Confirm the BP readings by auscultation
d. Order a kidney ultrasound with doppler

Question Three

Answer: *d. Confirm the BP by auscultation*

Blood pressure definitions in children are based on BP results by auscultation. Oscillometry is good for screening since most children will have normal BPs on both oscilllometry and auscultation. Abnormal blood pressures by oscillometry should be confirmed by auscultation, however, since automated blood pressure devices may overestimate both systolic and diastolic blood pressures in children. It would be most important to confirm that this child does indeed have high blood pressure readings to guide your next steps.

Aspects of the perinatal and family history would be important to obtain but would be most germane if hypertension is confirmed.

Similarly, four extremity BPs and ultrasound with doppler would both be part of this girl's initial evaluation for hypertension once high blood pressure was actually confirmed.

Take Home Messages

NEPHROTIC SYNDROME

- Most children and younger adolescents with nephrotic syndrome can be empirically treated with steroids without a kidney biopsy
- Response to steroids is usually rapid (within 4 weeks) but frequent relapses and steroid dependency is extremely common
- MMF, rituximab, and tacrolimus are now being used most often as second line agents
- Although most children enter periods of lengthy remission, occasional relapses as an adult can be expected
- Steroid resistant nephrotic syndrome is generally secondary to FSGS, and although CNIs can often lead to a partial remission, eventual progression to ESKD is frequent

Take Home Messages

HYPERTENSION

- Hypertension in pre-adolescent children is defined statistically and is based on BPs by auscultation in an upper extremity
- Sizing of blood pressure cuffs can be problematic, especially if cuffs are chosen based on age rather than size of the upper extremity
- Although kidney parenchymal scarring once mediated most pediatric hypertension, the epidemic of obesity in children has changed the epidemiology
- In children with significant hypertension, a basic evaluation to look for secondary causes of hypertension is still advised
- Most children tolerate calcium channel blockers and angiotensin blockade well and without reported side effects

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