Pursuing Research in Pediatric Nephrology
Challenges & Opportunities for Young Researchers

Division of Nephrology, Department of Pediatrics

All India Institute of Medical Sciences, New Delhi

Why pursue research, at all..!?

For the love of it?

To satisfy intellectual curiosity

Passion for research

To stand out

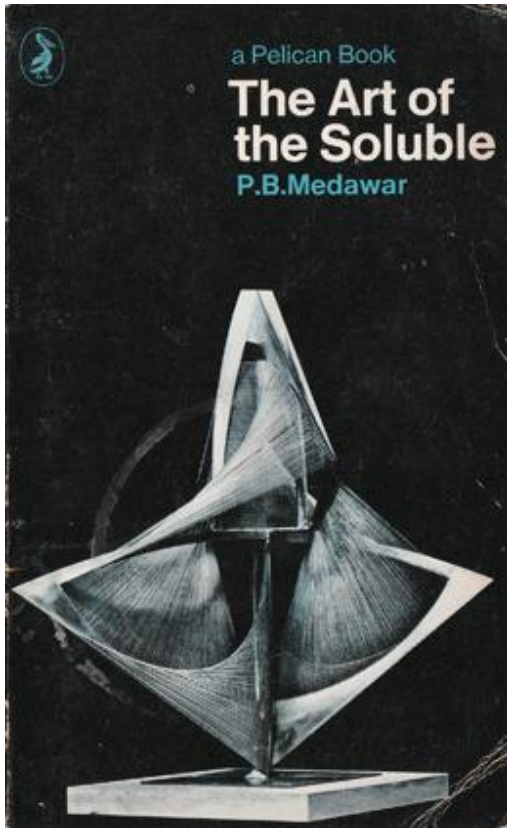
Ambition to do more

Acquire more skills

Improve one's CV

As an obligation…

MD and DM programs



1967: *Essays on*

Creativity and originality in science

The logical connections between creative and critical thought

The ethology of scientists & the anatomy of scientific behavior

Does research make better doctors?

Helps develop skills

Learn laboratory, statistical or clinical skills

Learn to work methodically

Rationale → Question → Objectives → Methods → Outcomes → Impact

Nurture intellectual curiosity

Ask questions, not accept as 'matter of fact'

Foster critical thinking

Synthesize relevant objectives from questions of the most importance ('so what?')

Life skills

Learn to deliver on commitment

Establishes expertise

Teach a man to fish…

Helps stand out

Publication; letters of recommendation

Make informed career choices

Academics vs. practice?

Improves patient care

During study participation
Methods that improve working protocols
Results that make an impact

Opens mind to accepting advances

Reduces research-to-practice gap!

What topic requires study?

- Acute kidney injury
- Chronic kidney disease
- Transplantation
- Hypertension
- Glomerular diseases
- Critical care nephrology
- Kidney replacement therapy including dialysis, continuous renal replacement therapies
- Electrolyte disorders

- Renal genetics
- Tubular diseases
- Cystic kidney disease
- Nephrolithiasis
- Congenital anomalies of kidney and urinary tract
- Urinary tract infections
- Renal imaging techniques
- Kidney development
- Renal pathology
- Immunology; complement biology

What are the options for research?

Descriptive Research

Aim: To understand the disease or condition

Examples: Studies of disease burden, risk factors, determinants and pathogenesis mechanisms

Development research

Aim: Develop interventions for screening, diagnosis, prevention, treatment of diseases or conditions;

To make existing interventions simpler, safer, more efficacious, or more affordable

Examples: Development of point-of-care tests, molecular diagnostic tests, animal models for diseases appropriate dosage and formulations, artificial intelligence & machine learning predictive tools/ models, phase 2/3 (or equivalent phase) clinical trials

Discovery research

Aim: Find novel mechanisms of disease (basic research), methods of diagnosis, or interventions in experimental or human studies.

Examples: Pre-clinical and phase-I studies on new pharmaceuticals or traditional medicines

Genomic methods, algorithms or tools for personalized medicine

Delivery research or implementation research

Aim: At learning how to overcome barriers in delivering effective interventions to the people who need them
Examples: Health system-based interventions to increase access, and to successfully implement national health program or schemes, reducing inequity and improve quality of health care

Barriers to Research..

Lack of…..

Time

Funding: Personnel; resources

Infrastructure: Techniques; set-up

Skillset: Lab; clinical; statistical

Mentorship

Personal interest in research

Survey of physicians, n=603

Question Category	*n*	Percentage
1. Current involvement		
Yes, presented research	152	71.03
No, have not presented research	62	28.97
Yes, published research	65	30.95
No, have not published research	145	69.05
Yes, given time to conduct	72	34.95
No, not given time to conduct	134	65.05
Yes, given compensa		
No, not given compe		
2. Interest		
Yes, interested in pre		
No, not interested in		
Yes, interested in pub		
No, not interested in		
3. Primary barriers (top		
Lack of time		
Lack of research men		
Lack of opportunity		
4. Would conduct if no		
Yes		
No		
N/A (I already condu		
5. Importance		
Very important	120	19.58
Important	223	36.38
Somewhat important	210	34.26
Not at all important	60	9.79

Lack of

Time	47.58%
Research mentorship	12.58%
Opportunity	11.94%
Interest	6.13%
Research community	5.32%
Knowledge	3.71%
Appropriate protections (e.g., IRB)	3.39%
Research ideas	1.29%

Fear of making a mistake 1.29%

Behavior Analysis in Practice 2020; 13: 894-904

Survey of medical students, China (n=200)

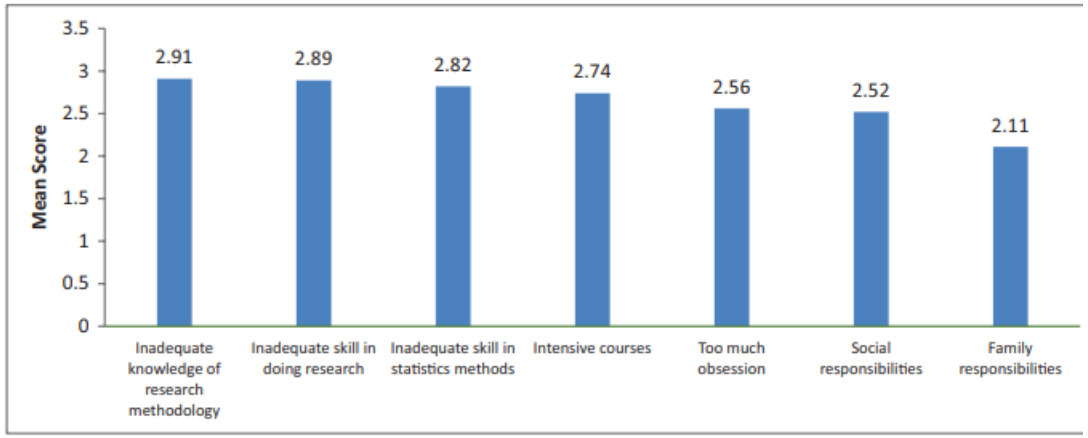


Figure 1: Mean score of personal barriers to research activities

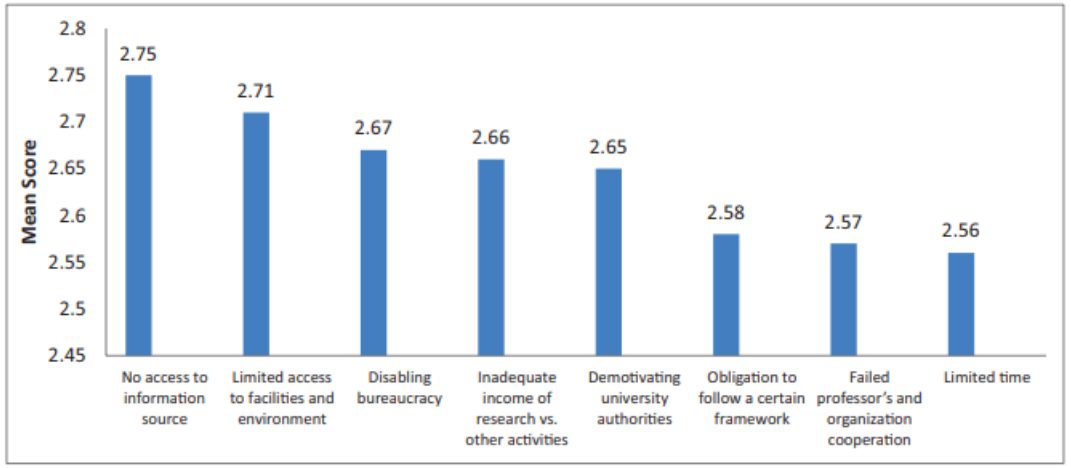


Figure 2: Mean score of organizational barriers to research activities

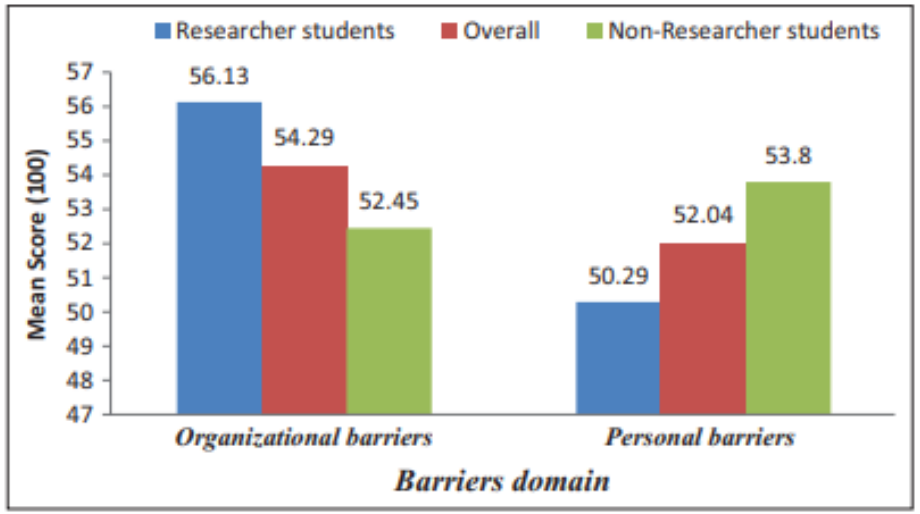


Figure 3: Researcher and non-researcher students' mean scores of barriers to research activities

Most prevalent personal barriers

Inadequate knowledge of research methodology

Inadequate skill in research conduction

Most prevalent organizational barriers

Limited access to information sources

Researcher students: More the organizational barriers

Non-researcher students: More of the personal barriers

Avicenna J Med 2019;9:8-14

Recommendations to Beat Barriers to Research..

Barriers	Recommendations and Resources
Lack of protections (access to an IRB/RRC)	• Start an RRC (LeBlanc et al., 2018). • Explore work settings with an existing research infrastructure.
Lack of time	• Develop a schedule and stick to it. • Remove distractions during writing and thinking time. • Create a task analysis. • Identify small, accomplishable daily goals on each project (Silvia, 2017).
Lack of research ideas and lack of knowledge	• Use clinical practice as an opportunity to identify applied research questions. • Expand research opportunities (e.g., literature reviews, practice guidelines). • Identify problems in your clinical activities and ask questions to solve them.
Lack of mentorship and lack of opportunity	• Find an internal mentor. • Reach out to external mentors in the field with similar research interests. • Contact professionals in academia to identify opportunities for collaboration and mentorship.
Lack of research community	• Create a research community internally (e.g., volunteer research lab, reading group, journal club).
Fear of making mistakes	• View applied research flexibly (i.e., uncontrolled conditions, participant dropout). • Be patient (research in applied settings will take time).

Behavior Analysis in Practice 2020; 13: 894-904

The essential ingredient.. Is not the resources

Attributes of a good researcher

Interest	Drive to excel
Motivation	Knowledge
Inquisitiveness	Recognition
Commitment	Scholarly approach
Sacrifice	Integrity

Asking the right question

Addressing them the right way..

Question
Hypothesis
Methods

J Invest Surg. 2012 Aug;25(4):201-2

Learning from patients: At many levels..

Etiology of disease

Mechanisms of disease

Natural history, determinants of disease severity

Research takes many forms:
Study what you can…

Humble questions, answered carefully, can inform, impact practice..

Case reports: Instructive small steps…

1. Unique Cases: Describe unique or rare cases that cannot be explained by known diseases or syndromes

2. Variations and Unexpected Events: Highlight important variations of diseases or conditions and unexpected events that may provide new or useful information·

3. Complex Cases: Detail instances where a patient has two or more unexpected diseases or disorders

4. **Problem-Solving Skills**: Present real-world scenarios that require critical thinking and analysis.

5. Application of Knowledge: Allow students and professionals to apply theoretical knowledge to practical situations

6. **Learning from Real-Life Examples**: Provide concrete, contextual, in-depth knowledge about specific subjects, making learning more relatable and impactful

Case Reports > Pediatr Nephrol. 2010 Oct;25(10):2171-4. doi: 10.1007/s00467-010-1518-x. Epub 2010 Apr 24.

Frasier syndrome: early gonadoblastoma and cyclosporine responsiveness

Aditi Sinha [1], Sonika Sharma, Ashima Gulati, Alok Sharma, Sandeep Agarwala, Pankaj Hari, Arvind Bagga

Review > Pediatr Nephrol. 2021 Jun;36(6):1353-1364. doi: 10.1007/s00467-020-04695-0. Epub 2020 Jul 10.

Calcineurin inhibitors in nephrotic syndrome secondary to podocyte gene mutations: a systematic review

Georgia Malakasioti [1], Daniela Iancu [2], Kjell Tullus [3]

Results: Data of 178 genetic SRNS cases from 22 studies were analyzed; 35% responded (fully or partially) to CNI with minimal change being the commonest biopsy pattern among responders. Full responders had superior kidney survival compared with partial and non-responders (log-rank test $\chi^2 = 10.7$; $P < 0.01$). WT1 variant carriers were most likely to respond to CNI compared with any other mutation [OR 4.7 (2.0-11.3); $P < 0.01$].

No experience required..

MBBS student led research!

RESEARCH PAPER

Etiology and Outcome of Crescentic Glomerulonephritis

ADITI SINHA, KRITI PURI, PANKAJ HARI, *AMIT KUMAR DINDA AND ARVIND BAGGA
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Correspondence to: Dr Arvind Bagga, Professor, Division of Nephrology, Department of Pediatrics, 3053, Teaching Block, All India Institute of Medical Sciences, New Delhi. arvindbagga@hotmail.com
Received: June 07, 2012; Initial review: June 26, 2012; Accepted: August 02, 2012.

RESEARCH PAPER

Disease Course in Steroid Sensitive Nephrotic Syndrome

ADITI SINHA, PANKAJ HARI, PIYUSH KUMAR SHARMA, ASHIMA GULATI, MANI KALAIVANI*, MUKTA MANTAN, AMIT KUMAR DINDA†, RAJENDRA N SRIVASTAVA AND ARVIND BAGGA
*From Departments of Pediatrics, *Biostatistics and †Pathology, All India Institute of Medical Sciences, New Delhi, India. Correspondence and offprint requests to: Prof. Arvind Bagga, MD, Department of Pediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India. arvindbagga@hotmail.com*
Received: December 7, 2011; Initial review: December 23, 2011; Accepted: February 10, 2012.

Retrospective cohort study

Sequential rituximab therapy sustains remission of nephrotic syndrome but carries high risk of adverse effects

Background

Rituximab induces remission of nephrotic syndrome (NS) lasts 6-18 months and repeat therapy is required
Significant adverse events have been reported following multiple rituximab doses

Methods

Nephrotic syndrome (NS)
Difficult-to-treat steroid dependence (n=127)
CNI-dependent/refractory steroid resistance (n=123)

Therapy
≥2 sequential courses of IV rituximab, given annually *or* at B-cell repopulation

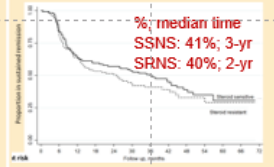
Screened for adverse events (AE)
Human antichimeric antibodies (HACA)
Response to two vaccines

Results

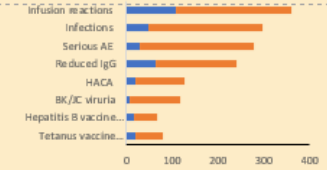
250 patients (72% boys); median age 10 years

Efficacy
Relapses fewer by 2.0 (95% CI 1.8-2.2) per person-yr
Prednisone dose reduced by 59%; oral medications withdrawn in 62%

Sustained remission



Adverse events 0.20 (0.17-0.23)/person-yr



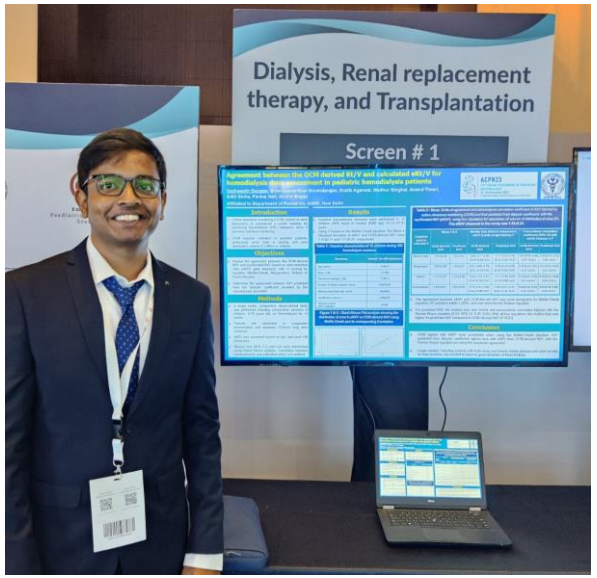
Age <10-yr: Risk of relapse, therapy failure, hypogammaglobulinemia

Conclusion

Sequential rituximab therapy enables sustained remission in difficult-to-treat steroid- &/or CNI-dependent NS
Therapy carries modest risk of infusion reactions, infections, development of HACA & low levels of IgG
Patients <10-yr-old are at higher risk of hypogammaglobulinemia and treatment failure

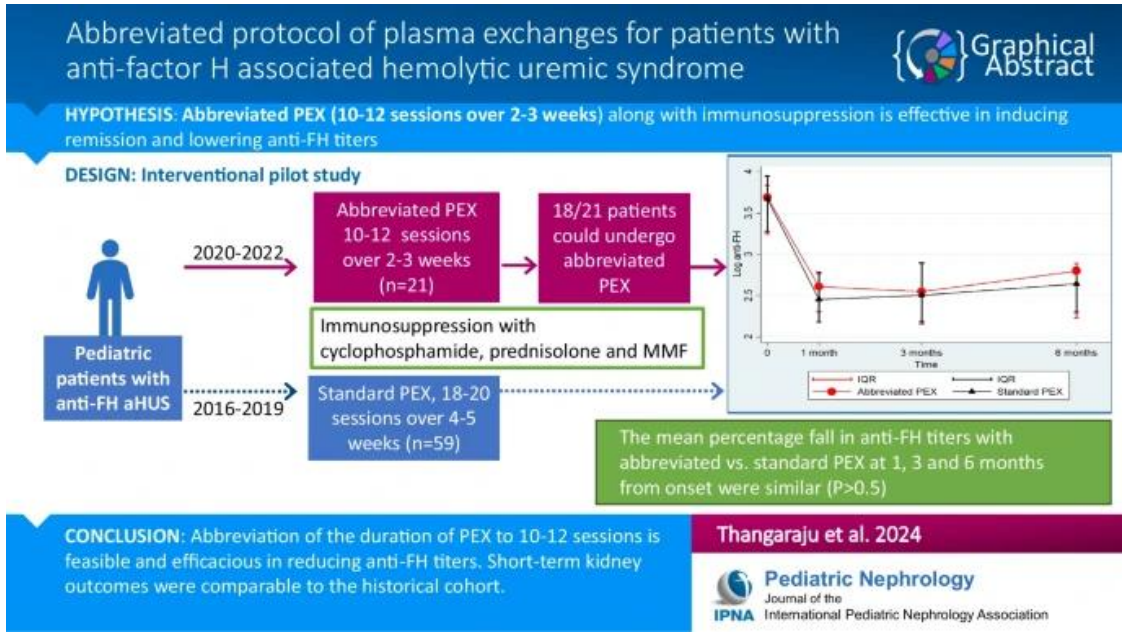
ERA nephrology dialysis transplantation

Sinha, A., et al. NDT (2022)
@NDTSocial



Single limb prospective studies: Particularly relevant to rare conditions or events

Lower level of evidence because of lack of comparator
Useful in situations of rare events
Can couple to detailed or expensive studies infeasible on large scale



› Indian J Pediatr. 2023 Apr;90(4):355-361. doi: 10.1007/s12098-022-04214-z. Epub 2022 Jul 4.

Feasibility and Efficacy of Sustained Low-Efficiency Dialysis in Critically Ill Children with Severe Acute Kidney Injury

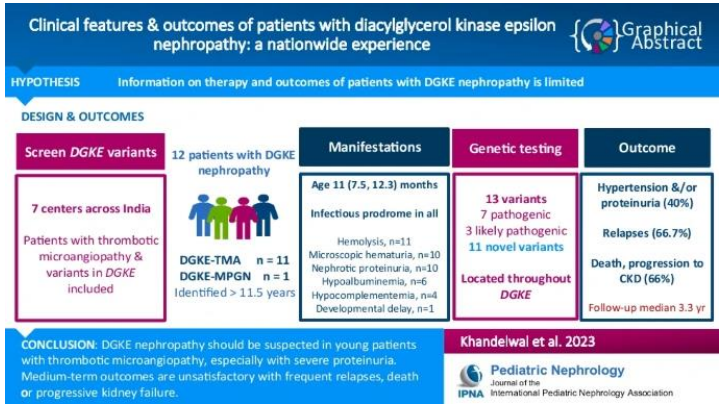
Menka Yadav [1], Anand N Tiwari [1], Rakesh Lodha [2], Jhuma Sankar [2], Priyanka Khandelwal [1], Pankaj Hari [1], Aditi Sinha [3], Arvind Bagga [1]

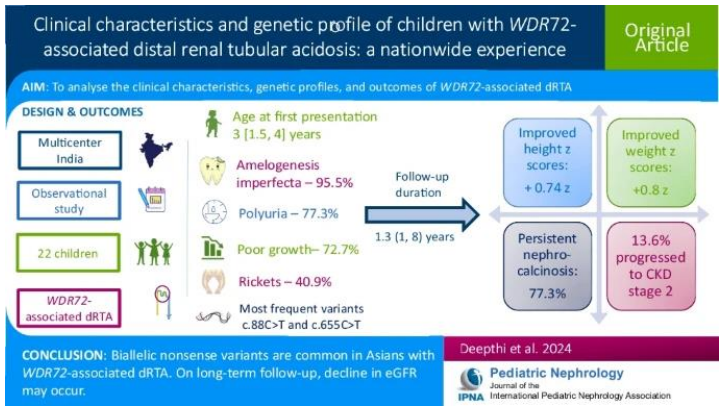
Collaborative studies: A positive outcome of networking

Especially useful in studying rare diseases

Cross-sectional surveys: Understand prevalence of problems, etiology of disease

Registries: Inform on natural history, impact of therapies, outcomes

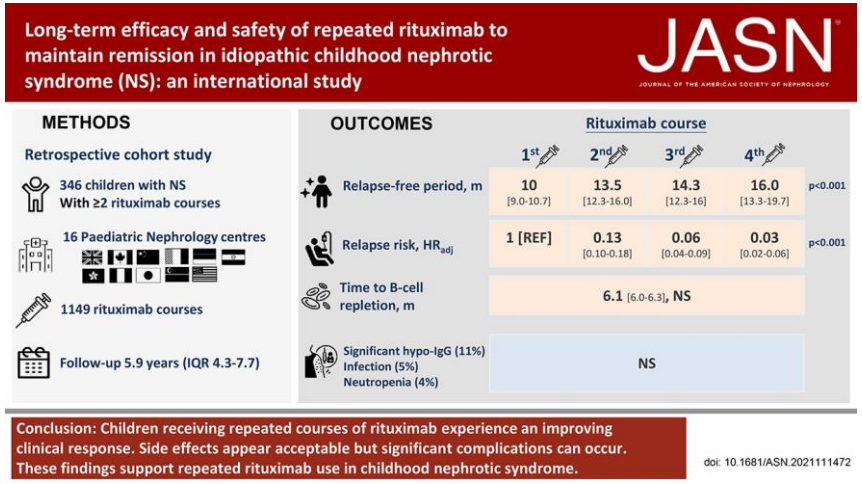




› Indian J Nephrol. 2012 Mar;22(2):121-4. doi: 10.4103/0971-4065.97130.

Modality of choice for renal replacement therapy for children with acute kidney injury: Results of a survey

A Vasudevan [1], A Iyengar, K Phadke



Exploring the Clinical and Genetic Spectrum of Steroid Resistant Nephrotic Syndrome: The PodoNet Registry

Agnes Trautmann[1], Beata S. Lipska-Ziętkiewicz[2] and Franz Schaefer[1] on behalf of the PodoNet Consortium*

Multicenter study on the genetics of glomerular diseases among southeast and south Asians: Deciphering Diversities - Renal Asian Genetics Network (DRAGoN)

Liangjian Lu, Yok-Chin Yap, Duc Quang Nguyen, Yiong-Huak Chan, Jun-Li Ng, Yao-Chun Zhang, Chang-Yien Chan, Mya Than, Isaac Desheng Liu, Sadaf Asim, Khemchand Moorani ... See all authors

› Front Immunol. 2019 Jun 7:10:1282. doi: 10.3389/fimmu.2019.01282. eCollection 2019.

Clinical and Immunological Profile of Anti-factor H Antibody Associated Atypical Hemolytic Uremic Syndrome: A Nationwide Database

Mamta Puraswani [1], Priyanka Khandelwal [1], Himanshi Saini [1], Savita Saini [1], Bahadur Singh Gurjar [2], Aditi Sinha [1], Rajashri Pramod Shende [3], Tushar Kanti Maiti [4], Abhishek Kumar Singh [4], Uma Kanga [5], Uma Ali [6], Indira Agarwal [7], Kanav Anand [8], Narayan Prasad [9], Padmaraj Rajendran [10], Rajiv Sinha [11], Anil Vasudevan [12], Aniti Saxena [13], Sanjay Agarwal [14], Pankaj Hari [1], Arvind Sahu [3], Satyajit Rath [3] [15], Arvind Bagga [1]

Collaborative randomized studies

Clinical Trial > Am J Kidney Dis. 2023 Feb;81(2):145-155.e1. doi: 10.1053/j.ajkd.2022.05.012. Epub 2022 Jul 14.

Lumasiran for Advanced Primary Hyperoxaluria Type 1: Phase 3 ILLUMINATE-C Trial

Mini Michael [1], Jaap W Groothoff [2], Hadas Shasha-Lavsky [3], John C Lieske [4], Yaacov Frishberg [5], Eva Simkova [6], Anne-Laure Sellier-Leclerc [7], Arnaud Devresse [8], Fitsum Guebre-Egziabher [9], Sevcan A Bakkaloglu [10], Chebl Mourani [11], Rola Saqan [12], Richard Singer [13], Richard Willey [14], Bahru Habtemariam [14], John M Gansner [14], Ishir Bhan [14], Tracy McGregor [14], Daniella Magen [15]

Randomized Controlled Trial > Kidney Int. 2015 Jan;87(1):217-24. doi: 10.1038/ki.2014.240. Epub 2014 Jul 16.

Extending initial prednisolone treatment in a randomized control trial from 3 to 6 months did not significantly influence the course of illness in children with steroid-sensitive nephrotic syndrome

Aditi Sinha [1], Abhijeet Saha [2], Manish Kumar [3], Sonia Sharma [1], Kamran Afzal [4], Amarjeet Mehta [5], Mani Kalaivani [6], Pankaj Hari [1], Arvind Bagga [1]

Clinical Trial > BMC Nephrol. 2018 Aug 10;19(1):199. doi: 10.1186/s12882-018-0998-y.

Effect of haemodiafiltration vs conventional haemodialysis on growth and cardiovascular outcomes in children - the HDF, heart and height (3H) study

Rukshana Shroff [1], Aysun Bayazit [2], Constantinos J Stefanidis [3], Varvara Askiti [3], Karolis Azukaitis [4], Nur Canpolat [5], Ayse Agbas [5], Ali Anarat [2], Bilal Aoun [6], Sevcan Bakkaloglu [7], Devina Bhowruth [8], Dagmara Borzych-Dużałka [9], Ipek Kaplan Bulut [10], Rainer Büscher [11], Claire Dempster [8], Ali Duzova [12], Sandra Habbig [13], Wesley Hayes [8], Shivram Hegde [14], Saoussen Krid [15], Christoph Licht [16], Mieczyslaw Litwin [17], Mark Mayes [8], Sevgi Mir [10], Rose Nemec [16], Lukasz Obrycki [17], Fabio Paglialonga [18], Stefano Picca [19], Bruno Ranchin [20], Charlotte Samaille [21], Mohan Shenoy [22], Manish Sinha [23], Colette Smith [24], Brankica Spasojevic [25], Enrico Vidal [26], Karel Vondrák [27], Alev Yilmaz [28], Ariane Zaloszyc [29], Michel Fischbach [29], Franz Schaefer [30], Claus Peter Schmitt [30]

Collaborative research: A word of caution

Multicenter *versus* single center studies

Larger sample size
Higher reproducibility
Larger generalizability
Higher scrutiny: Improved study quality
Lower risk of bias

Expensive; slower; often infeasible
Less efficient resource utilization
Heterogenous skillsets; commitment..

More consistent data collection
Higher rates of protocol adherence
Investigator commitment

Inflated treatment effects
Confirmation bias

Data is as good as the investigators..

Remember risks of selective reporting; falsification

Important to ensure data accuracy & completeness

Data quality checks; review of case records

Choose collaborators carefully

Credibility at stake is of the corresponding author!

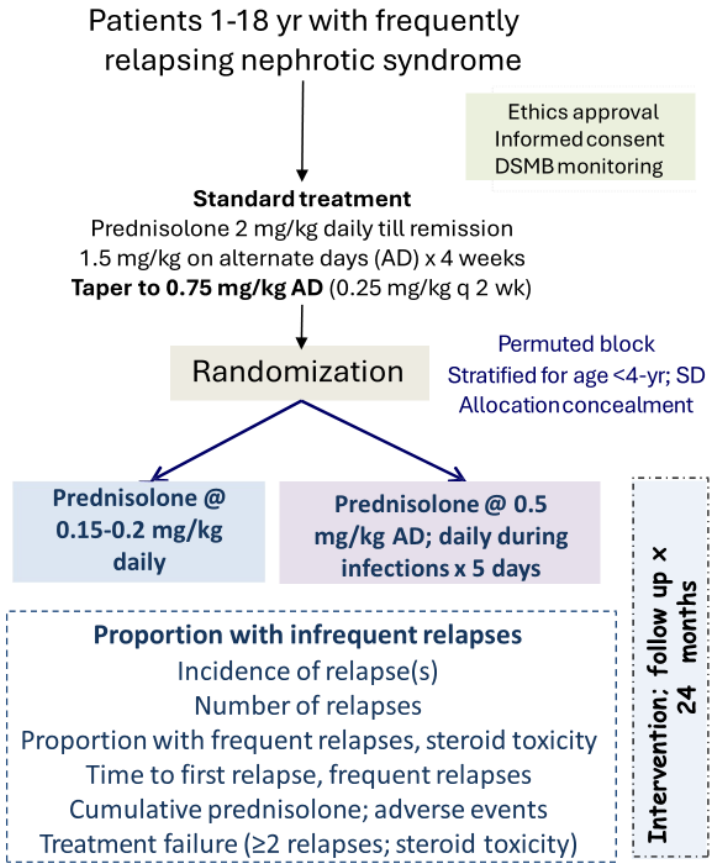
Crit Care 2023; 27: 465; *BMJ* 2012;344:e813

Randomized studies: Not 'All in a day's work'

Test of

- Skills
- Commitment
- Integrity
- Ethical practices
- Statistical skills

Open label RCT to compare efficacy of low(*er*) dose daily versus AD prednisolone, made daily during infections



CTRI/2019/1/518

IEC approval	June 2018
CTRI registration	December 2018
Enrolment begun	February 2019
Interrupted (pandemic)	**March 2020-April 2022**
Expected enrolment completion	**September 2025**
Study completion expected	**September 2027**

Baseline Characteristics, n=121 (Sample size 160)

Characteristics	AD prednisolone (n=59)	Low dose daily prednisolone (n=62)
Boys (%)	40 (67.8)	45 (72.5)
Age at onset, months	36 (28,3, 70.8)	34.8 (26.8, 63.3)
Age at randomization, months	60.8 (51.9, 93.1)	63 (50.2, 82.3)
Age at randomization <4-yr	16 (27.1)	17 (27.4)
Relapses in year prior	3 (3, 4)	3 (3, 4)
Steroid dependence (%)	6 (10.2)	10 (16.1)
Weight, kg	21.5 (15.5, 26.9)	20.5 (15.5, 21.3)
Height, cm	117 (106.5, 125)	112 (102, 116,5)
Creatinine, mg/dl	0.35 (0.3, 0.4)	0.3 (0.3, 0.4)

Randomized studies: Not infeasible for Residents

Randomized Controlled Trial > Am J Kidney Dis. 2009 May;53(5):760-9.

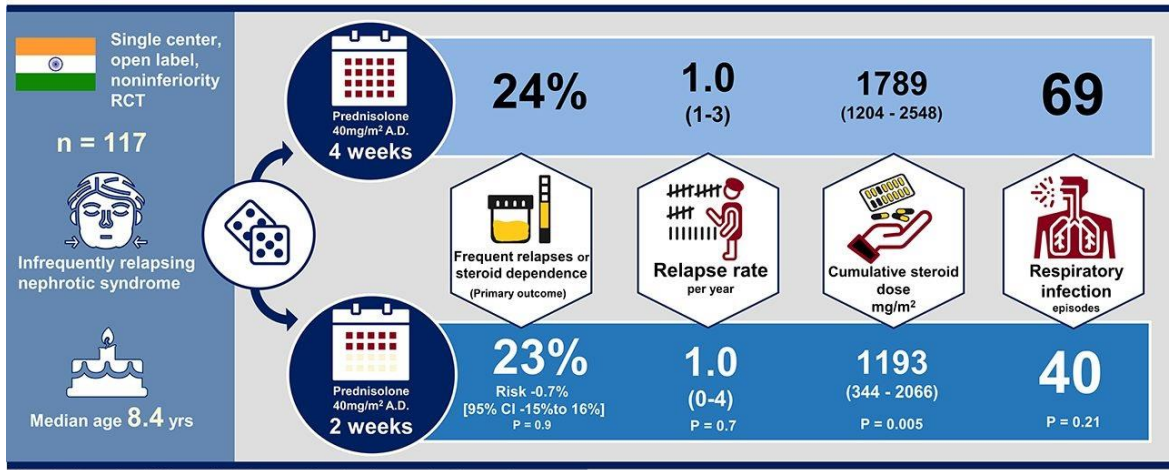
doi: 10.1053/j.ajkd.2008.11.033. Epub 2009 Mar 5.

Efficacy and safety of tacrolimus versus cyclosporine in children with steroid-resistant nephrotic syndrome: a randomized controlled trial

Swati Choudhry [1], Arvind Bagga, Pankaj Hari, Sonika Sharma, Mani Kalaivani, Amit Dinda

Is short-duration prednisolone effective in treatment of nephrotic syndrome relapse in children?

CJASN
Clinical Journal of the American Society of Nephrology



Conclusions: In children with infrequently relapsing nephrotic syndrome, a short steroid treatment for relapse led to a similar proportion of patients developing frequent relapses or steroid dependence; however, its non-inferiority could not be established.

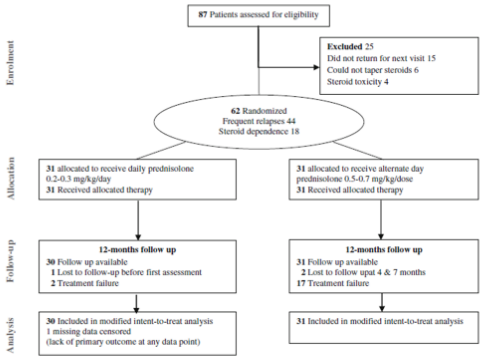
Deepika Kainth, Pankaj Hari, Aditi Sinha, et al. ***Short-Duration Prednisolone in Children with Nephrotic Syndrome Relapse***. CJASN doi: 10.2215/CJN.06140420. **Visual Abstract by Divya Bajpai, MD, PhD**

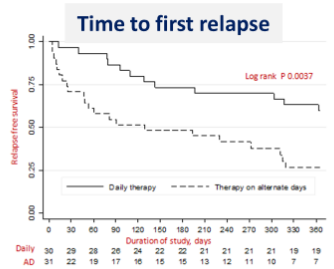
Efficacy of low-dose daily versus alternate-day prednisolone in frequently relapsing nephrotic syndrome: an open-label randomized controlled trial

Pediatr Nephrol 2019;34:829-35

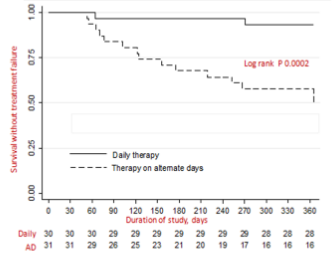
2–18 years; frequent relapses, n=**61**
12 months

Intervention 0.26±0.02 mg/kg/day
Control 0.51±0.05 mg/kg alternate day





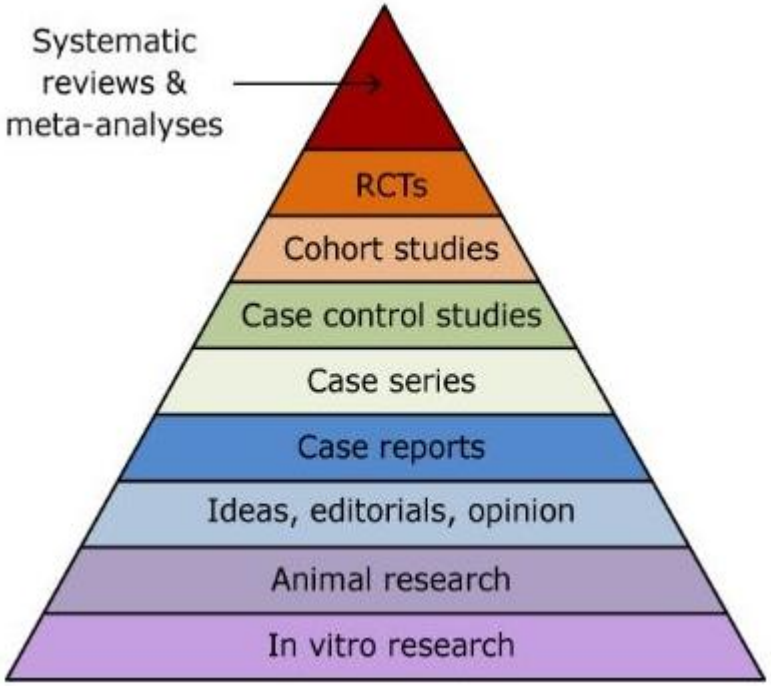
Time to treatment failure
Frequent relapses; steroid toxicity



NNT: 3 to enable sustained remission; 2 to prevent treatment failure

Incidence rate (95% CI)	Intervention	Control	Incidence rate ratio	*P*
Relapse/person yr	0.55 (0.3, 0.9)	1.94 (1.4, 2.6)	0.28 (0.2, 0.5)	<0.001
Infection associated relapses/person-yr	0.31 (0.1, 0.6)	1.15 (0.8, 1.7)	0.27 (0.1, 0.6)	<0.001

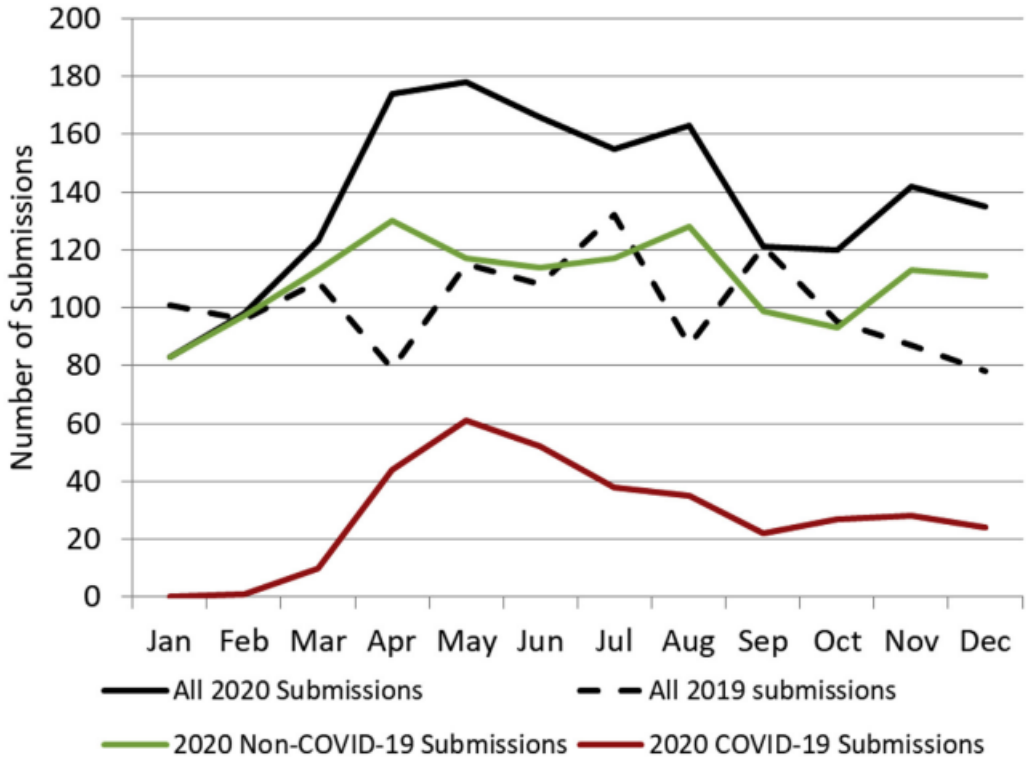
Meta-analysis: The highest level of evidence?



Potential misunderstanding	Background
A meta-analysis is an objective procedure	Every meta-analysis is characterized by decisions regarding research question, eligibility criteria, risk of bias analysis, and statistical approach. These decisions should be reasonable and transparently reported. Probably, no single best and ultimately objective procedure exists. For this reason, different meta-analyses on the same topic may come to different conclusions
A meta-analysis provides the highest level of evidence	A meta-analysis is generally considered to provide high-level evidence. However, the validity of a meta-analysis depends largely on the validity of included studies ("garbage in—garbage out"); a meta-analytic design is thus not a guarantee for highest level evidence
Study quality is synonymous with risk of bias	Study quality is about the question whether a study has been optimally performed; risk of bias relates to threats of validity. A study can be high quality but still have a high risk of bias for certain bias domains. An example is a comparison between two surgical techniques; even if the study is optimally performed, it cannot, by design, be blinded
A risk of bias analysis resolves the bias	A risk of bias analysis mainly displays this bias risk; such a display does not resolve it, although a sensitivity analysis restricted to low risk of bias studies can be considered
Random effects models solve heterogeneity	Random effects models allow that different studies have a different underlying true effect; the random effects model thus does not explain, solve, or even remove heterogeneity
Assuming homogeneity between studies when the statistical test fails to show heterogeneity	In the presence of few studies only, tests for heterogeneity have low power; the presence of a nonsignificant test does thus not provide strong evidence for true homogeneity between studies. This is especially the case if the review includes <10 studies
Present the I^2 statistic as if it was a test	The I^2 statistic is formally not a test that can reject a null hypothesis. It provides a quantitative measure of the heterogeneity between studies beyond chance[13]

When life gives you lemons..

The publication pandemic



Review > Minerva Med. 2021 Oct;112(5):631-640. doi: 10.23736/S0026-4806.21.07489-9.

Scientometric analysis of medical publications during COVID-19 pandemic: the twenty-twenty research boom

Ankita Aggarwal [1], Edoardo Agosti [2], Preet M Singh [3], Amrutha Varshini [4], Kanwaljeet Garg [5], Bipin Chaurasia [6], Luca Zanin [2], Marco M Fontanella [2]

Affiliations + expand

PMID: 34814634 DOI: 10.23736/S0026-4806.21.07489-9

Free article

Abstract

Introduction: There was significant surge in the academic publications after the onset of COVID-19 outbreak. The aim of this study was to scientometrically analyze all the medical publications on COVID-19 in 2020 as well as the top 100 cited articles.

Evidence acquisition: We performed a search of the "Web of Science" database using the keywords "COVID," and "corona" on December 20, 2020.

Evidence synthesis: Our search retrieved a total of 45,420 articles on the topic COVID-19 in the year 2020. Corresponding authors from 143 countries contributed to these articles. The highest number of articles were contributed by corresponding authors from the USA (N.=10299), whereas 50 articles in

Comment | Published: 09 September 2024

What we should learn from pandemic publishing

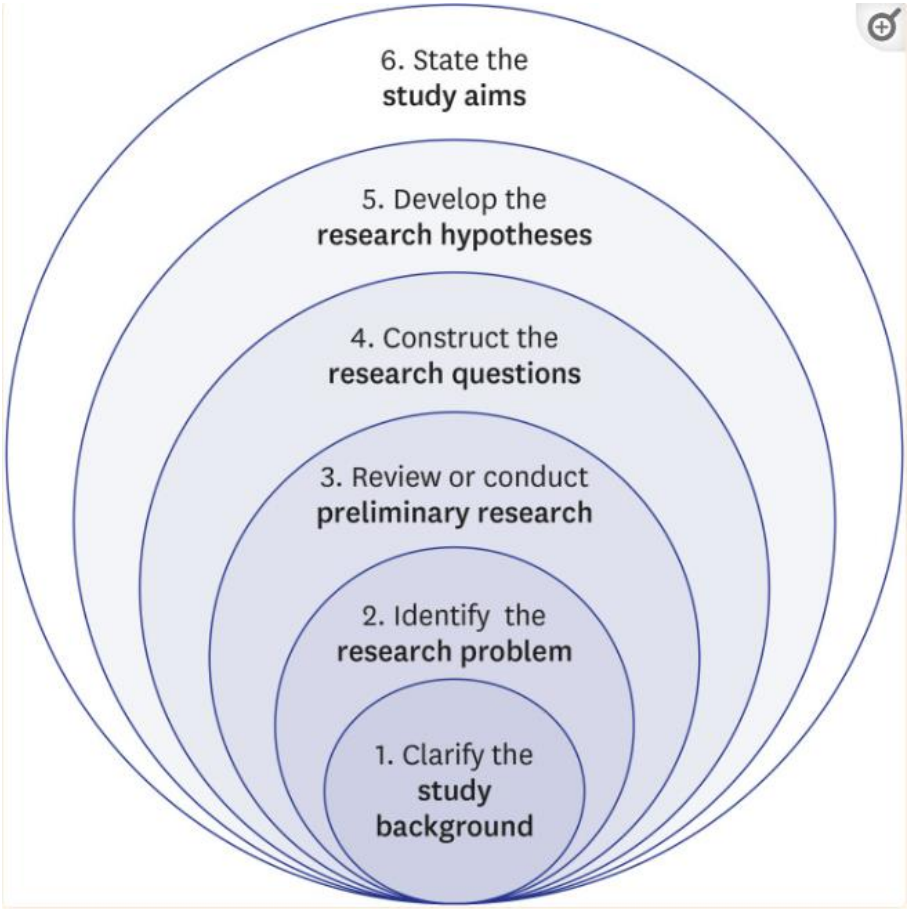
Satyaki Sikdar, Sara Venturini, Marie-Laure Charpignon, Sagar Kumar, Francesco Rinaldi, Francesco Tudisco, Santo Fortunato & Maimuna S. Majumder

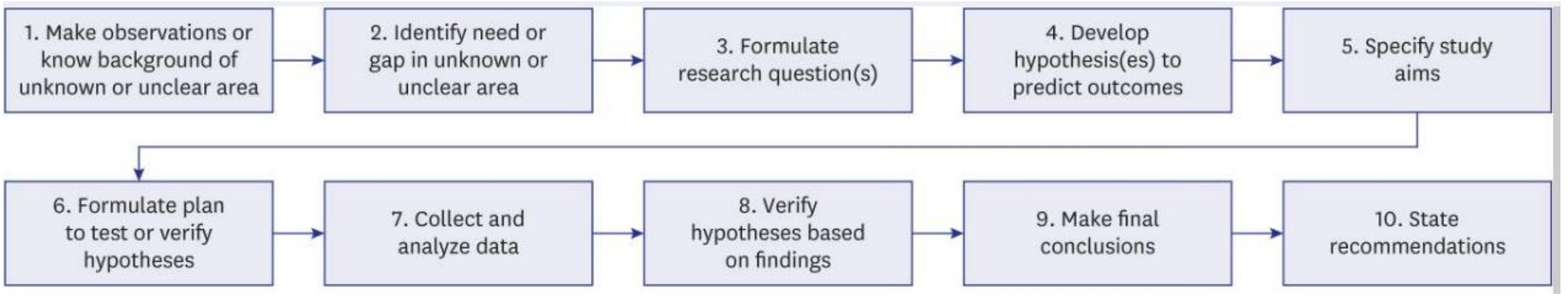
Nature Human Behaviour (2024) | Cite this article

277 Accesses | 12 Altmetric | Metrics

Authors of COVID-19 papers produced during the pandemic were overwhelmingly not subject matter experts. Such a massive inflow of scholars from different expertise areas is both an asset and a potential problem. Domain-informed scientific collaboration is the key to preparing for future crises.

Developing a study protocol





Formulate a hypothesis to address your query..

Quantitative research hypotheses
Simple hypothesis
- Predicts relationship between single dependent variable and single independent variable
If the dose of the new medication (single independent variable) is high, blood pressure (single dependent variable) is lowered.
Complex hypothesis
- Foretells relationship between two or more independent and dependent variables
The higher the use of anticancer drugs, radiation therapy, and adjunctive agents (3 independent variables), the higher would be the survival rate (1 dependent variable).
Directional hypothesis
- Identifies study direction based on theory towards particular outcome to clarify relationship between variables
Privately funded research projects will have a larger international scope (study direction) than publicly funded research projects.
Non-directional hypothesis
- Nature of relationship between two variables or exact study direction is not identified
- Does not involve a theory
Women and men are different in terms of helpfulness. (Exact study direction is not identified)

Definiti
Quant
Descri
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Causal hypothesis
- An effect on dependent variable is predicted from manipulation of independent variable
A change into a high-fiber diet (independent variable) will reduce the blood sugar level (dependent variable) of the patient.
Null hypothesis
- A negative statement indicating no relationship or difference between 2 variables
There is no significant difference in the severity of pulmonary metastases between the new drug (variable 1) and the current drug (variable 2).
Alternative hypothesis
- Following a null hypothesis, an alternative hypothesis predicts a relationship between 2 study variables
The new drug (variable 1) is better on average in reducing the level of pain from pulmonary metastasis than the current drug (variable 2).
Working hypothesis
- A hypothesis that is initially accepted for further research to produce a feasible theory
Dairy cows fed with concentrates of different formulations will produce different amounts of milk.
Statistical hypothesis
- Assumption about the value of population parameter or relationship among several population characteristics
- Validity tested by a statistical experiment or analysis
The mean recovery rate from COVID-19 infection (value of population parameter) is not significantly different between population 1 and population 2.

Avoid ambiguity..

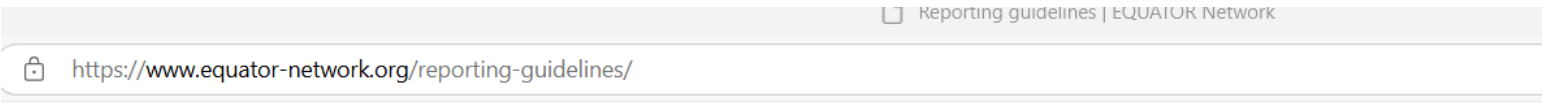
Examples of ambiguous research question and hypothesis that result in unclear and weak research objective in qualitative research, how to transform them into clear and good statements, and points to avoid

Variables	Unclear and weak statement (Statement 1)	Clear and good statement (Statement 2)	Points to avoid
Research question	Does disrespect and abuse (D&A) occur in childbirth in Tanzania?	How does disrespect and abuse (D&A) occur and what are the types of physical and psychological abuses observed in midwives' actual care during facility-based childbirth in urban Tanzania?	1) Ambiguous or oversimplistic questions
			2) Questions unverifiable by data collection and analysis
Hypothesis	Disrespect and abuse (D&A) occur in childbirth in Tanzania.	Hypothesis 1: Several types of physical and psychological abuse by midwives in actual care occur during facility-based childbirth in urban Tanzania.	1) Statements simply expressing facts
		Hypothesis 2: Weak nursing and midwifery management contribute to the D&A of women during facility-based childbirth in urban Tanzania.	2) Insufficiently described concepts or variables
Research objective	To describe disrespect and abuse (D&A) in childbirth in Tanzania.	"This study aimed to describe from actual observations the respectful and disrespectful care received by women from midwives during their labor period in two hospitals in urban Tanzania."[17][a]	1) Statements unrelated to the research question and hypotheses
			2) Unattainable or unexplorable objectives

Examples of ambiguous research question and hypothesis that result in unclear and weak research objecti in quantitative research, how to transform them into clear and good statements, and points to avoid

Variables	Unclear and weak statement (Statement 1)[a]	Clear and good statement (Statement 2)[b]	Points to avoid
Research question	Which is more effective between smoke moxibustion and smokeless moxibustion?	"Moreover, regarding smoke moxibustion versus smokeless moxibustion, it remains unclear which is more effective, safe, and acceptable to pregnant women, and whether there is any difference in the amount of heat generated."[16]	1) Vague and unfocused questions
			2) Closed questions simply answerable by yes or no
			3) Questions requiring a simple choice
Hypothesis	The smoke moxibustion group will have higher cephalic presentation.	"Hypothesis 1. The smoke moxibustion stick group (SM group) and smokeless moxibustion stick group (-SLM group) will have higher rates of cephalic presentation after treatment than the control group.	1) Unverifiable hypotheses
		Hypothesis 2. The SM group and SLM group will have higher rates of cephalic presentation at birth than the control group.	2) Incompletely stated groups of comparison
		Hypothesis 3. There will be no significant differences in the well-being of the mother and child among the three groups in terms of the following outcomes: premature birth, premature rupture of membranes (PROM) at	3) Insufficiently described variables or outcomes

How to report your data?



equator network

Enhancing the QUAlity and Transparency Of health Research

Toolkits

This section provides practical help and resources to support you in:

- Writing research
- Selecting the appropriate reporting guideline
- Peer reviewing research
- How to develop a reporting guideline
- Using guidelines in your journal

Reporting guidelines for main study types

Randomised trials	CONSORT	Extensions
Observational studies	STROBE	Extensions
Systematic reviews	PRISMA	Extensions
Study protocols	SPIRIT	PRISMA-P
Diagnostic/prognostic studies	STARD	TRIPOD
Case reports	CARE	Extensions
Clinical practice guidelines	AGREE	RIGHT
Qualitative research	SRQR	COREQ
Animal pre-clinical studies	ARRIVE	
Quality improvement studies	SQUIRE	Extensions
Economic evaluations	CHEERS	Extensions

Take-away.. Research and you

Helps you find answers to questions that irk you

Requires (chiefly) an inquisitive mind and a committed soul

Not only for academicians & life-long researchers

Cross-sectional and retrospective studies can provide meaningful information

Collaborative research: More efficient; can be more or less biased than single center studies, depending on the invetsigators!

Prospective research: Demands commitment, tenacity, skills, integrity and adherence to ethical practices

Study what you feel passionately about! The methods will follow..

Acute Kidney Injury

Early Diagnosis: What Every Pediatrician Should Know

Division of Nephrology, Department of Pediatrics
All India Institute of Medical Sciences, New Delhi

Overview

- Definition
- Epidemiology
- Diagnosis; early recognition
- Risk stratification
- Prevention
- Outcomes

Recognizing AKI is important

Serum creatinine

Varies: age, gender, race, muscle, diet

Doesn't depict dysfunction

immediately; rises after 50% lost

Secretion overestimate function

Effect of drugs (cimetidine, trimethoprim)

Effect of fluid overload: Dilutional fall

Methods of estimation vary

Easily dialyzed

Baseline creatinine not known

Urine output

The canary in the coal mine

Duration: prognostic value

No need for 'baseline'

Enables early diagnosis

Improves management

Caveats

Not all AKI is oliguric

Not validated prospectively

Diuretic use

Cumbersome to measure accurately

Defining AKI: Emerging Consensus?

Stage	Creat change	Urine output
1	≥ 0.3 mg/dl or 1.5- to 2-fold	< 0.5 ml/kg/h for > 6 h
2	> 2- to 3-fold	< 0.5 ml/kg/h for ≥ 12 h
3	> 3-fold	< 0.3 ml/kg/h for ≥ 24 h or anuria ≥12 h

AKIN criteria

Stage	serum creatinine	Urine output
1	0.3 mg/dl in 48 h or 1.5-1.9 within 7d	< 0.5 ml/kg/h for 6–12 h
2	2-2.9 times	< 0.5 ml/kg/h for ≥ 12 h
3	≥ 3 times baseline or ≥ 4 mg/dl or dialysis	< 0.3 ml/kg/h for ≥ 24 h or Anuria ≥ 12 h

KDIGO criteria

RIFLE criteria

pRIFLE criteria

Stage	eCCL	Urine output
R	↓ by 25%	<0.5 ml/kg/h for 8 h
I	↓ by 50%	<0.5 ml/kg/h for 16 h
F	↓ by 75%	<0.3 ml/kg/h for 24 h or anuric for 12 h
L: F > 4 wks; E: F > 3 months		

pROCK criteria

Stage	serum creatinine change
1	≥ 0.23 mg/dl + 30% rise
2	≥ 0.45 mg/dl + 60% rise
3	≥ 0.90 mg/dl + 120% rise

pRIFLE, AKIN, KDIGO 2012 broadly similar

Scheme	Stage	Creatinine Criteria	Urine Output Criteria
RIFLE		GFR decrease ≥25% or sCr increase by 1.5x	<0.5 mL/kg/h for 8 h
		GFR decrease ≥50% or sCr increase by 2x	<0.5 mL/kg/h for 16 h
		GFR decrease ≥75% or sCr increase by 3x or >4 mg/dL	<0.3 mL/kg/h for 24 h (anuria 12 h)
		Persistent failure >4 weeks	
		Persistent failure >3 months	
Pediatric RIFLE		eCCl decrease >25%	<0.5 mL/kg/h for 8 h
		eCCl decrease >50%	<0.5 mL/kg/h for 16 h
		eCCl decrease >75% or eCCl <35 mL/min/1.73 m²	<0.3 mL/kg/h for 24 h (anuria 12 h)
		Persistent failure >4 weeks	
		Persistent failure >3 months	
AKIN	1	Increase >0.3 mg/dL or to 150%-200% baseline	<0.5 mL/kg/h for 6 h
	2	Increase to 200%-300% baseline	<0.5 mL/kg/h for 12 h
	3	Increase to >300% baseline or >4 mg/dL with an acute increase of 0.5 mg/dL	<0.3 mL/kg/h 24 h (anuria 12 h)
KDIGO	1	Increase >1.5-1.9x baseline (or >0.3 mg/dL increase)	<0.5 mL/kg/h for 6-12 h
	2	Increase >2-2.9x baseline	<0.5 mL/kg/h for >12 h
	3	>3x baseline	<0.3 mL/kg/h >24 h (anuria 12 h)
		Initiation of CRRT	
		Decrease in eGFR to <35 mL/min/1.73 m²	

Kidney Int 2007;71:1028-35
Crit Care 2007;11:R31
Kidney Int 2012;2(Suppl):1–138

Acute kidney injury

Sudden loss of renal function, over hours to days, with deranged fluid balance, acid base & electrolytes

AWARE Study

32 ICUs, N = 4683

AKI: **26.9%**

Severe AKI: **11.6%**

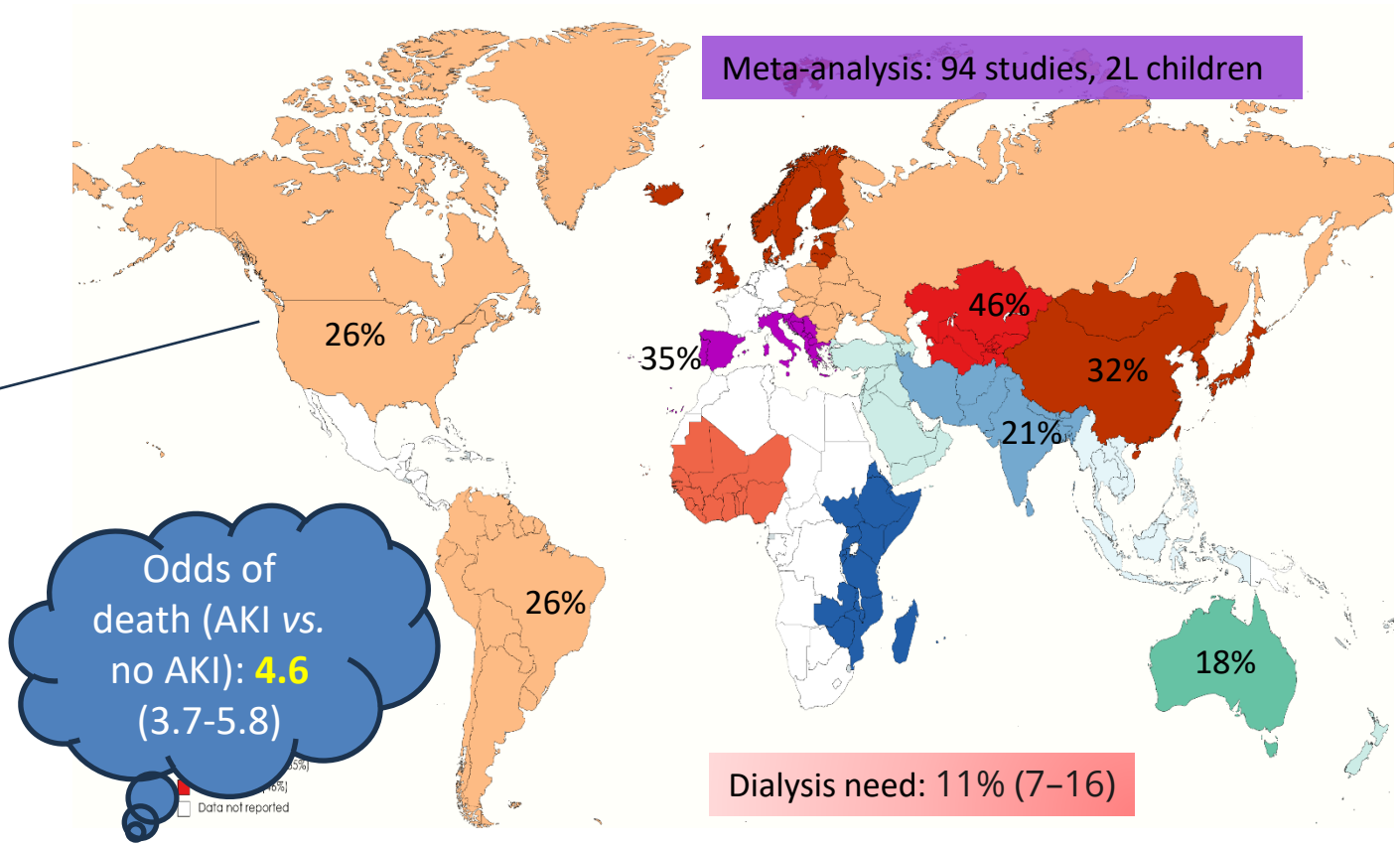
Mortality

Stage 1: **4%**

Stage 2: **8%**

Stage 3: **20%**

Dialysis: **31%**



Pediatrics 2023

AKI definition: urine output vs creatinine

Table 2. Outcomes for patients with maximum AKI severity by UO, SC, or both (*n*=23,866)

Characteristic	No AKI (*n*=8179)	Maximum AKI Severity			*P* Value[c]
		UO (*n*=14,177)	SC (*n*=4694)	Both (*n*=4995)	
Duration of stage 3 AKI (d), mean (SD)	N/A	1.3 (0.6)	3.5 (4)	5.6 (6.9)	<0.001
RRT during hospital stay	4 (0)	304 (2.1)	232 (4.9)	1251 (25)	<0.001
Length of stay (d), median (Q1, Q3)[a]					
ICU	3 (2–4)	5 (3–9)	4 (2–6)	7 (4–15)	<0.001
Hospital	7 (5–11)	13 (8–22)	14 (8–24)	22 (12–38)	<0.001
Mortality					
Hospital	350 (4.3)	1761 (12.4)	788 (16.8)	1597 (32)	<0.001
30 days[b]	425 (5.2)	1822 (12.9)	808 (17.2)	1375 (27.5)	<0.001
90 days[b]	596 (7.3)	2710 (19.1)	1074 (22.9)	1890 (37.8)	<0.001
1 year[b]	1064 (13)	3966 (28)	1498 (31.9)	2395 (47.9)	<0.001

Diagnosis of AKI would have been missed in 67% of cases, if using only plasma creatinine

Mortality was higher among patients with stage III AKI defined according to urine output

Serum creatinine diluted during fluid overload…

Adjusted serum creatinine =

$$\textbf{Measured creatinine} \times \left\{1 + \frac{\textbf{cumulative net fluid balance}}{\textbf{total body water}}\right\}$$

TBW = 0.6 $\times$ body weight (kg)

JASN 2015

AWARE study, Pediatrics 2023

Emphasis on early recognition

Any of the following

Increase in SCr by ≥0.3 mg/dl within 48 hr

Increase in SCr to ≥1.5 times baseline, known or presumed to have occurred within prior 7 d

Urine volume <0.5 ml/kg/hr for 6 hr

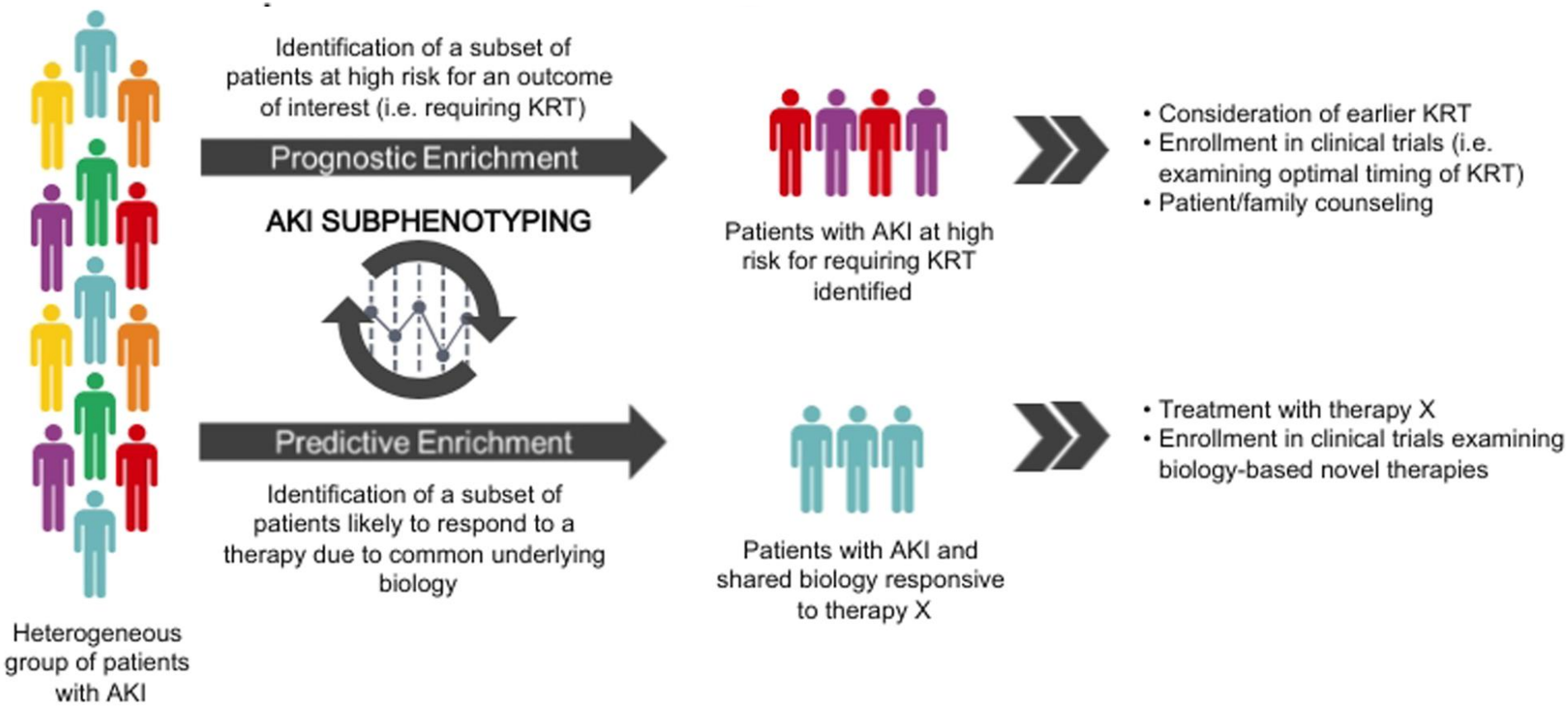
AKI in neonates defined differently

Serum creatinine reflects mom's GFR; GFR dynamic

Urine output often preserved

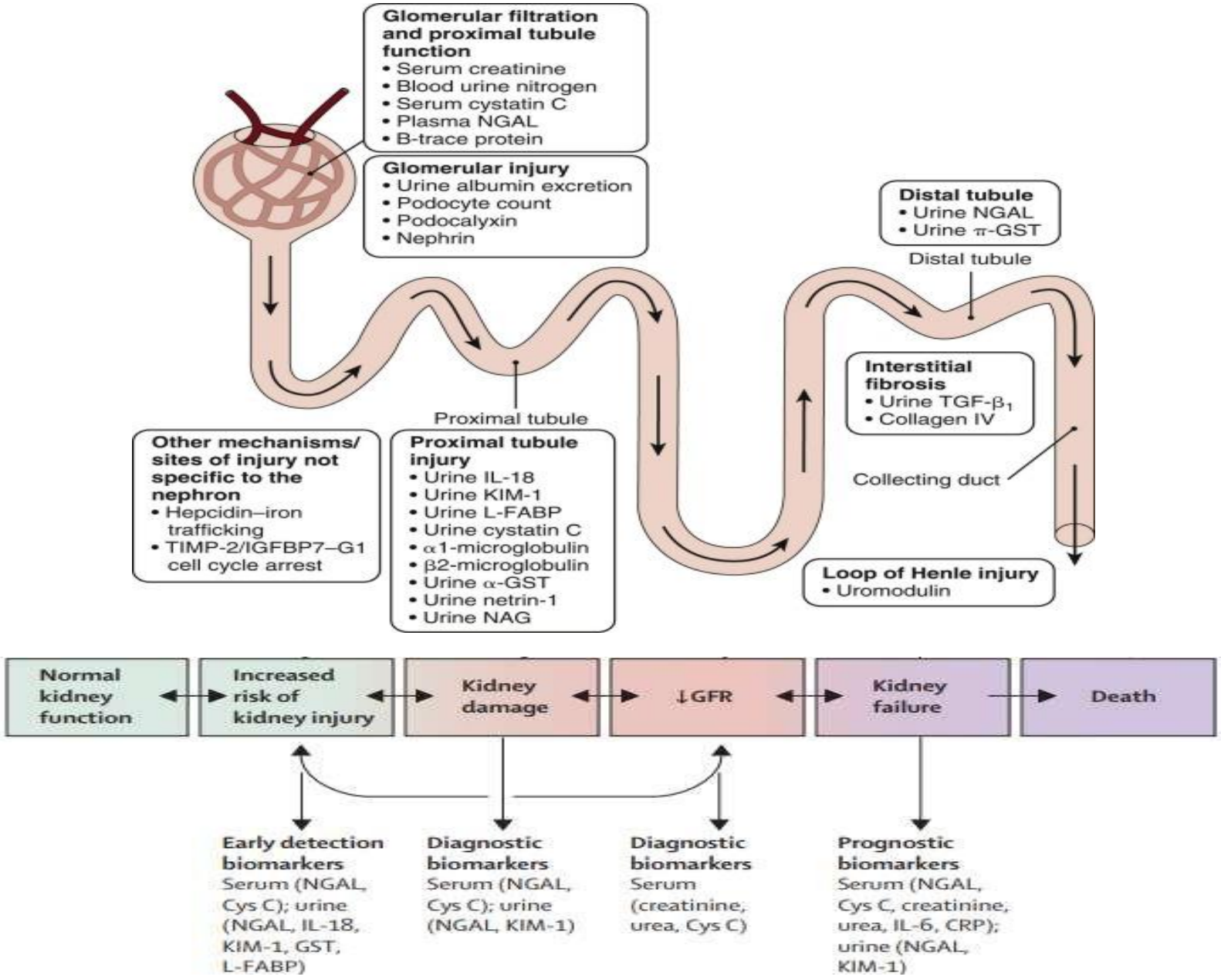
Definition	Stage	Serum creatinine	Urine output over 24-h
KDIGO	1	↑ by ≥0.3 mg/dl in ≤48-hr or to 1.5–1.9 times the baseline within 7 days	≤1 ml/kg/h
	2	↑ to 2.0–2.9 times the baseline within 7 days	≤0.5 ml/kg/h
	3	≥3 times the baseline, or to ≥2.5 mg/dl, or initiation of KRT	≤0.3 ml/kg/h, or anuria
	Stage	**eCrCl**	**Urine output over 24-h**
nRIFLE	Risk	↓ by 25% (Risk)	<1.5 ml/kg/h
	Injury	↓ by 50% (Injury)	<1.0 ml/kg/h
	Failure	↓ by 75% (Failure)	<0.7 ml/kg/h or anuria x 12-h
	Term	**Serum creatinine (SCr)**	
Abbreviated or short definition	SCr rise	↑ by ≥0.3 mg/dl from reference value	
	Peak SCr	Peak creatinine ≥1.5 mg/dl	
	Nadir SCr	Nadir creatinine ≥0.5 mg/dl at discharge or day 30	

Sub-phenotypes of AKI

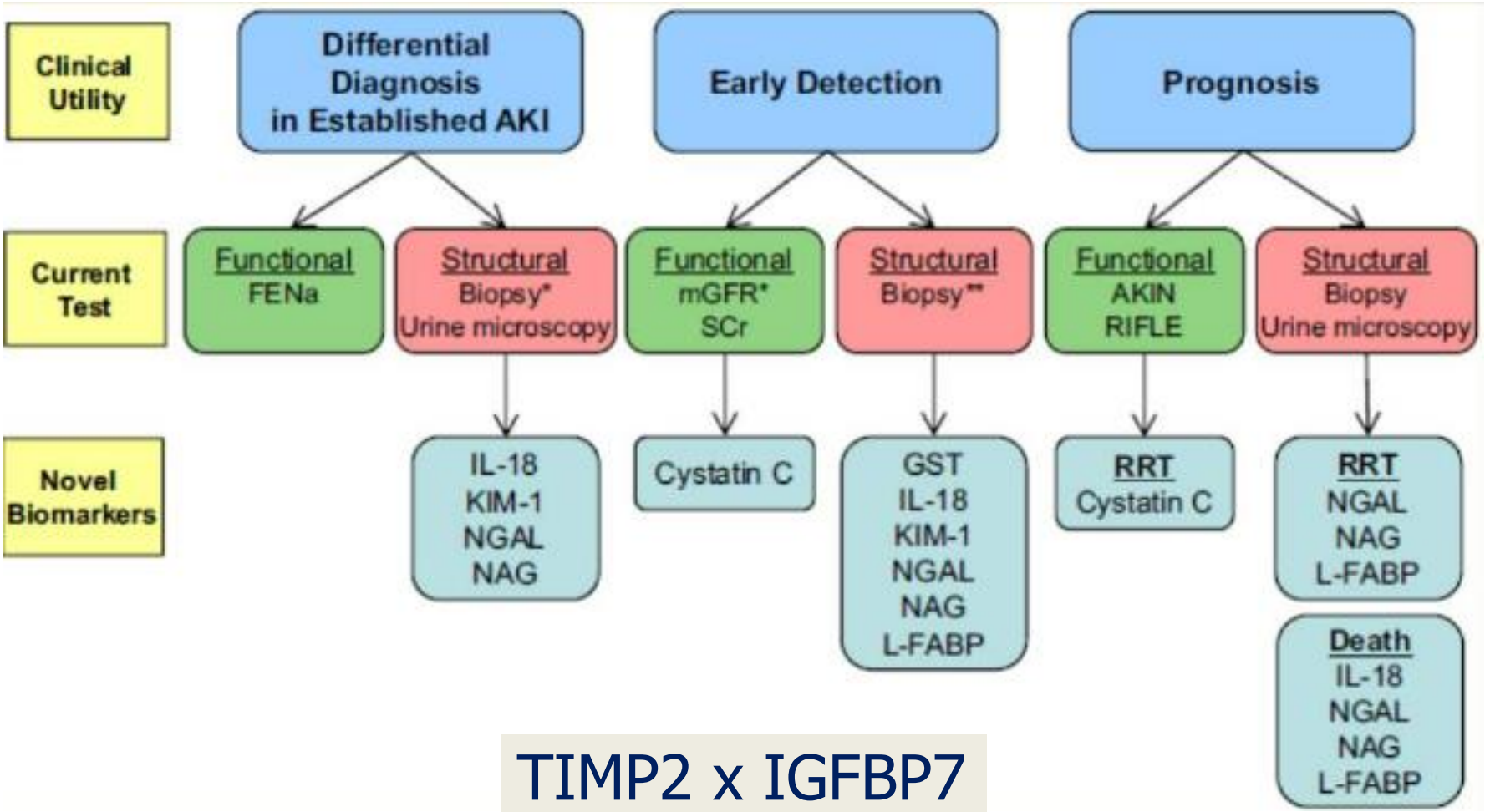


Crit Care. 2022

Early detection: Biomarkers

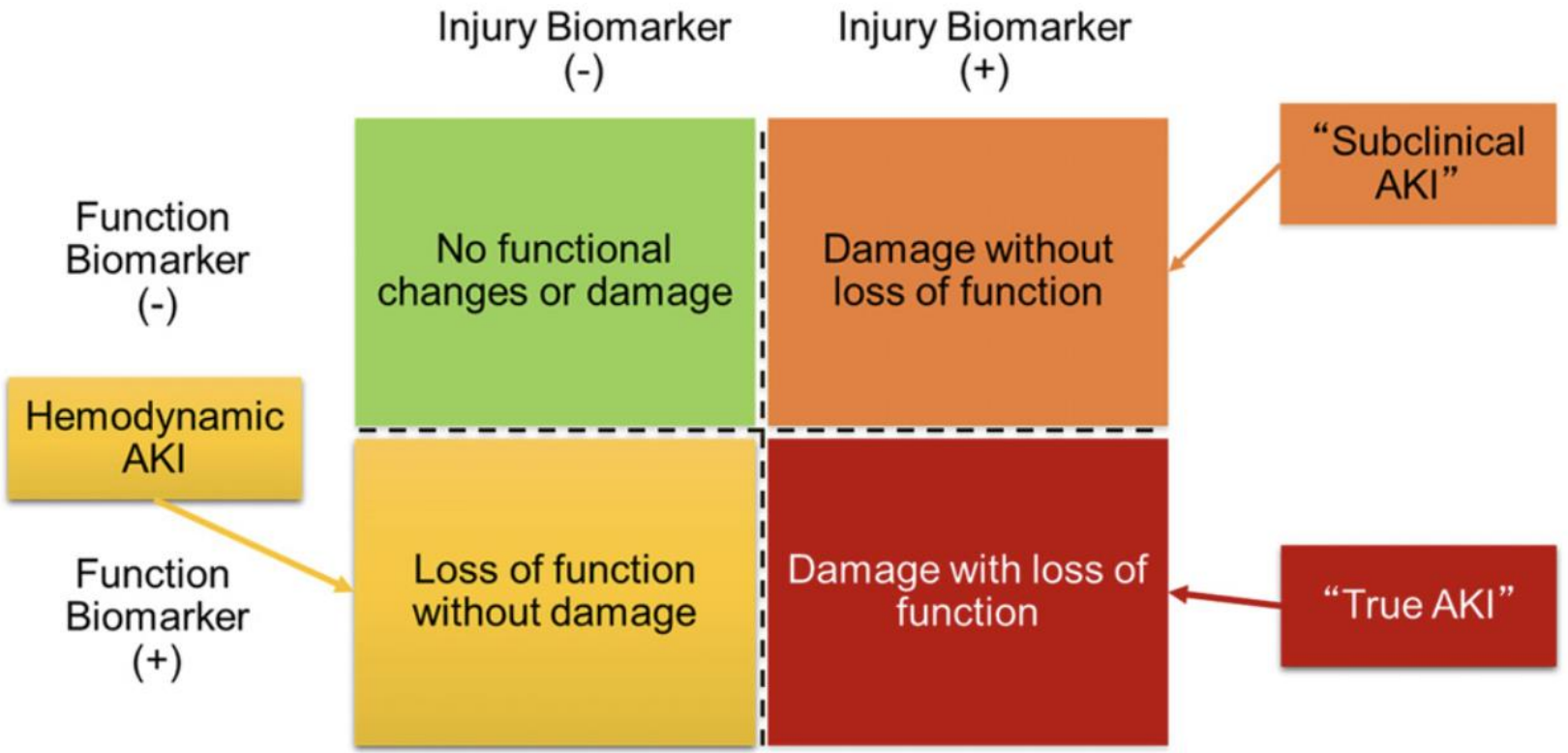


Utility of biomarkers



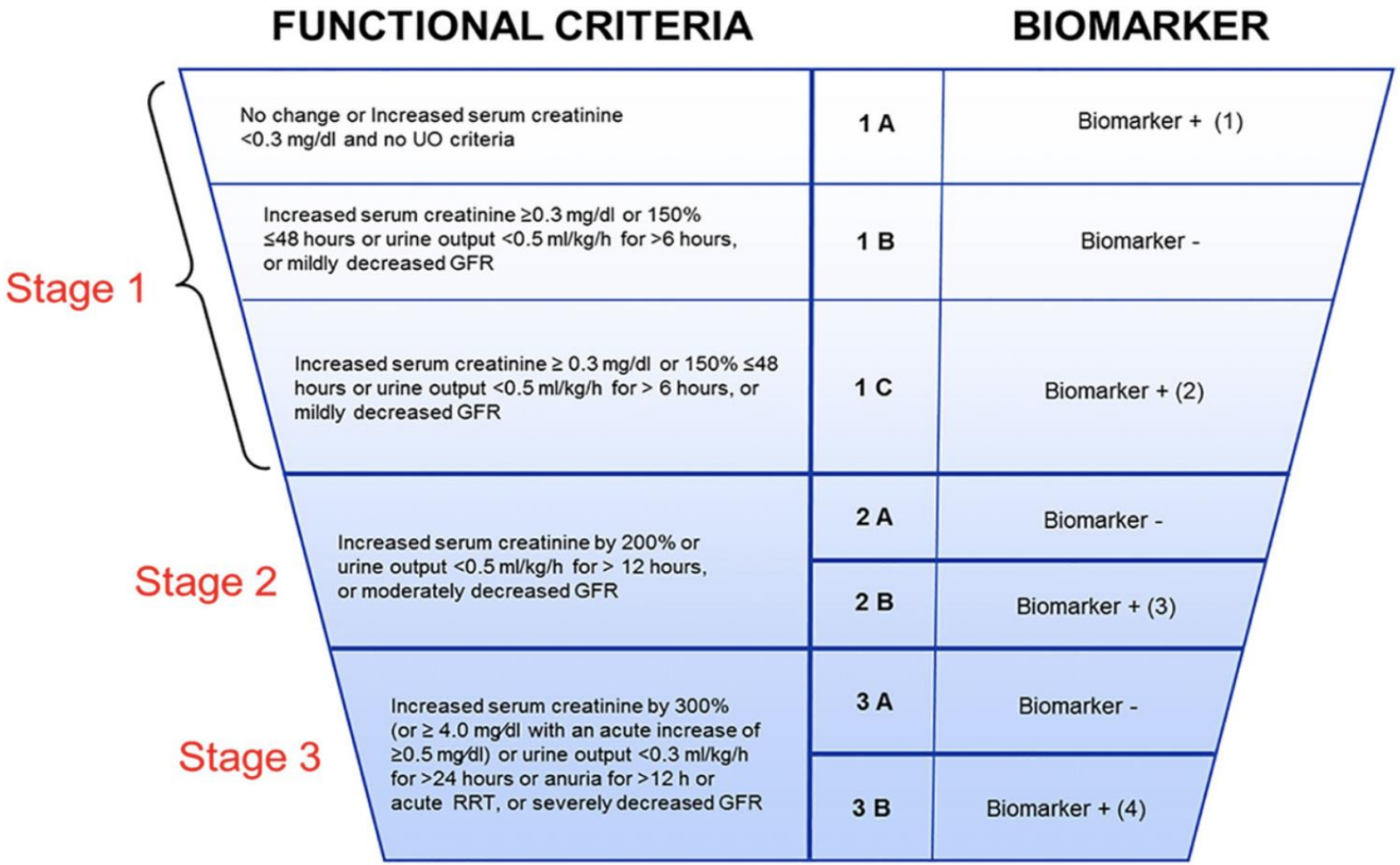
TIMP2 x IGFBP7

Biomarker based definitions



ADQI 2024

Redefining AKI definitions

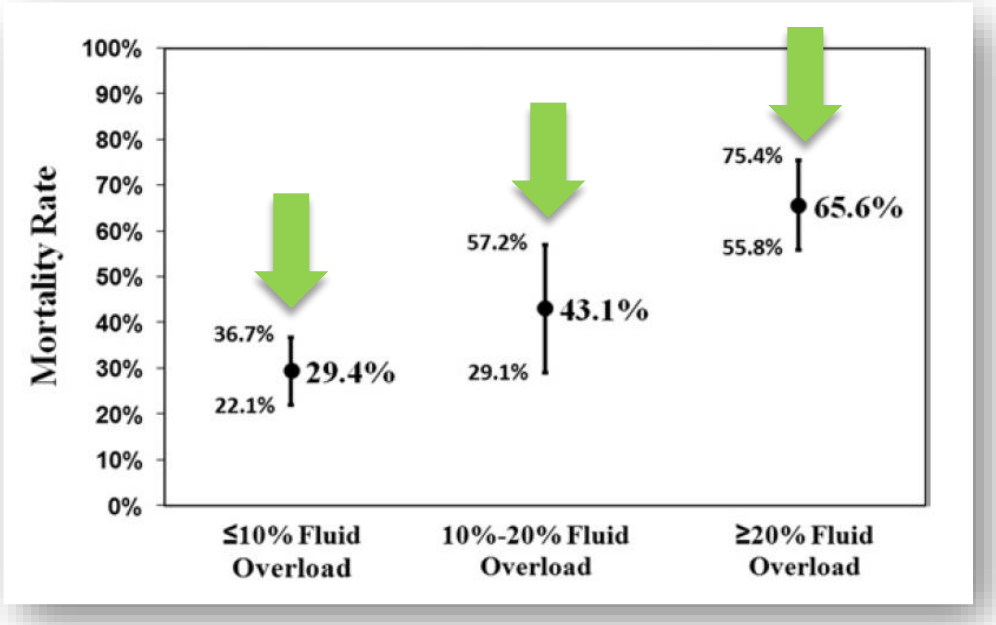


ADQI 2024

Detecting Risk of Severe AKI

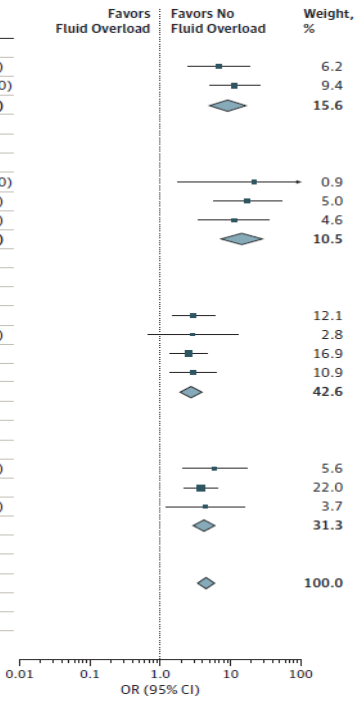
(A) % Fluid Overload

Σ (fluid input – fluid output),L / admission weight, kg X 100



PPCRRT Registry; 13 centers; Nat Rev Nephrol 2010;6:190

Source	Log (OR)	SE	OR (95% CI)
Definition 1 (%FO >5% in 24 h)			
Li et al,[6] 2016	1.9313	0.4969	6.90 (2.60-18.27)
Chen et al,[24] 2016	2.4368	0.4052	11.44 (15.17-25.30)
Subtotal (95% CI)			**9.35 (5.05-17.29)**
Heterogeneity: $\chi^2_8 = 0.62$, ($P = .43$); $I^2 = 0\%$			
Test for overall effect: $z = 7.12$, ($P < .001$)			
Definition 2 (%FO >10% during PICU admission)			
Ketharanathan et al,[40] 2014	3.1023	1.2792	22.25 (1.81-273.00)
Naveda et al,[44] 2016	2.8856	0.5574	17.91 (6.01-53.41)
Sutawan et al,[52] 2016	2.4384	0.5790	11.45 (3.68-35.63)
Subtotal (95% CI)			**15.02 (7.09-31.82)**
Heterogeneity: $\chi^2_8 = 0.41$, ($P = .81$); $I^2 = 0\%$			
Test for overall effect: $z = 7.07$, ($P < .001$)			
Definition 3 (%FO >10% at CRRT initiation)			
Gillespie et al,[31] 2004	1.1053	0.3570	3.02 (1.50-6.08)
Selewski et al,[49] 2012	1.0922	0.7478	2.98 (0.69-12.91)
Modem et al,[43] 2014	0.9442	0.3021	2.57 (1.42-4.65)
de Galasso et al,[27] 2016	1.0963	0.3765	2.99 (1.43-6.26)
Subtotal (95% CI)			**2.83 (1.95-4.10)**
Heterogeneity: $\chi^2_8 = 0.16$, ($P = .98$); $I^2 = 0\%$			
Test for overall effect: $z = 5.46$, ($P < .001$)			
Definition 4 (%FO >20% at CRRT initiation)			
Hayes et al,[35] 2009	1.8036	0.5252	6.07 (2.17-17.00)
Sutherland et al,[51] 2010	1.3604	0.2643	3.90 (2.32-6.54)
Jhang et al,[38] 2014	1.4956	0.6452	4.46 (1.26-15.80)
Subtotal (95% CI)			**4.29 (2.78-6.62)**
Heterogeneity: $\chi^2_8 = 0.57$, ($P = .75$); $I^2 = 0\%$			
Test for overall effect: $z = 6.56$, ($P < .001$)			
Total (95% CI)			**4.62 (3.63-5.90)**
Heterogeneity: $\chi^2_8 = 23.08$, ($P = .02$); $I^2 = 52\%$			
Test for overall effect: $z = 12.34$, ($P < .001$)			
Test for subgroup differences: $\chi^2_3 = 21.31$, ($P < .001$); $I^2 = 85.9\%$			

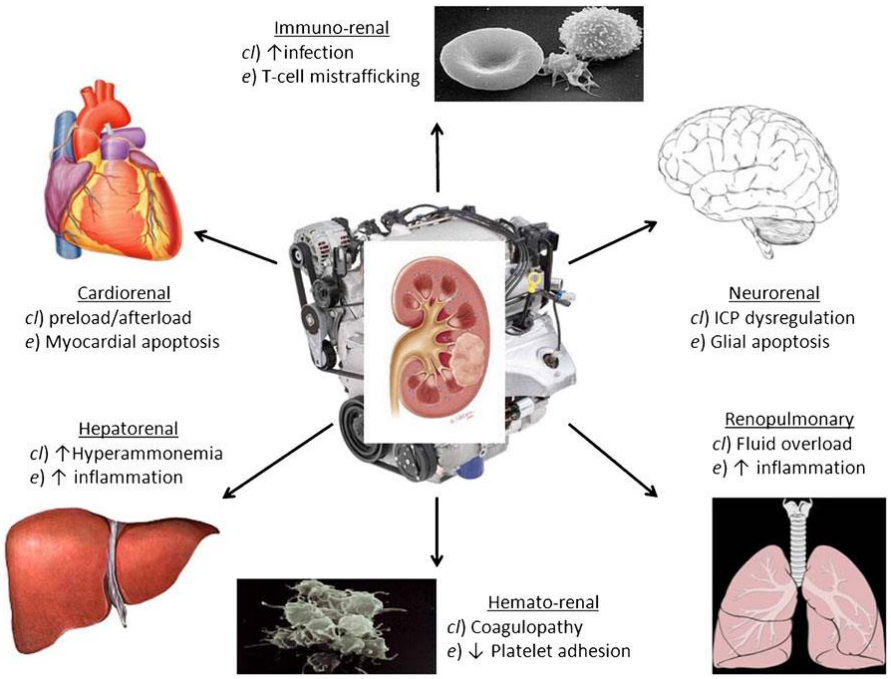


JAMA Pediatrics 2018

FO >10% is independently associated with increased risk of mortality

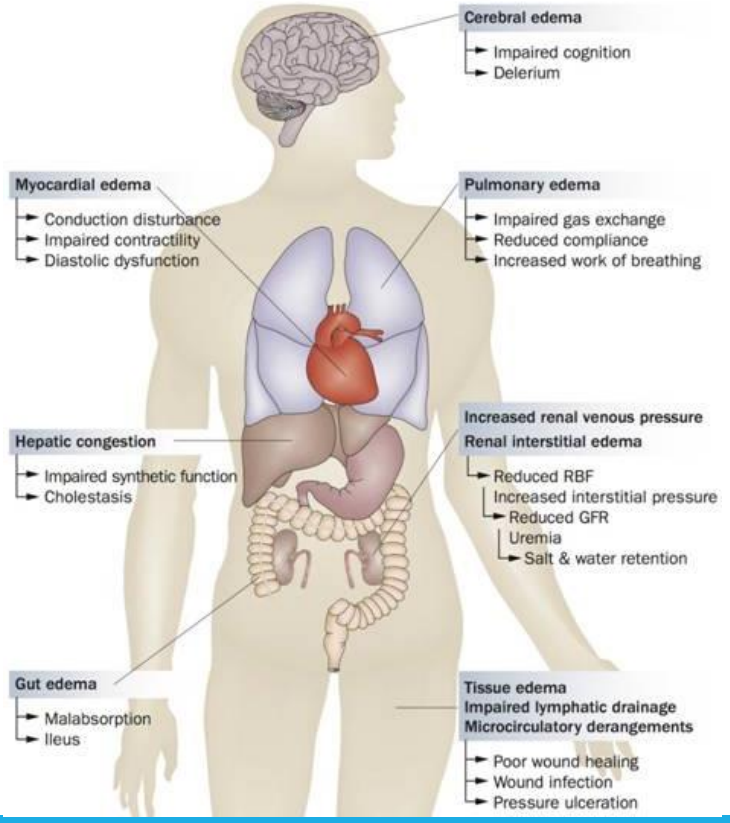
Fluid Overload and the Kidney: Innocent victim or malicious culprit?

Clinical (*cl*) & experimental (*e*) effects



Pediatr Nephrol (2013) 28:2239–2248

Sequelae of fluid overload



Prediction of severe AKI

(B) Renal angina index

AKI Risk Tranche

Risk Factor	Risk Tranche	Risk Score
ICU Admission	Medium	1
History of Transplantation (Solid Organ or Bone Marrow)	High	3
Vasoactive Support & Mechanical Ventilation	Very High	5

X = Renal Angina Index (Range 1-40)

AKI Injury Tranche

Change in Creatinine	Fluid Overload %	Injury Score
<0	< 0 – 5%	1
1.0 – 1.49x	5 – 9.99%	2
1.5 – 1.99x	10 – 14.99%	4
> 2x	≥ 15%	8

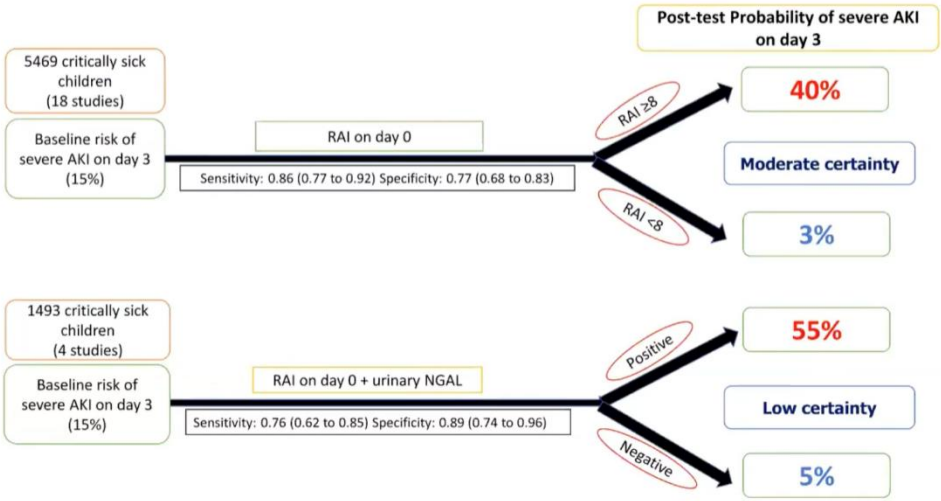
RAI > 8 predicts AKI stage 2 or 3 on day 3

Sensitivity 85%

Specificity 79%

Assessed 12h after ICU admission

Adding RAI to biomarkers improved their predictive accuracy



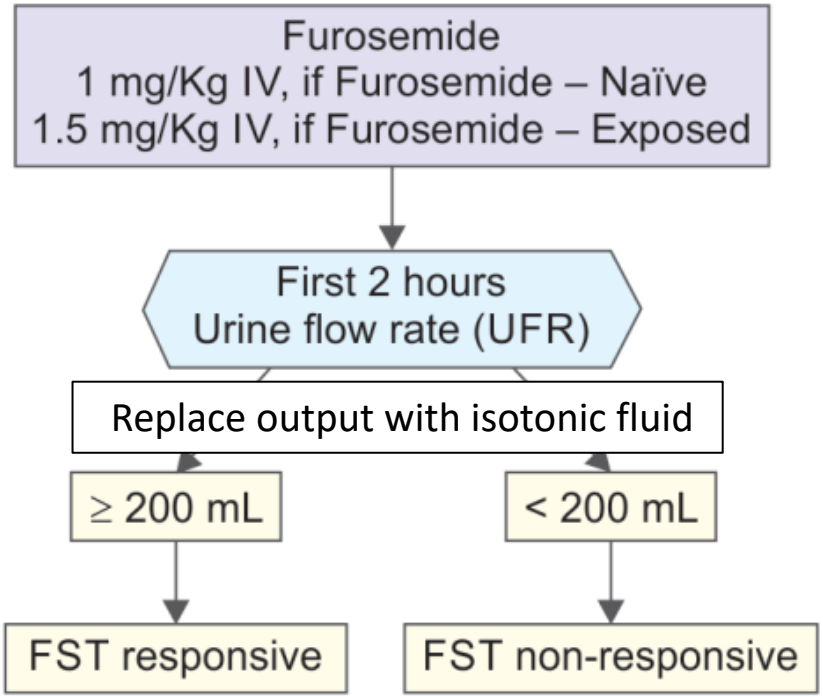
Prediction of severe AKI

(C) Furosemide stress test

Test of integrated renal function

Renal blood flow, organic anion secretion, luminal patency

Patients with AKI stage 1, 2



Predict AKI stage 3 within 14 days

Sensitivity 87%, specificity 84%, AUC 0.87

Urinary threshold not yet determined in children

Pediatric studies upcoming; AUC from pediatric studies for AKI 3:

< 2 ml/kg within 2 h: 0.92

< 0.5 ml/kg within 2 h: 0.84

< 3 ml/kg within 4 h: 0.75

Nephron 2016;134:191–194
J Am Soc Nephrol 26: 1762–1764, 2015

Furosemide stress test to predict acute kidney injury progression in critically ill children

Graphical Abstract

HYPOTHESIS: Furosemide stress test (FST) may predict stage 3 acute kidney injury (AKI) in critically ill children

DESIGN & OUTCOMES

Prospective cohort

Critically ill children admitted to ICU having AKI stage 1 or 2

IV Furosemide 1 mg/kg after catheterization (FST)

Hourly urine output x 6h; Urine volume < 2 mL/kg at 2h deemed FST non-responsive

480 children screened over 2 years

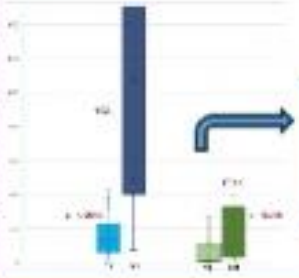
51 developed AKI stage 1-2, underwent FST

FST non-responsive (NR) n = 9

AKI 3: n = 8 (89%)
KST: n = 7 (78%)
Death: n = 5 (56%)

FST responsive (FR) n = 42

AKI 3: n = 5 (12%)
KST: n = 2 (5%)
Death: n = 3 (7%)



NGAL and PENK biomarkers higher in FST non-responsive group

AUC of FST for predicting
AKI stage 3: 0.93
KST need: 0.96
Mortality: 0.93

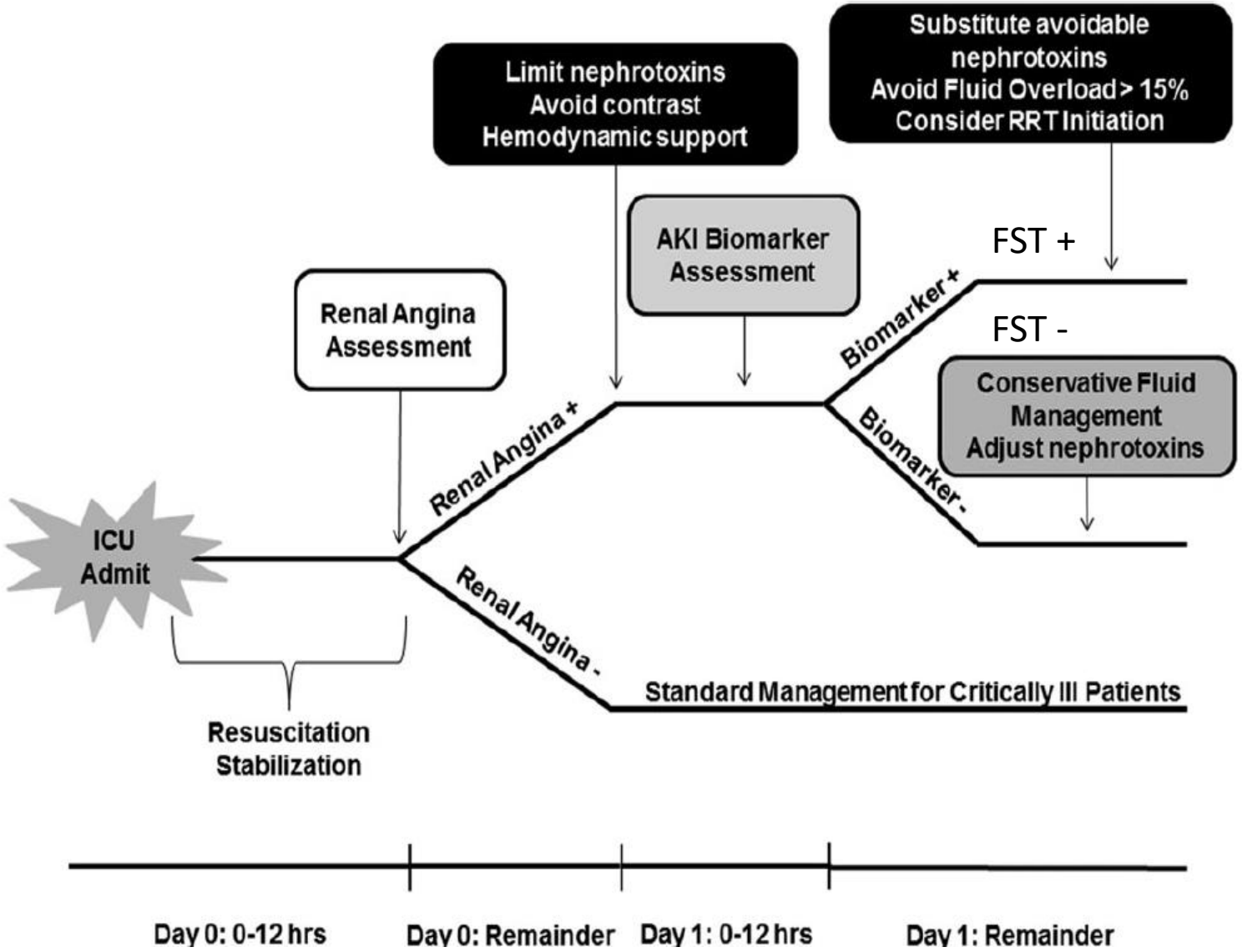
KST: Kidney support therapy

CONCLUSION: Furosemide stress test is a simple, inexpensive and robust biomarker for predicting stage 3 AKI and KST need in critically ill children. FST outperformed the other blood biomarkers NGAL and PENK; addition of biomarkers to FST did not improve the diagnostic accuracy.

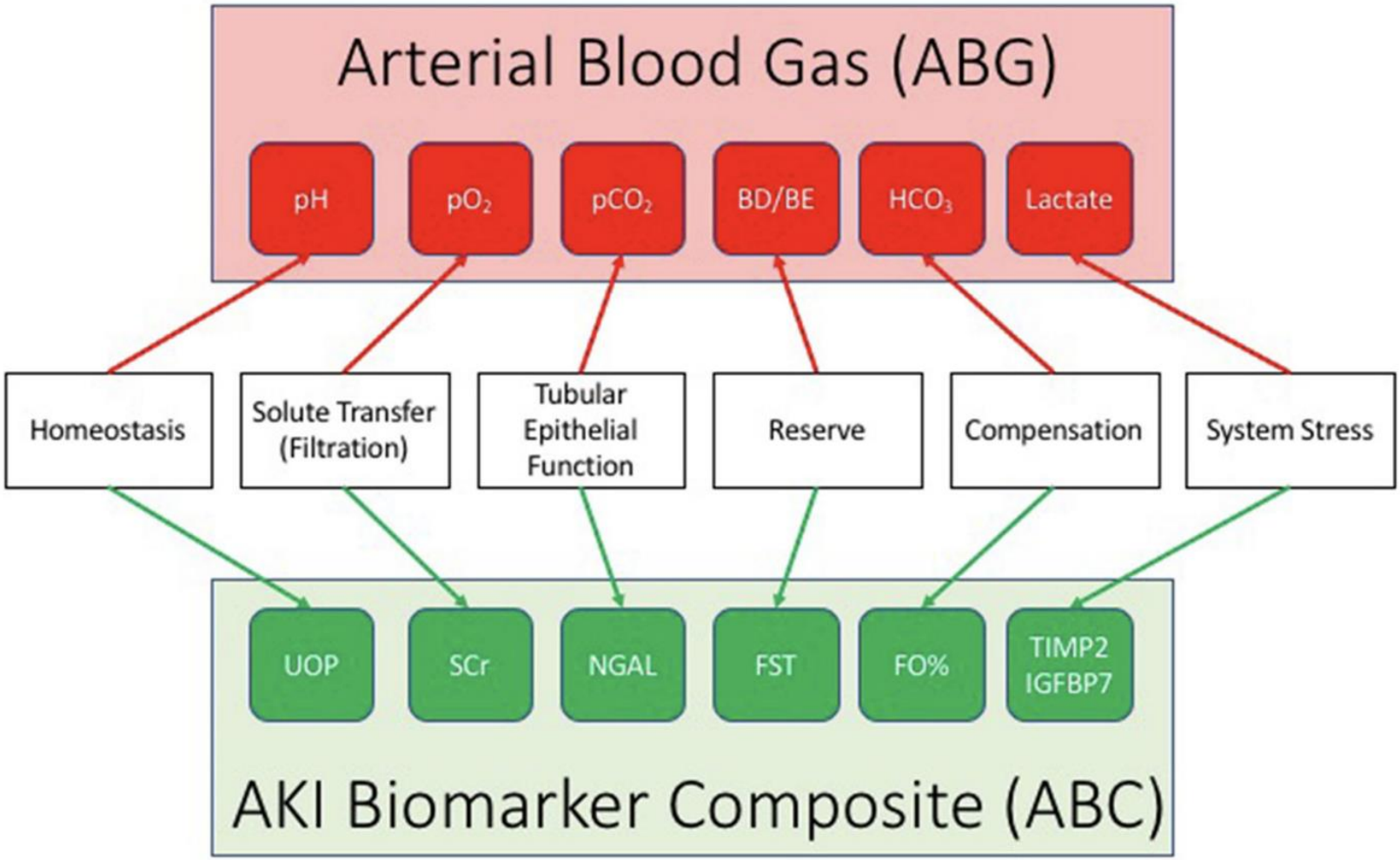
Krishnasamy et al. 2024

Pediatric Nephrology
Journal of the International Pediatric Nephrology Association
IPNA

Diagnosis of AKI and Assessing Risk of Progression: Changing Paradigms

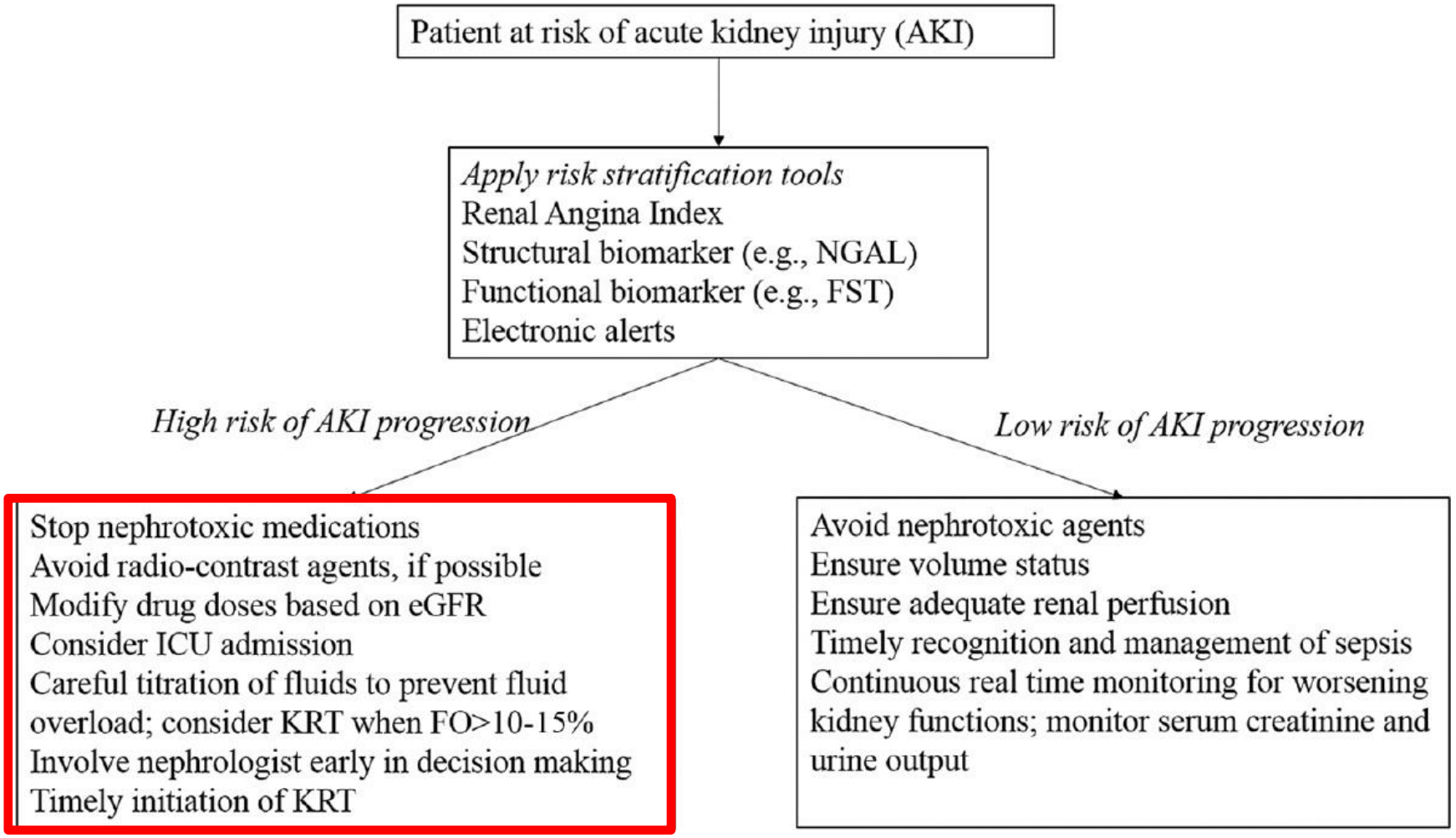


ABC approach for AKI severity assessment



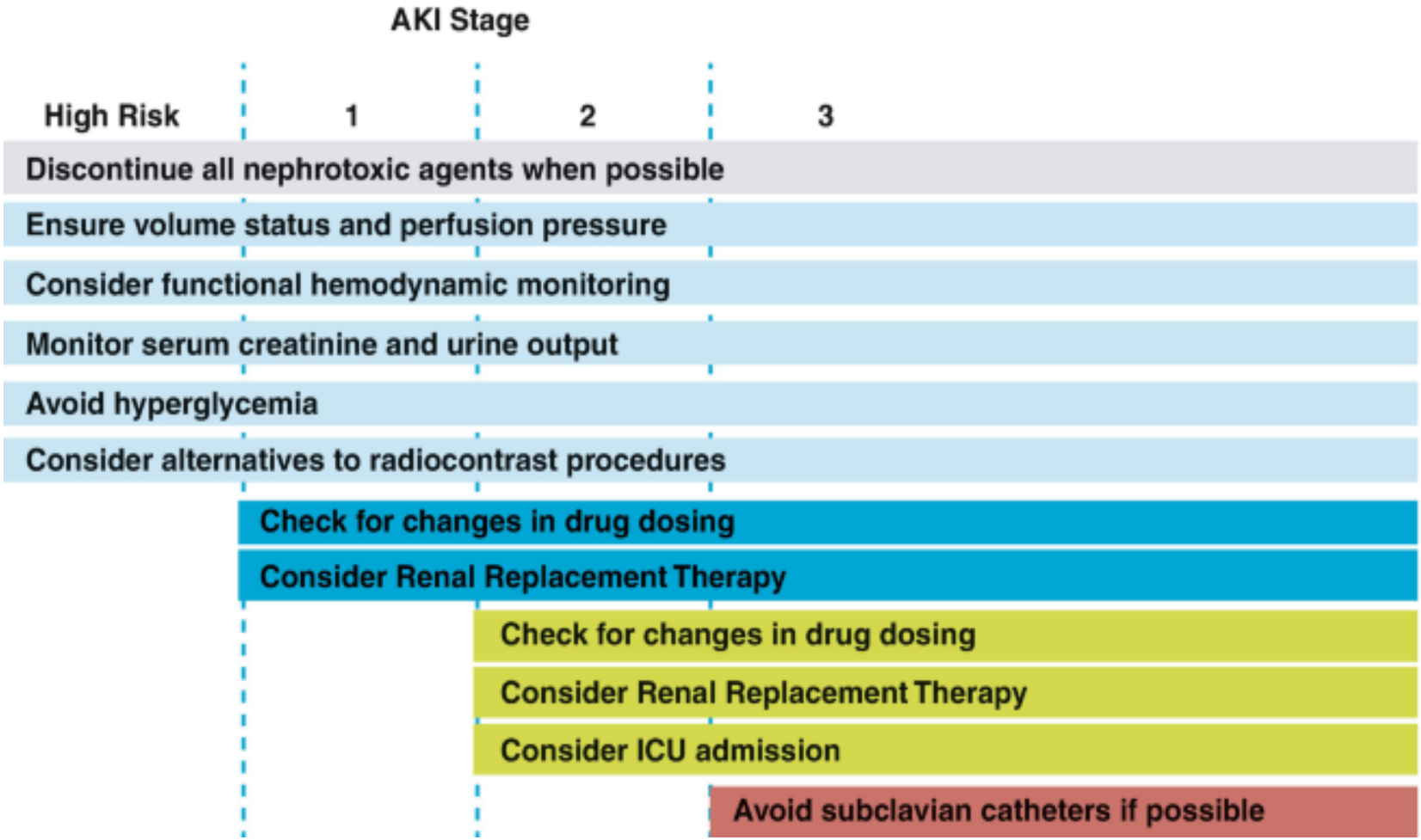
Front Pediatr 2020

Diagnosis of AKI and Assessing Risk of Progression: Changing Paradigms



Asian J Pediatr Nephrol 2022

AKI: Strategies for Prevention



Kidney Int. Suppl. 2012

Electronic alerts

Nephrotoxic Injury Negated by Just-in-time Action (NINJA)

Automatic alerts to treating physicians if aminoglycosides given for ≥ 3 days or ≥ 3 nephrotoxic medications given simultaneously

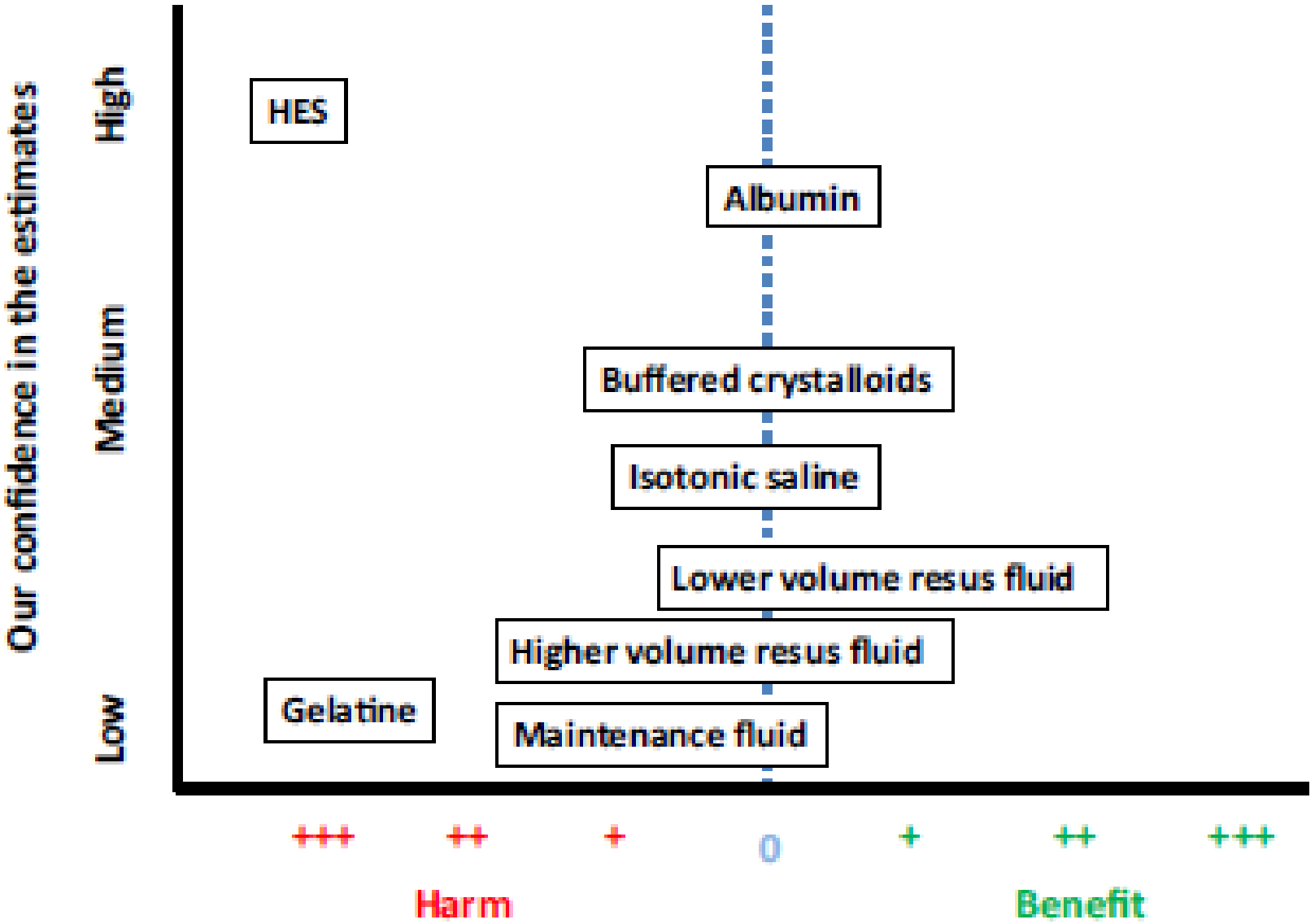
AKI rate decreased by 64%

Baby NINJA: AKI rate reduced from 30.9% to 11%

Acyclovir	Enalapril[d]	Ioxilan[c]	Polymixin B
Amikacin[b]	Enalaprilat[d]	Ketorolac	Sirolimus
Amphotericin liposomal[c]	Foscarnet	Lisinopril[d]	Sulfasalazine
Amphotericin B	Ganciclovir	Lithium	Tacrolimus
Aspirin	Gentamicin[b]	Losartan[d]	Tenofovir
Captopril[d]	Ibuprofen	Mesalamine	Ticarcillin–clavulanate
Carboplatin	Ifosfamide	Methotrexate	Tobramycin[b]
Celecoxib[d]	Indomethacin	Mitomycin	Topiramate
Cidofovir[c]	Iodixanol[c]	Nafcillin	Valacyclovir
Cisplatin	Iohexol[c]	Naproxen	Valganciclovir
Cyclosporine	Iopamidol[c]	Pamidronate	Valsartan[d]
Colistiethate	Iopromide[c]	Pentamidine	Vancomycin[b]
Deferasirox	Ioversol[c]	Piperacillin	Zoledronic acid
Diatrizoate meglumine[c]	Ioxaglate meglumine–Diatrizoate sodium[c]	Piperacillin–tazobactam	Zonisamide

Kidney Int 2020

Prevent & treat renal ischemia



Intensive Care Med (2017) 43:807–815

Prevent & treat renal ischemia

Impact of fluid interventions on risk of AKI

Intervention	Conclusion	Process
HES solutions	Established nephrotoxicity in critically ill patients	RCTs; systematic reviews: High risk of AKI, RRT, death with HES versus crystalloids
Gelatine solutions	Increasing evidence of nephrotoxicity	Before-after studies, some RCTs (low quality, quantity of data)
Crystalloid solutions	Focus on benefits vs harm	Saline and physiologic buffered fluids: Before after studies; few RCTs
Fluid boluses	Focus on uncertain efficacy	Before after studies; large RCTs
Fluid volume	Risk of fluid overload	RCTs, systematic reviews

Normal saline *vs.* Balanced solutions

	Human plasma	0.9% Sodium chloride	Hartmann's	Ringer's lactate	Ringer's acetate	Plasma-Lyte 148	Plasma-Lyte A pH 7.4	Sterofundin/ Ringerfundin
Osmolarity (mOsm/l)	275–295	308	278	273	276	295	295	309
pH	7.35–7.45	4.5–7.0	5.0–7.0	6.0–7.5	6.0–8.0	4.0–8.0	7.4	5.1–5.9
Sodium (mmol/l)	135–145	154	131	130	130	140	140	145
Chloride (mmol/l)	94–111	154	111	109	112	98	98	127
Potassium (mmol/l)	3.5–5.3	0	5	4	5	5	5	4
Calcium (mmol/l)	2.2–2.6	0	2	1.4	1	0	0	2.5
Magnesium (mmol/l)	0.8–1.0	0	0	0	1	1.5	1.5	1
Bicarbonate (mmol/l)	24–32							
Acetate (mmol/l)	1	0	0	0	27	27	27	24
Lactate (mmol/l)	1–2	0	29	28	0	0	0	0
Gluconate (mmol/l)	0	0	0	0	0	23	23	0
Maleate (mmol/l)	0	0		0		0	0	5
Na:Cl ratio	1.21:1 to 1.54:1	1:1	1.18:1	1.19:1	1.16:1	1.43:1	1.43:1	1.14:1

Pediatric Nephrology July 2018

Risks of excess chloride

Buffered fluids: As safe & effective as saline based; SPLIT trial; *SALT-ED*

Cochrane Database Syst Rev 2012; NEJM 2018

Prevent renal injury

Nephrotoxic Injury Negated by Just-in-time-Action **NINJA** (PP AKI Research Group)

Table 4 | List of nephrotoxic medications

Acyclovir	Enalaprilat	Mesalamine
Ambisome[a]	Foscarnet	Methotrexate
Amikacin	Gadopentetate dimeglumine[a]	Nafcillin
Amphotericin B	Gadoextate disodium[a]	Piperacillin/tazobactam
Captopril	Ganciclovir	Piperacillin
Carboplatin	Gentamicin	Sirolimus
Cefotaxime	Ibuprofen	Sulfasalazine
Ceftazidime	Ifosfamide	Tacrolimus
Cefuroxime	Iodixanol [a]	Ticarcillin/clavulanic acid
Cidofovir[a]	Iohexol[a]	Tobramycin
Cisplatin	Iopamidol[a]	Topiramate
Colistimethate	Ioversol[a]	Valacyclovir
Cyclosporine	Ketorolac	Valganciclovir
Dapsone	Lisinopril	Vancomycin
Enalapril	Lithium	Zonisamide

[a]Medications counted for 7 days after administration toward exposure due to their long half-life. All other listed medications count for 48 additional hours after exposure.

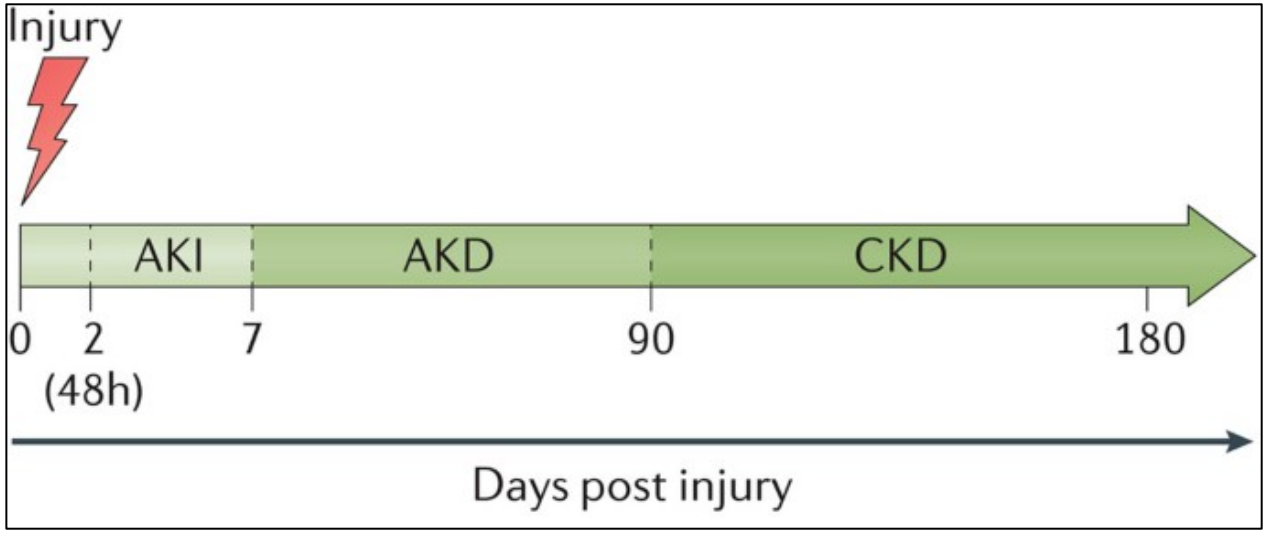
AKI reduction QI initiative

Identify hospitalized children receiving **nephrotoxic agents**: **≥3 days of aminoglycoside *or* 3 toxic agents**

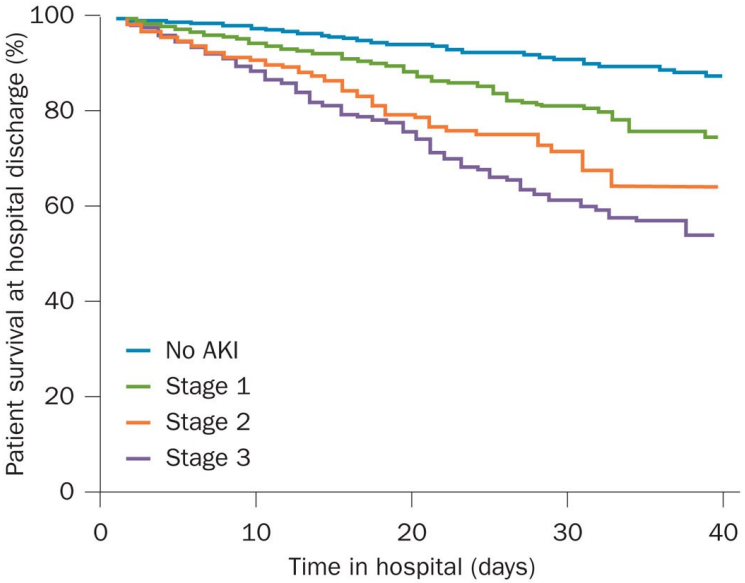
Daily creatinine

Reduced nephrotoxic agents exposure; **reduced incidence of AKI**

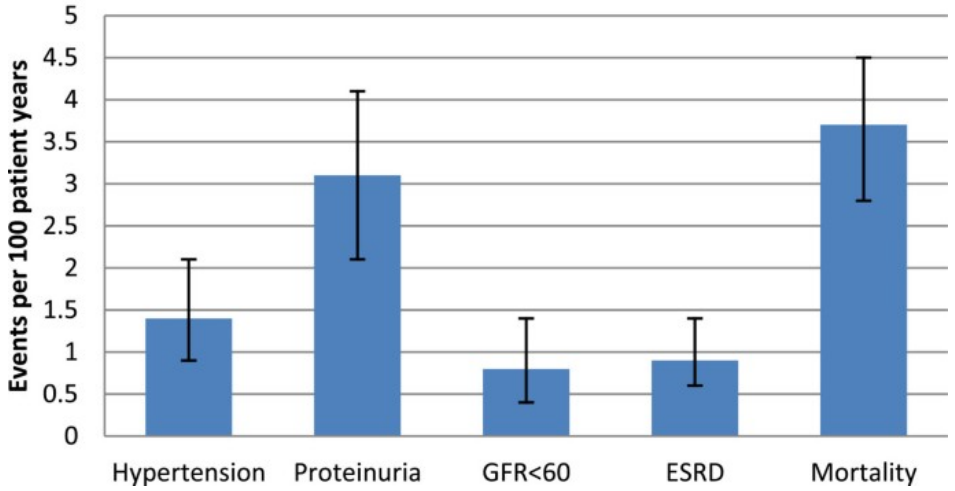
Outcomes of AKI



↑ Mortality, ICU and hospital stay



Long-term outcomes



Nat Rev Nephrol 2017
BMC Neph 2014

Take home messages

AKI occurs in 1 out of 4 children admitted to the ICU

Serum creatinine and urine output are the traditional biomarkers; albeit with limitations

Novel risk stratification tools have been identified; need further validation

AKI is independently associated with mortality and long-term adverse outcomes

Prevention of AKI is the key to improve overall outcomes

Slides courtesy: Prof A Bagga, Prof P Hari, Srinivasavaradan G, Sudarsan Krishnasamy (Division of Nephrology, Department of Pediatrics, AIIMS, New Delhi)

Fluid and electrolytes- Potassium

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Total body water(TBW) - divided between 2 main compartments

1.intracellular fluid (ICF) 2. extracellular fluid (ECF)

Fetus & newborn : ECF volume larger than ICF volume

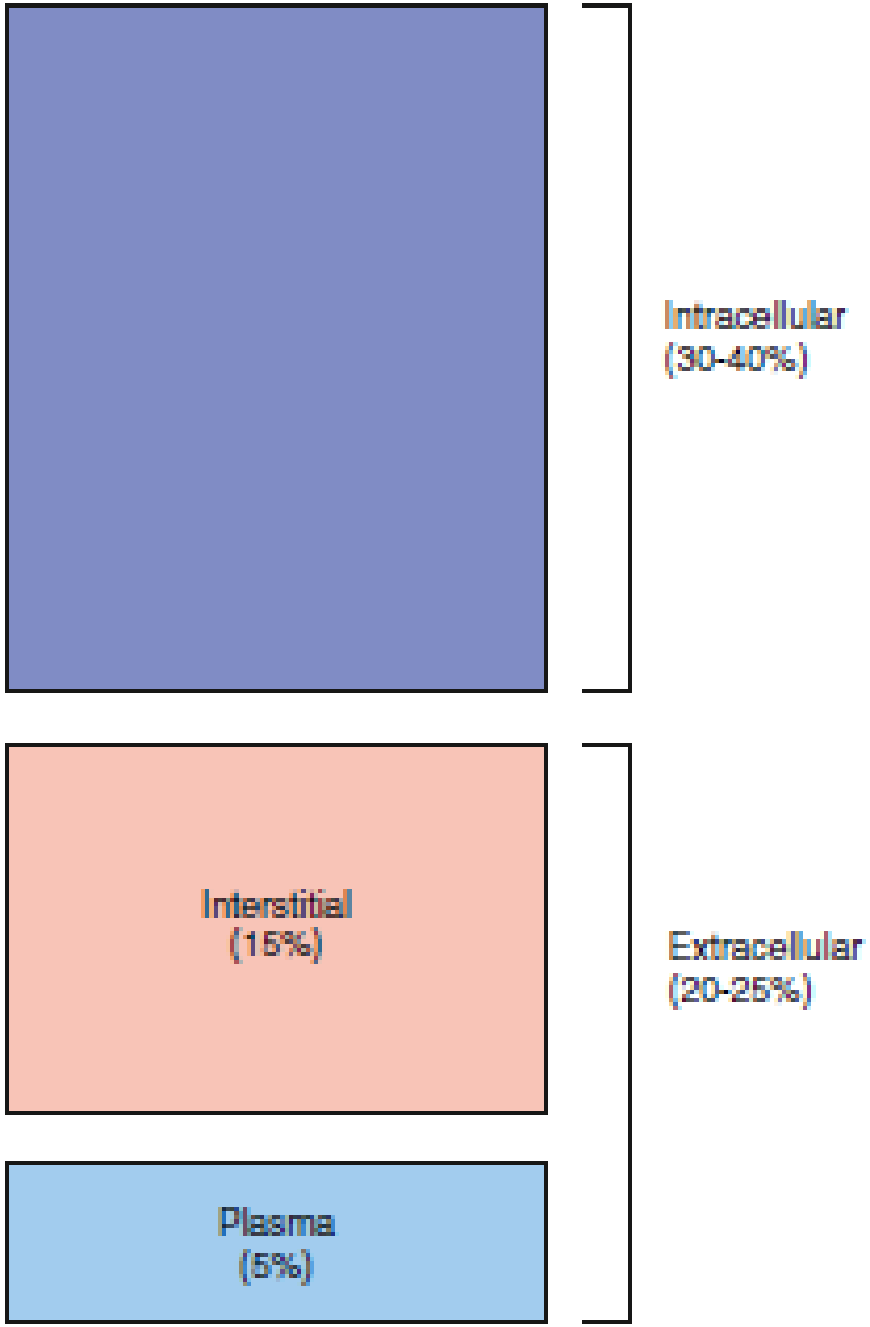
- Postnatal diuresis - immediate ECF volume decrease → continued ICF expansion from cellular growth

By 1 year: ratio of ICF to ECF volume ↣ adult levels

ECF volume - 20–25% of body weight

ICF volume - 30–40% of body weight

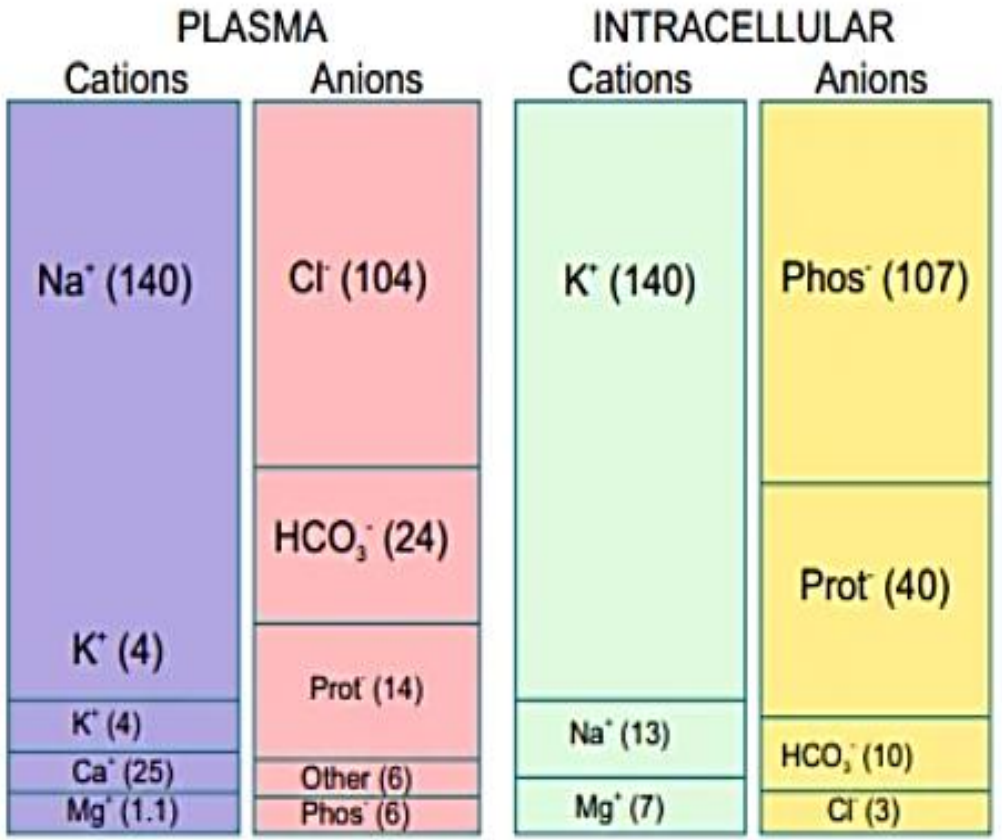
With puberty - increased muscle mass of males - higher ICF volume than females.

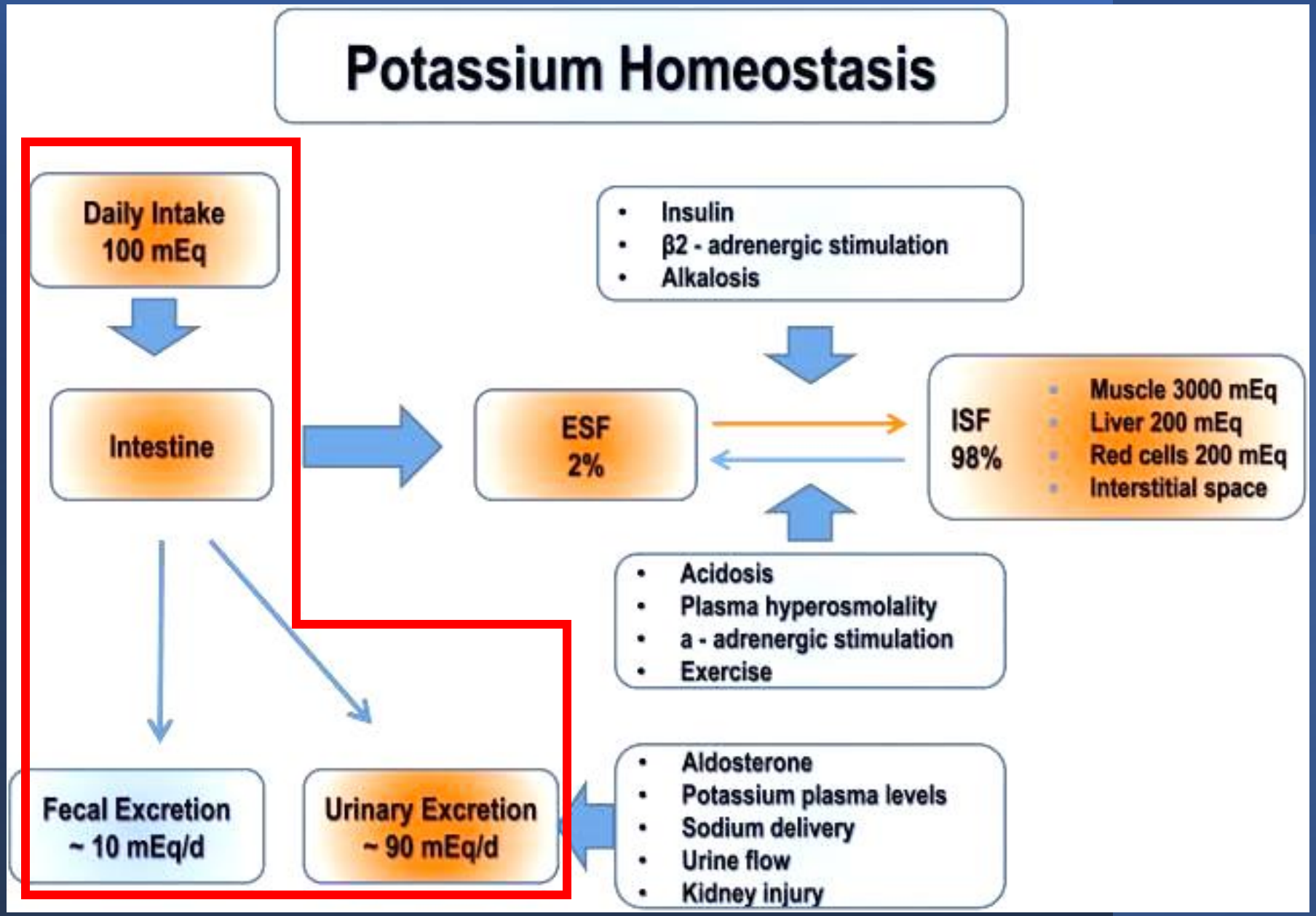


Potassium

Potassium (K+) most abundant cation in ICF :
30 times higher conc than in ECF

Age	Range (mEq/L or mmol/L)
Preterm	4 to 6.5
Newborn	3.7 to 5.9
Infant	4.1 to 5.3
Child >1 year old	3.5 to 5




Potassium Homeostasis
Daily Intake
100 mEq
Intestine
ESF
2%
ISF
98%
Muscle 3000 mEq
Liver 200 mEq
Red cells 200 mEq
Interstitial space
Insulin
β2 - adrenergic stimulation
Alkalosis
Acidosis
Plasma hyperosmolality
a - adrenergic stimulation
Exercise
Fecal Excretion
~ 10 mEq/d
Urinary Excretion
~ 90 mEq/d
Aldosterone
Potassium plasma levels
Sodium delivery
Urine flow
Kidney injury

Potassium: Body Content and Physiologic Function

Intracellular [K+] –Approximately 150 mEq/L - much higher than plasma [K+]

- Majority of body K+ in muscle
- Increased muscle mass ↣ increase in body K+ (puberty & males)

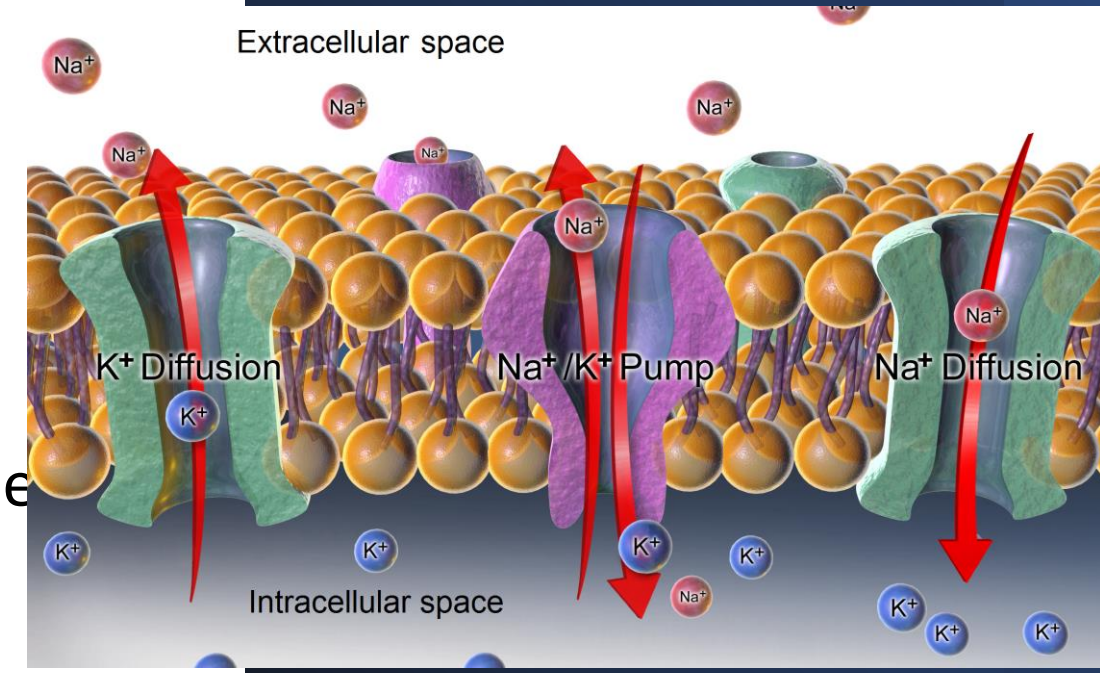
Majority of extracellular K+ : bone

<1% total body K+ in plasma

Intracellular to extracellular K+ ratio: determines threshold for cell to : generate an action potential & rate of cellular repolarization

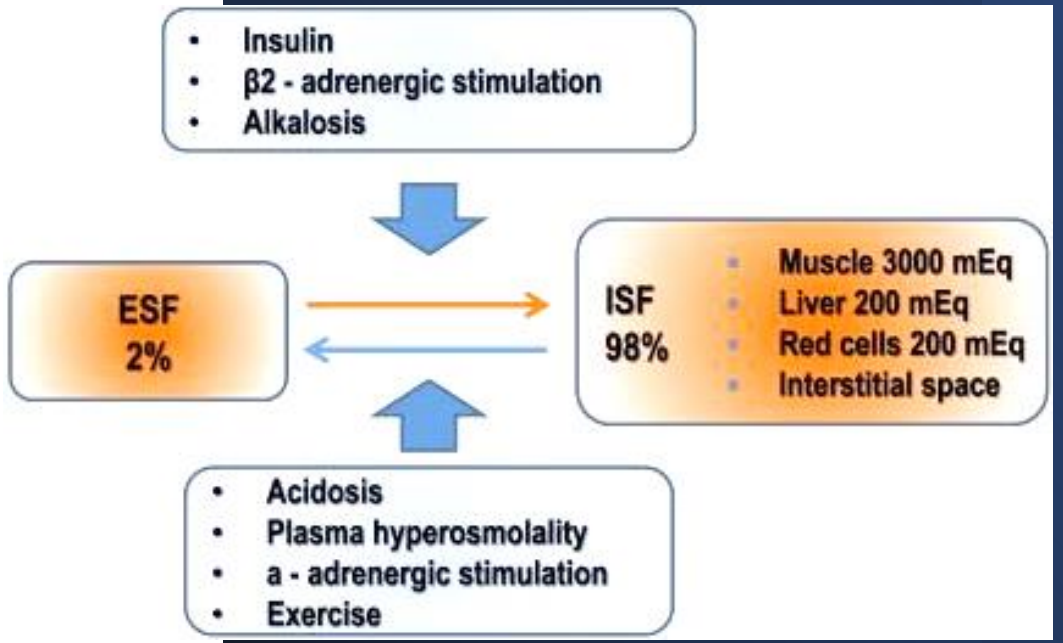
K+ necessary for maintaining cell volume - contribution to intracellular osmolality

- Na+,K+ -ATPase maintain high intracellular [K+] -
  - Pumps Na+ out of cell and K+ into cell
  - Balances normal leak of K+ out of cells via potassium channels - driven by favorable chemical gradient
- Resulting chemical gradient -produce resting membrane potential of cells
- K+ necessary
  - electrical responsiveness of nerve & muscle cells
  - contractility of cardiac, skeletal, smooth muscle
  - Above cells susceptible to changes in serum [K+]
- Conditions altering intracellular & extracellular compartments- alter distribution of K+



Factors altering K+ status

- Acid-base status affects K+ distribution: K+ channels & Na+K+ATPase
  - Acidosis drives potassium extracellularly
  - Alkalosis drives potassium intracellularly
- Insulin : activate Na+K+-ATPase : ↑ K+ movement into cells : post meal K+ absorption stimulates insulin secretion- mitigate hyperkalemia
- β-Adrenergic agonists stimulate Na+K+-ATPase: increase cellular uptake of K+ : increase protection (hyperkalemia stimulates adrenal release of catecholamines)
- α-Adrenergic agonists and exercise - net movement of K+ out of ICS
- Increase in plasma osmolality (mannitol infusion) →leads to water movement out of ICS(cells) → K+ follows - solvent drag
- Serum [K+] increases : approximately 0.6 mEq/L with each 10 mOsm rise in plasma osmolality



GIT role in Potassium homeostasis

Potassium - plentiful in food : 1-2 mEq/kg - recommended intake

90% of ingested K+ absorbed - small intestine

Colon exchanges body K+ for luminal Na+: Renal failure, aldosterone, glucocorticoids -↑ colonic secretion of K+

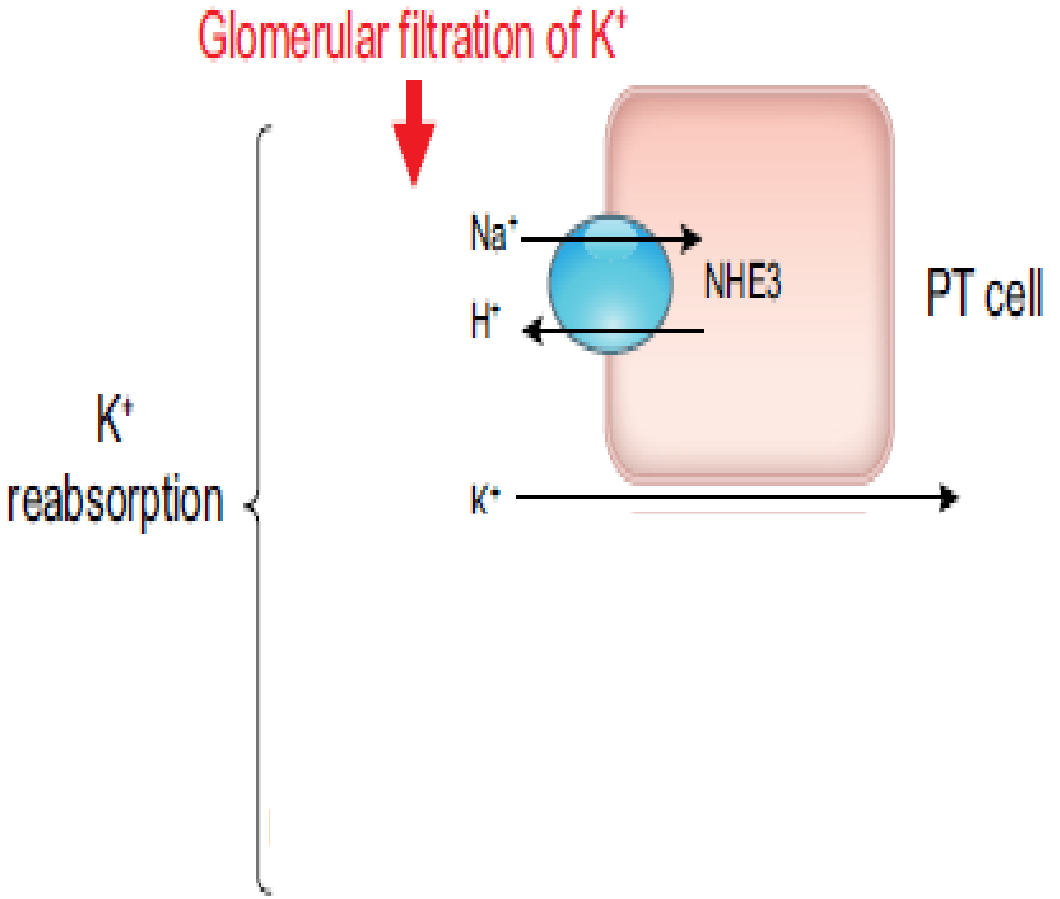
Regulation of intestinal losses - minimal role in maintaining potassium homeostasis –
increase in intestinal losses in renal failure & hyperkalemia, which stimulates aldosterone production - clinically significant -protect against hyperkalemia.

Potassium Excretion

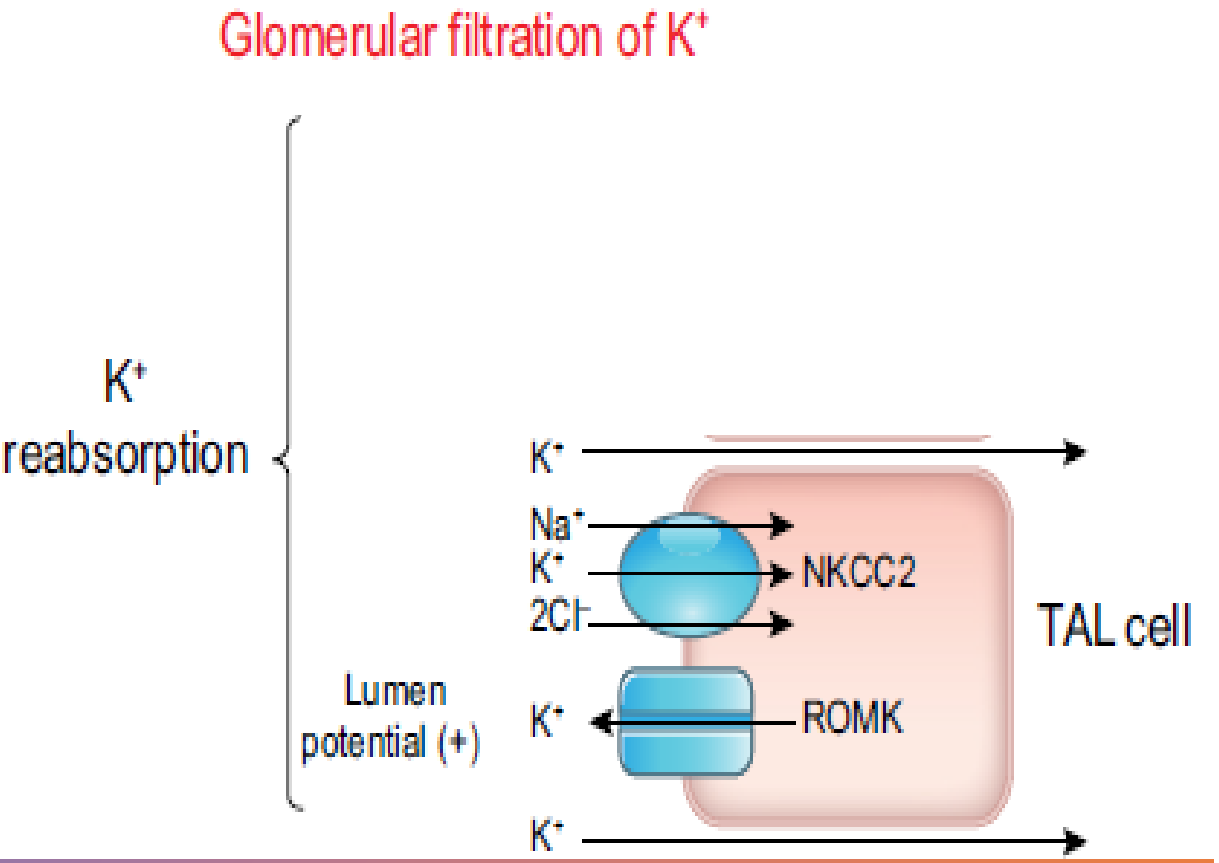
- Loss of K+ in sweat - minimal
- Colon – some ability to eliminate K+
- kidneys regulate long-term K+ balance - primarily responsible for maintaining total body potassium content
  - Most ingested K+ excreted in urine
  - Postprandial insulin shifts dietary potassium into cells by increasing Na+-K+-ATPase activity -till kidney excretes potassium load

Renal K+ handling- proximal tubule reabsorbtion

- > 90% filtered K+ reabsorbed- proximal tubule (PT) & thick ascending limb (TAL) of loop of Henle
- In early proximal tubule: passive K+ reabsorption paracellularly through “solvent drag,” - secondary to Na & H2O reabsorption
- In late proximal tubule : luminal voltage shifts from negative to positive - provide additional driving force for paracellular reabsorption of K+



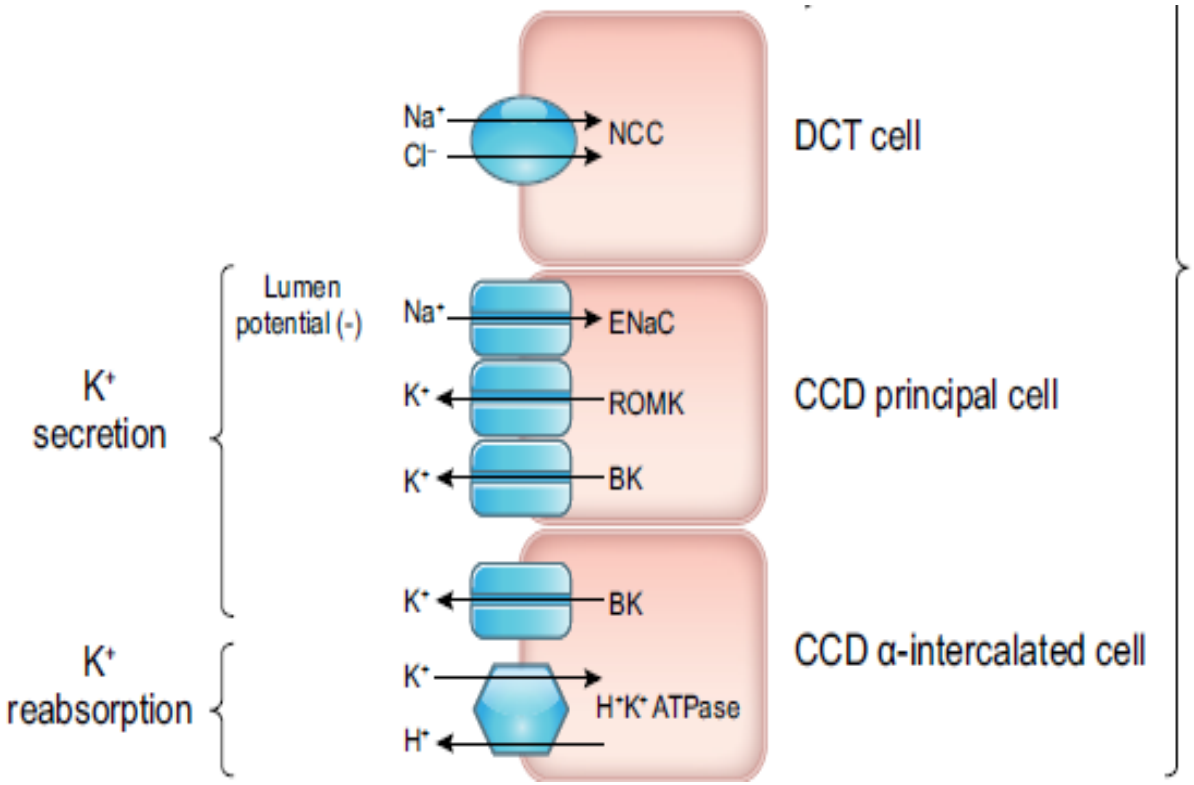
Renal K+ handling- thick ascending limb of loop of Henle reabsorbtion



- Reabsorption of K+ by proximal tubule & Thick ascending limb : paracellular & transcellular reabsorbtion : relatively constant - on average- (~10%) of filtered K load reaches distal nephron-
- **Major apical transporter-Na-K-2Cl cotransporter (NKCC2)** reabsorbs Na, K, Cl : driving force : low intracellular Na concentration generated by basolateral Na-K-ATPase
- Activity depends on K recycling from cell to tubular lumen by renal outer medullary K channel (ROMK, also called Kir1.1) : K+ recycling through ROMK → positive luminal charge – provide additional driving force for paracellular K+ reabsorption

Distal nephron K+ handling(secretion)

- K+ secretion determined by
  - intracellular & luminal K+ concentrations
  - Voltage difference across apical plasma membrane & its K+ permeability
- K secretion mediated by
  - K chloride cotransporters (KCC)
  - Renal outer medullary K channel (ROMK)
  - “big” K (BK) channels
- K secretion
  - increases in cells that express ENaC(epithelial sodium channels) & renal outer medullary K channel (ROMK) - especially principal cells in collecting duct
  - result of electrochemical coupling of Na+ reabsorption by ENaC to K secretion by ROMK (electrogenic secretion)

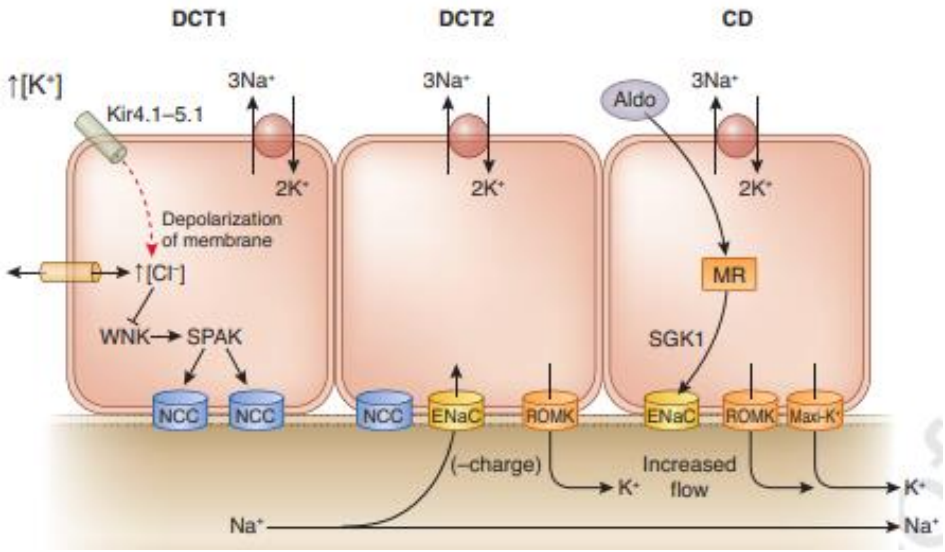


Under K depletion : H-K-ATPase in intercalated cells switch distal nephron function : from K+ secretion to K+ reabsorption

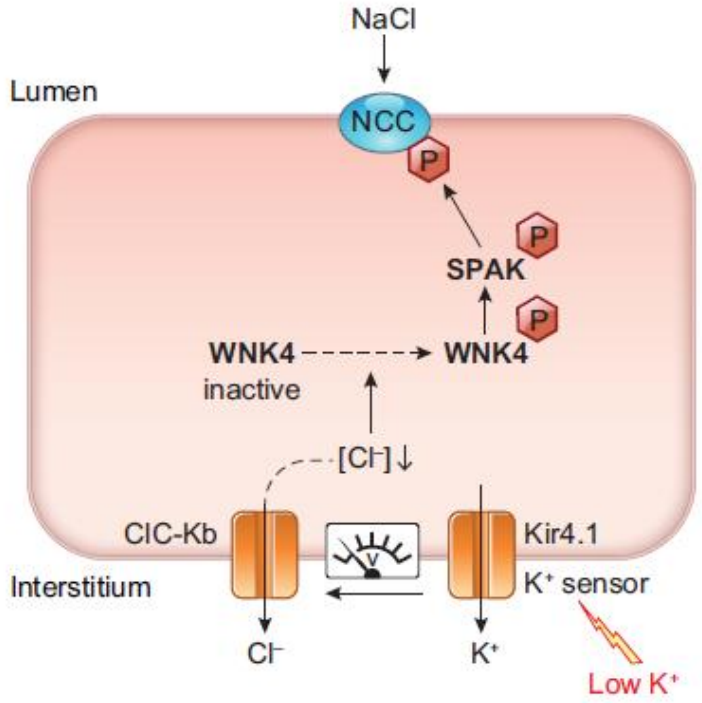
Aldosterone

- Principal hormone regulating K+ secretion- released response to ↑plasma K+
- Main site of action - cortical collecting duct- stimulates Na+ movement from tubule into cells - movement creates a negative charge in tubular lumen - facilitate K+ excretion
- big-K channels (BK, or “maxi-K” channels) -also regulated by aldosterone
- ↑ intracellular Na+ stimulates basolateral Na+,K+-ATPase →→more K+ to move into cells lining cortical collecting duct

Potassium Excretion IN HYPERKALEMIA



Potassium (Ex/Se)cretion IN HYPOKALEMIA



In response to low extracellular K → intracellular K moves out of DCT cells through Kir4.1 -result in membrane hyperpolarization and Cl efflux through ClC-Kb.

Resultant decrease in intracellular Cl relieves Cl-mediated inhibition of WNK4

Allow phosphorylation of SPAK and subsequently NCC(sodium-chloride cotransporter)

Leads to increased Na reabsorption in DCT, reducing distal Na delivery -limits K secretion and Kaliuresis

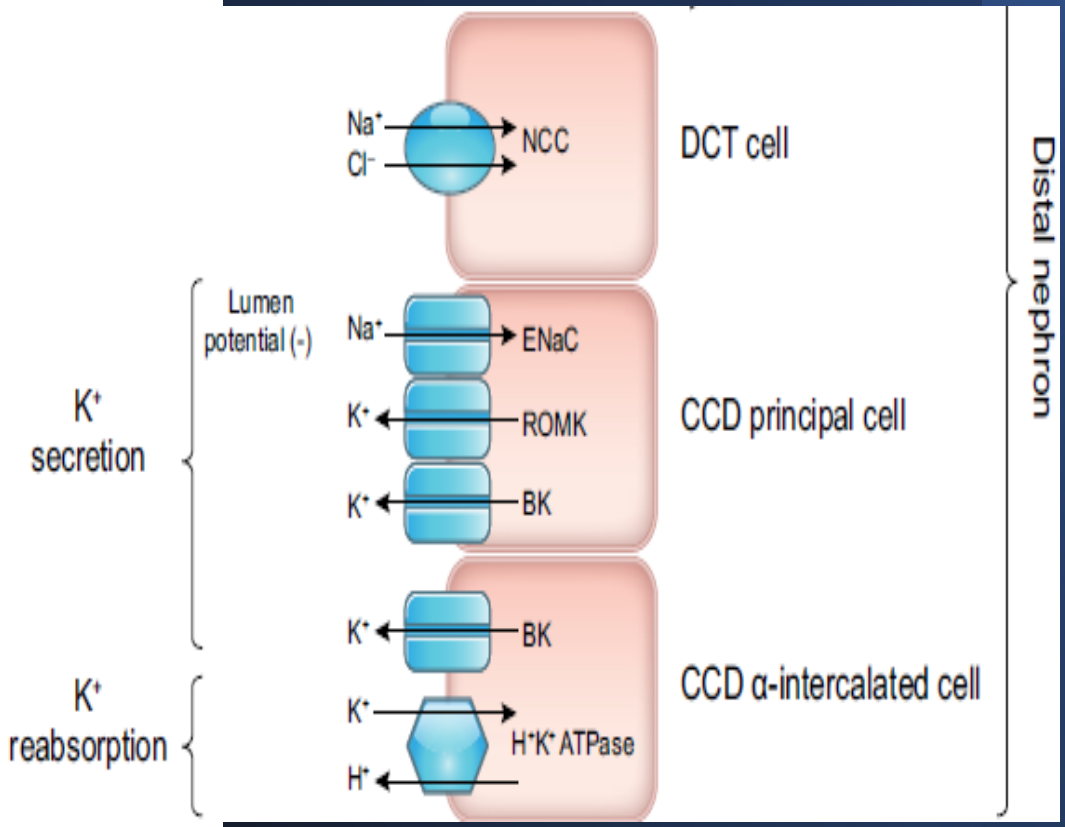
WNK, “with-no-lysine” kinases
SPAK(Ste20-related proline/alanine-rich kinase
SGK1; serum and glucocorticoid regulated kinase 1
ClC-kb: Chloride channel -Kb

Hoorn EJ, Gritter M, Cuevas CA, Fenton RA. Regulation of the renal NaCl cotransporter and its role in potassium homeostasis. Physiological reviews. 2020 Jan 1;100(1):321-56.

Renal K handling

In summary, K secretion in distal nephron primarily determined

- Plasma K+ concentration
- Distal Na+ delivery
- Tubular flow
- Aldosterone
- Interaction between ENaC, ROMK & BK channels
- Acid-base status



Hypokalemia

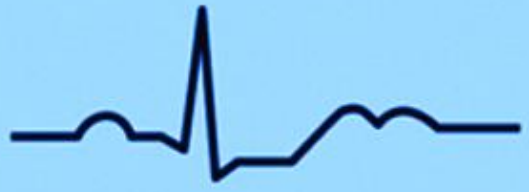
Hypokalemia

mild : potassium level from 3 to less than 3.5 mEq/L

moderate : potassium level 2.5 to less than 3 mEq/L

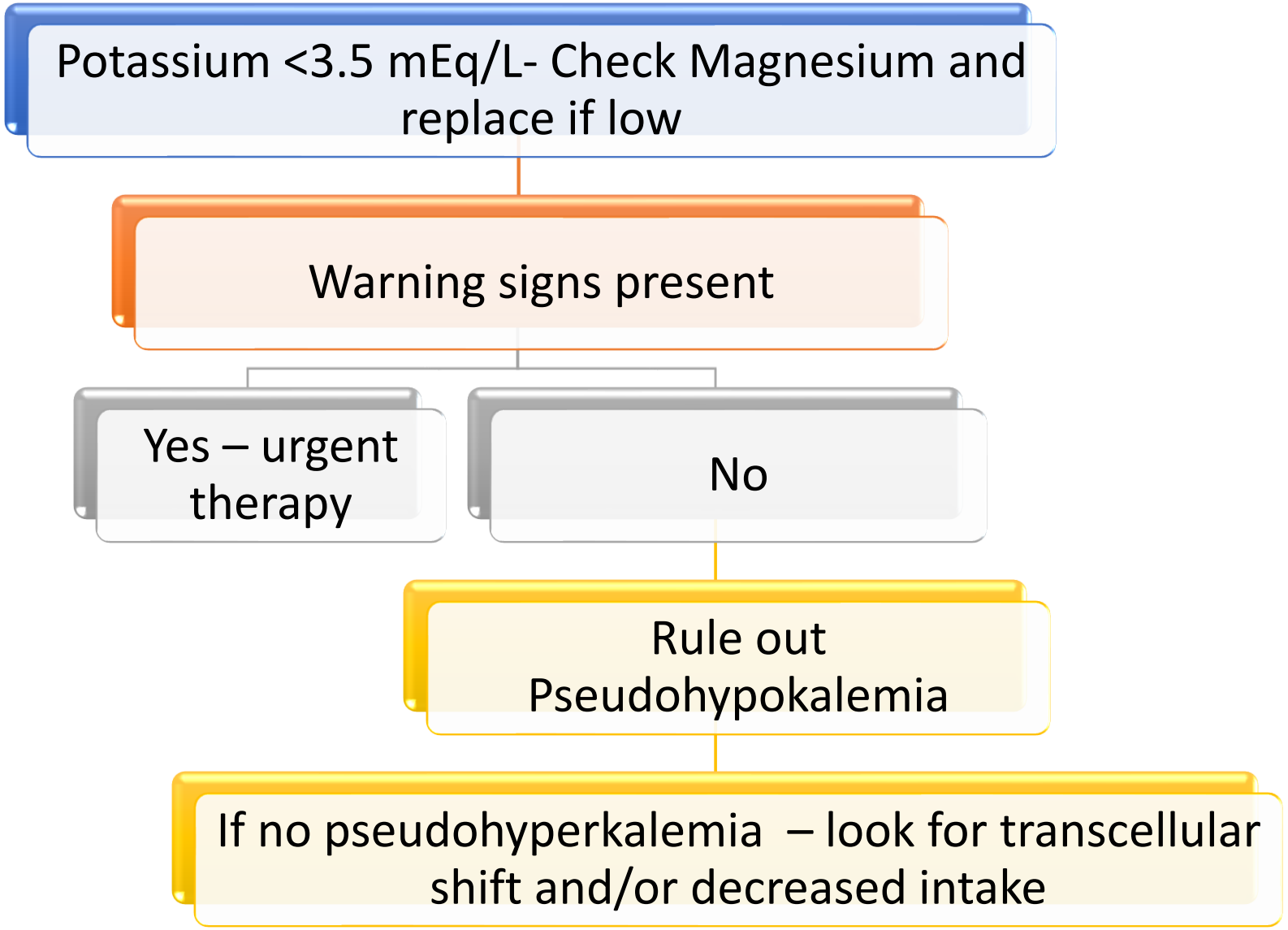
severe : potassium level less than 2.5 mEq/L

- **Hypokalemia –**
  - Decreased intake, extrarenal losses, renal losses -all associated with total body K+ depletion- most cases related to gastroenteritis
- **Spurious hypokalemia**
  - in leukemia & elevated WBC counts
  - if plasma for analysis left at room temperature - permit WBCs to take up K+ from plasma

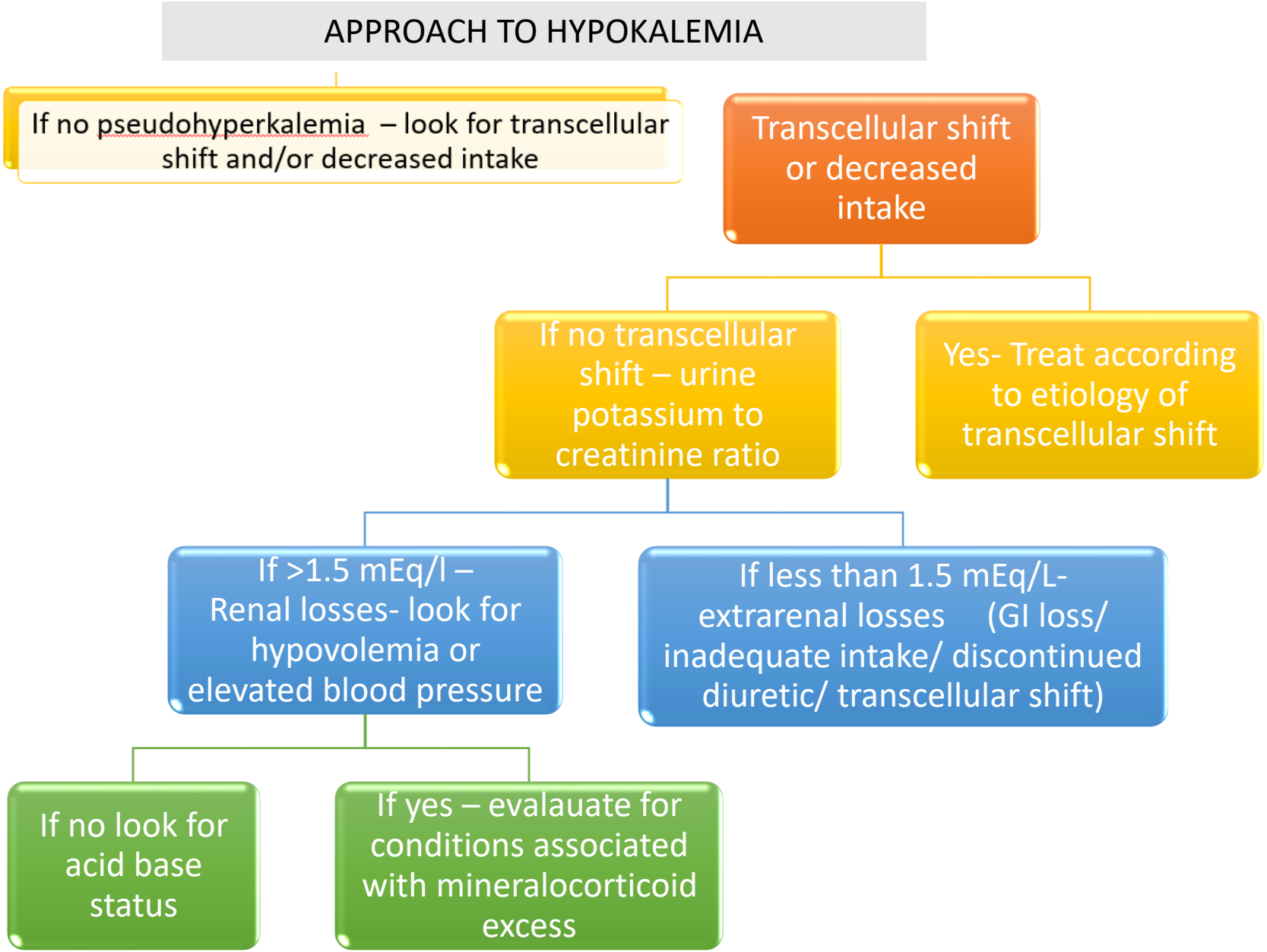
Hypokalemia		Depressed ST segment Diphasic T wave Prominent U wave
Normal		

APPROACH TO HYPOKALEMIA

Step 1

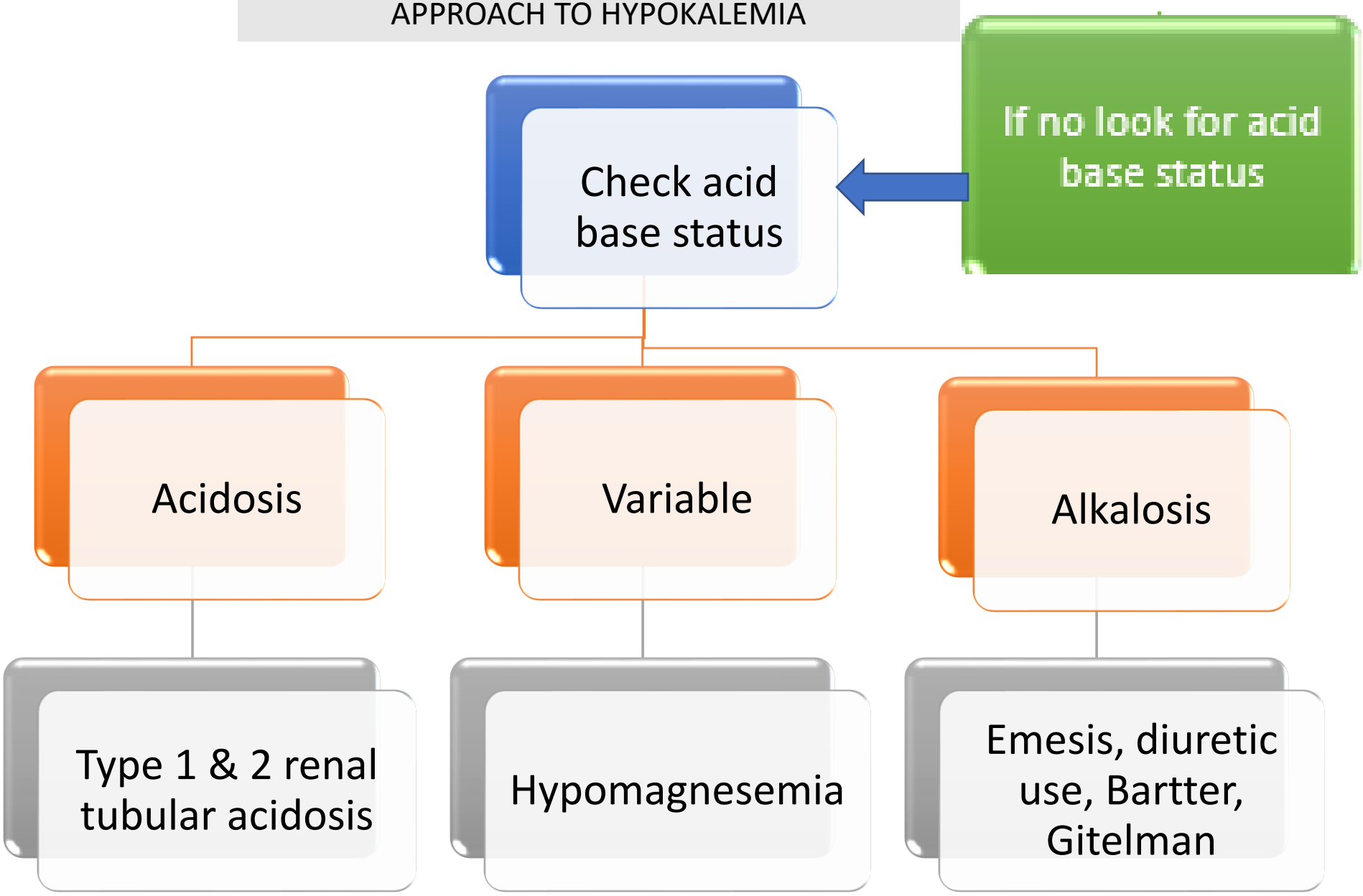


Step 2


APPROACH TO HYPOKALEMIA
If no pseudohyperkalemia – look for transcellular shift and/or decreased intake
Transcellular shift or decreased intake
If no transcellular shift – urine potassium to creatinine ratio
Yes- Treat according to etiology of transcellular shift
If >1.5 mEq/l – Renal losses- look for hypovolemia or elevated blood pressure
If less than 1.5 mEq/L- extrarenal losses (GI loss/ inadequate intake/ discontinued diuretic/ transcellular shift)
If no look for acid base status
If yes – evalauate for conditions associated with mineralocorticoid excess

APPROACH TO HYPOKALEMIA

Step 3

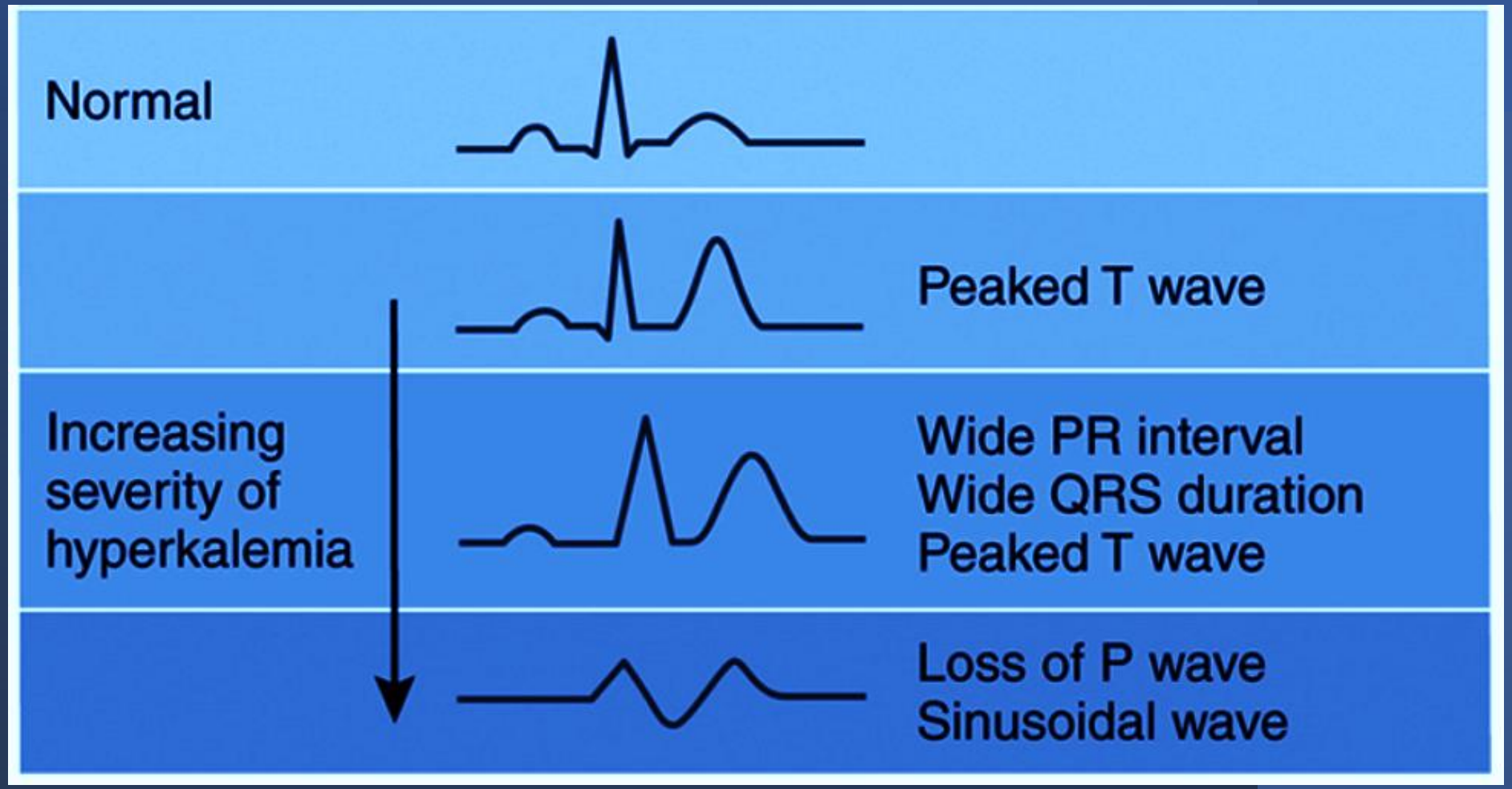


Hyperkalemia

Hyperkalemia	Pathophysiological correlation
Increased potassium intake (rare cause -with exception -children with chronic kidney disease)	Exposure to high potassium loads in intravenous fluids or medications Exposure to potassium-containing medications Massive transfusions of stored blood
Transcellular potassium movement	Structural cellular damage due to: Hemolysis /Rhabdomyolysis / Tumor lysis No structural cellular injury: Metabolic acidosis / Diabetic ketoacidosis / Hyperkalemia periodic paralysis
Abnormal renal potassium excretion	Decreased effective circulating volume Decreased RAAS activity: Cong adrenal hyperplasia/ Adrenal insufficiency Drug effect (ACE inhibitor/ARB, eplerenone, spironolactone or aliskiren) Significant renal impairment + either acute or chronic loss of GFR Impaired tubular potassium secretion: Reflux nephropathy /Obstructive uropathy / Sickle cell nephropathy / Drug effect (amiloride, triamterene) / Hypoaldosteronism (type IV renal tubular acidosis)
Pseudohyperkalemia	Hemolyzed specimen Leukocytosis or thrombocytosis

HYPERKALEMIA

- S.K+ normally 0.4 mEq/L higher than plasma value – secondary to K+ release from cells during clot formation
  - Exaggerated with thrombocytosis - K+ release from platelets
  - For every 100,000/m3 increase –S.K+ rise - 0.15 mEq/L
  - Elevated WBC counts, typically >200,000/m3- S.K+ dramatic elevation :
- Analysis of plasma sample - provides an accurate result.

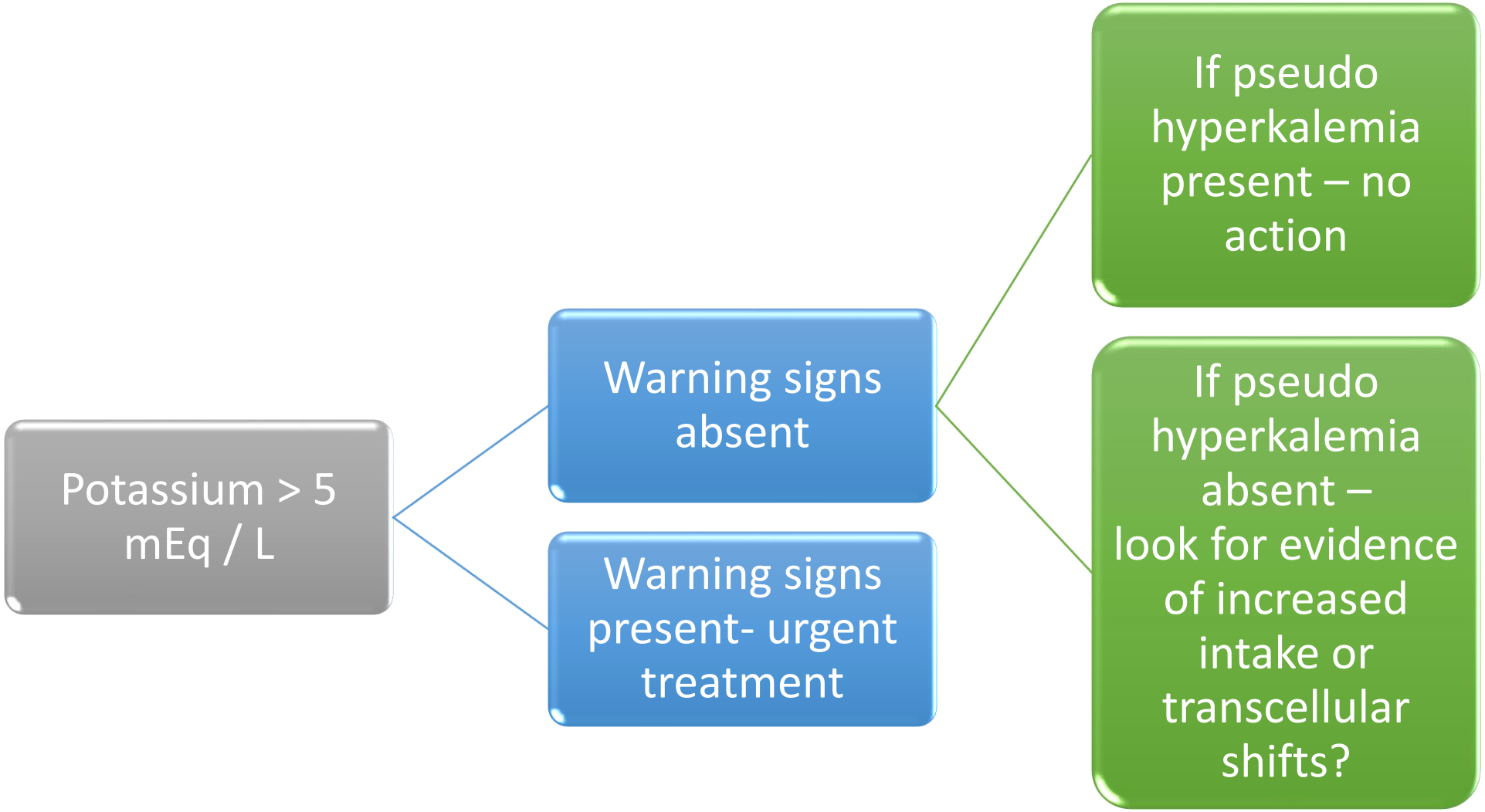

Normal
Peaked T wave
Increasing severity of hyperkalemia
Wide PR interval
Wide QRS duration
Peaked T wave
Loss of P wave
Sinusoidal wave

Pseudohyperkalemia

- Analyze sample promptly
  - to avoid K+ release from cells - occurs if sample is stored in cold
- Pneumatic tube transport - if cell membranes fragile (leukemia)- pseudohyperkalemia
- heparin causes lysis of leukemic cells - false elevation of plasma sample
- blood gas syringe - less heparin - more accurate reading than standard tube
- rare genetic disorders –cause in vitro leakage of K+ from red blood cells (RBCs) - causes familial **pseudohyperkalemia** (autosomal dominant; *ABCB6* gene).

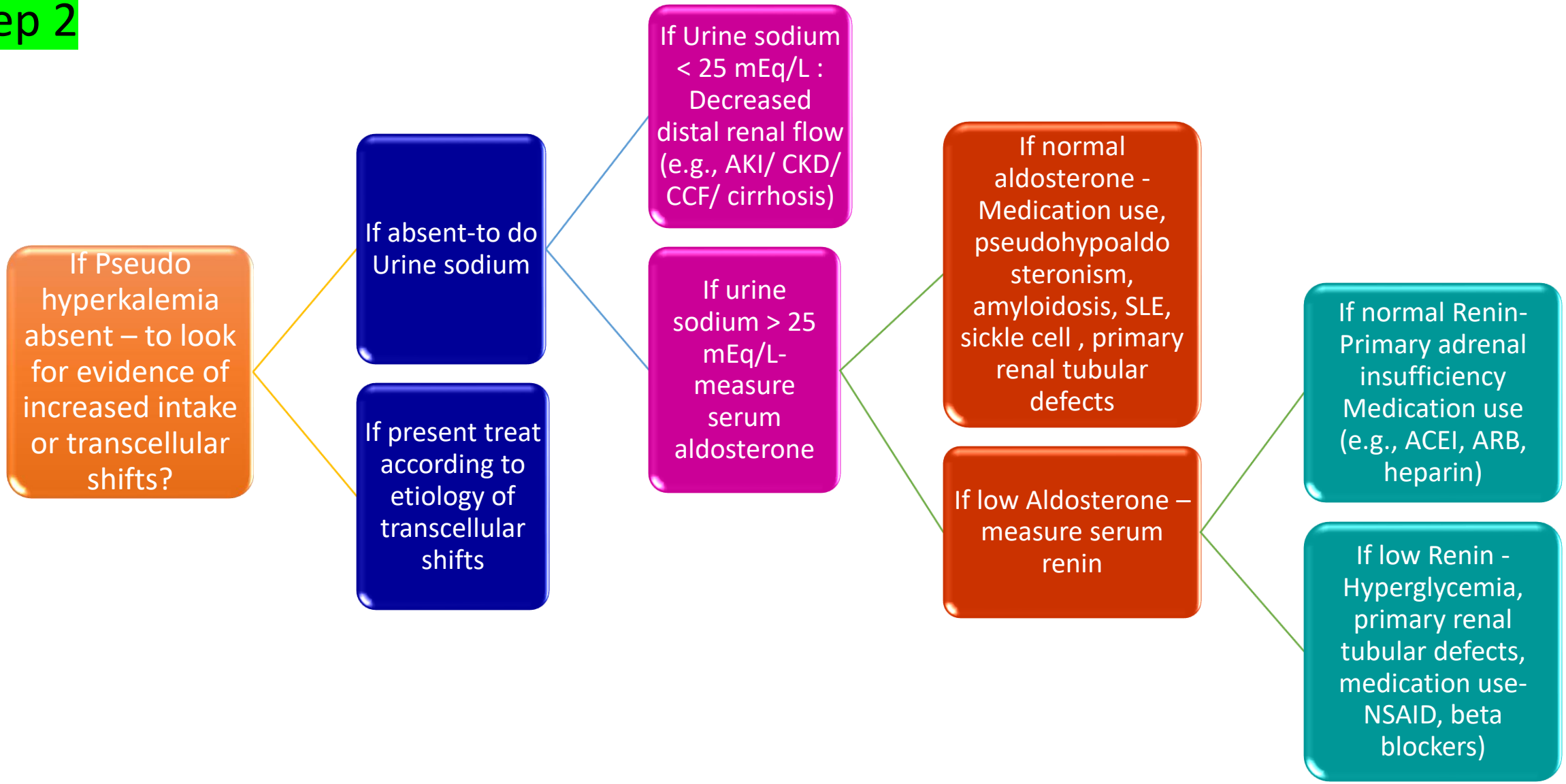
APPROACH TO HYPERKALEMIA

Step 1



APPROACH TO HYPERKALEMIA

Step 2



Thanking you

Approach to Polyuria in children

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NephKids 2024, Chennai, 15 Sept 2024

Approach to polyuria

- 9 months boy presents with
  - passing urine "very frequently" and "drinking excess of water" since 5 months of age

- Definitions
- Simplified approach to polyuria
- Case scenarios

Polyuria: Definition

- Physiological urine production differs across the lifespan
- Polyuria or inappropriately excessive urine volume relative to circulating volume and osmolality, is defined over a **24-h period** as

  > 6 ml/kg/hour or ~150 mL/kg in neonates,
  > 4 ml/kg/hour or ~100 mL/kg or 2L/m^2 in children
  > 2 ml/kg/hour or ~ 50 mL/kg in adults

Di Iorgi N, Napoli F, Allegri AEM, et al. Diabetes insipidus--diagnosis and management. Horm Res Paediatr. 2012;77(2):69-84.

Tony Huynh, et al. Paediatric perspectives in the diagnosis of polyuria-polydipsia syndrome. Clinical Endocrinology. 2023;1–13.

Polyuria

- Urine volumes

  - > 3 L / day in adults

  - > 2 L / m^2 in children

  OR

  - > 4 ml/kg/hour or > 100 ml/kg/day

  - > 6 ml/kg/hour in neonates

Polyuria in children

- Definition: Excessive urine output, greater than 4 ml/kg/hour

- To be differentiated from frequent urination
  - seen with UTI's,
  - dysfunctional voiding, or
  - physiological in infants due to small bladder capacity

- Nocturia / NE

Urine volumes not increased

Polyuria

- Difficult to quantify urine volumes in an infant

Is it polyuria or Not?

- Yes, It is Polyuria if
  - Urine volumes > 100 ml/kg/day (> 4ml /kg/hour)
  - Associated Nocturia
  - Associated polydipsia

For all practical purposes, absence of nocturia and polydipsia usually rules out polyuria

Polydipsia

- Normal intake ~ 1500 ml/m^2/ day based on the expected loss of water thru urine, and skin)

- Polydipsia: increased intake of liquids (> 3000 ml/m^2/day)

- Characterized by
  - excessive irritability in infants (which resolves after feeding water)

    and

  - drinking of liquids even at night (the child gets up frequently at night to drink water)

- Nocturnal polydipsia is significant

Is it polydipsia or Not?

Yes, it may be polydipsia if

- fluid intake of > 3000 ml/m^2/day (in older children)
- If associated with
  - Polyuria
  - Nocturnal Polydipsia
  - Failure to thrive
  - Chronic headache

Presenting features of polyuria

- Infants may present with
  - excessive crying, irritability [resolves with water]
  - weight loss,
  - constipation,
  - excessively wet diapers, and
  - failure to thrive.

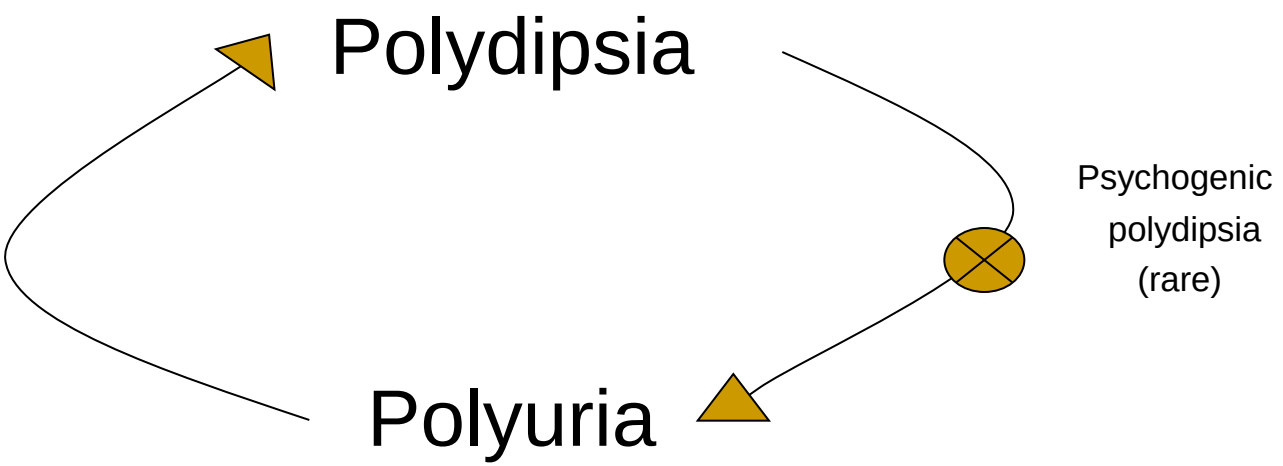
- Younger children often manifest with primary enuresis and difficulty in toilet training.

- Older children characteristically have high urine output and nocturia leading to disturbed sleep and easy fatigability.

Presenting features of polyuria

- Polydypsia may be intense or uncontrollable and may involve craving for ice.
- Anorexia due to preference of water over food results in loss of weight and failure to thrive.
- Irritability, fatigue due to disturbed sleep and affection of linear growth is seen in all age groups.
- Seizures due to severe hypernatremia, hyperosmolar dehydration and potential hypoxia may lead to neurological sequel in the form of intracranial bleed and developmental delay

What came first?



Polyuria – Polydipsia Syndrome

- In children three pathophysiologic mechanisms give rise to polydypsia and polyuria:

  - *Central* (vasopressin sensitive) DI caused by defective vasopressin synthesis and/or secretion.

  - *Nephrogenic* (vasopressin resistant) DI caused by defective renal tubular response to vasopressin action.

  - *Primary polydypsia* due to compulsive water drinking (psychogenic) or defective thirst mechanism (dipsogenic).

Approach to a child with Polyuria

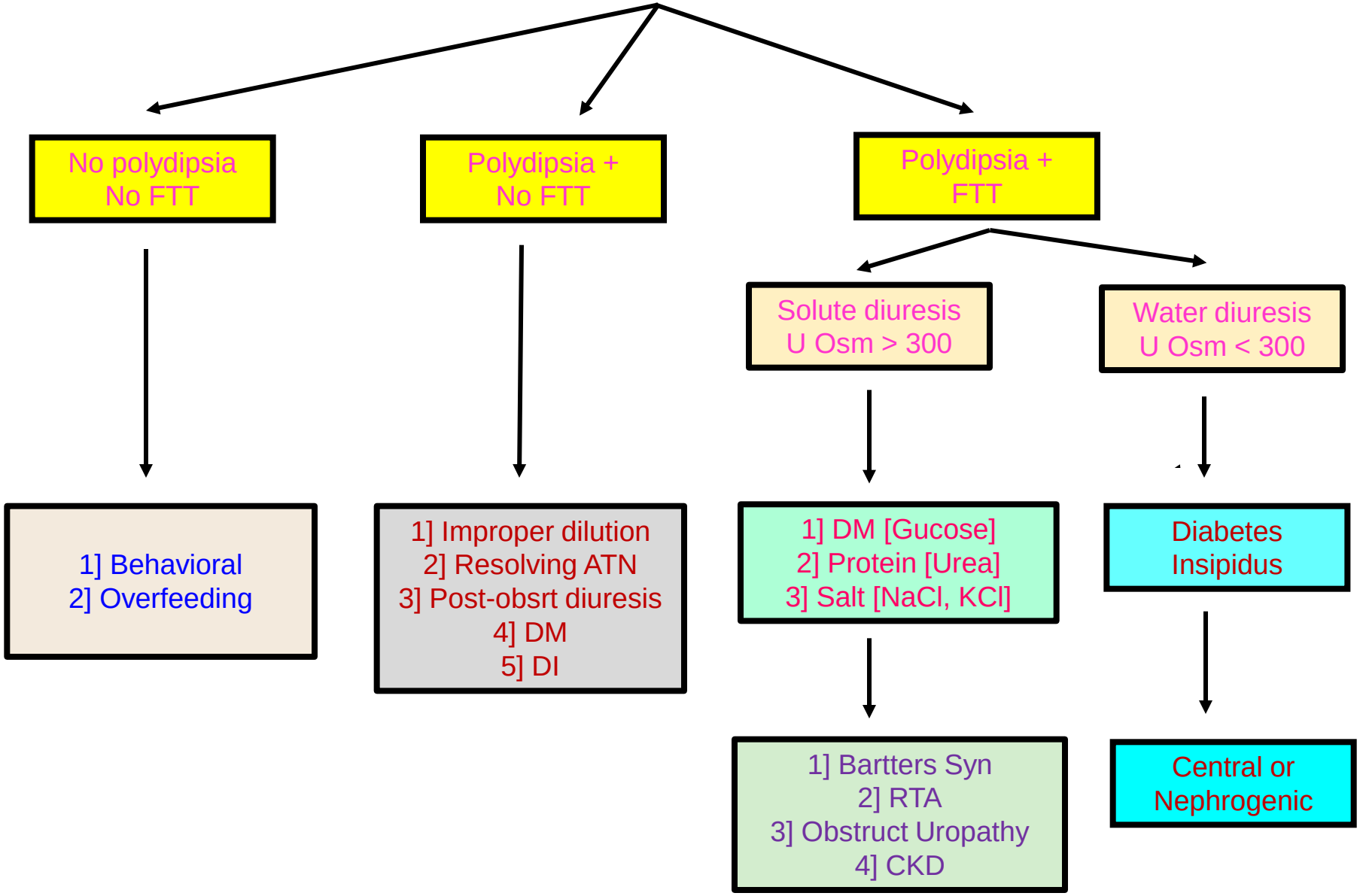
- Duration of polyuria?
- Is it associated with polydipsia?
- Is it associated with failure to thrive?

Transient Polyuria

- Improper dilution of formula feeds
- Resolving phase of ATN [Tubular Injury]
- Post-obstructive diuresis [Excretion of retained NaCl / Urea]
- Rarely, high protein diet (Enteral / TPN) in a hospitalized patient
- Mannitol therapy [Osmotic agent]

Acute history, and absence of FTT

Approach to a child with Polyuria



Approach to a child with Polyuria

1) Detailed history:

Quantify output [compare with siblings],

Nocturnal polyuria,

Polydipsia,

FTT,

Preparation of feeds, …

2) Physical exam:

Growth,

Signs of dehydration,

Renal or Bladder mass,

Ambiguous genitalia,

Rickets,

Fundus (older child – CDI)

Approach to a child with Polyuria

3) Investigations:

- CUE: **Specific gravity,** pH, protein, glucose, sediment
- Random Blood Sugar (FBS, PPBS)
- Serum creatinine, blood urea
- Serum electrolytes + Serum calcium
- Venous Blood Gas
- Spot urine electrolytes
- Urine osmolality

4) Abdominal USG: Renal size, hydronephrosis, nephrocalcinosis

5) Selected cases (DI is confirmed): Water deprivation test, MRI Brain

Step wise approach to polyuria

- Step 1: Is Polyuria associated with Polydispia +/- FTT
- Step 2: Complete urine examination (SG, Glucose) [Urinary concentrating ability]
- Step 3: Blood urea, Blood creatinine [Rule out CKD]
- Step 4: USG abdomen for kidney size, HN, HU, nephrocalcinosis
  [R/o Hypodysplasia, PUV]
- Step 5: Venous Blood Gas [Acidosis / Alkalosis]
- Step 6: Serum electrolytes, serum calcium, serum magnesium

Case 1

- 9 month boy with frequent urination,
  increased intake of water and
  irritability since 5 months age

- Upon enquiry, he was on breast feeds until 5 months of age and now, on
  Top feeds with intake of 120 ml 7-8 times a day + 100 ml water 3-4 times a day

- The mother does report constipation

- At night, the boy is usually dry and has an occasional bottle feed

- He was born at term with BW of 3.4 kgs, and there was no h/o polyhydramnios during pregnancy

Case 1 contd …

- On examination:
  - He was euvolemic with weight of 8.5 kg, length 70 cms, and developmentally age appropriate
  - There was no pallor or signs of rickets
  - Kidneys and bladder were not palpable
  - Normal male genitalia

- Estimated oral intake = 840 ml + 400 ml = 1240 ml (BSA ~ 0.42 m^2, 3000 ml/ m^2/day)

- CUE: 1010 / 5.5 / No protein / No sugar / occ WBC

Case 2

- 15 month boy with frequent urination,
  increased intake of water, and
  irritability since 3 months of age
- Upon enquiry, he was on breast feeds until 5 months of age and is currently on
  Formula feeds with intake of 90 ml 7-8 times a day + 50 ml water 3-4 times a day + Solid foods
- The mother does report constipation
- He voids with a forceful stream 2-3 times an hour during the day
- At night, the boy has 3-4 wet diapers and has 2-3 bottle feeds
- He was born at 36 weeks with BW of 2.2 kgs, and there was h/o polyhydramnios during pregnancy

Case 2 contd …

- On examination:
  - He was dehydrated with weight of 5.5 kg, length 65 cms, and developmentally slightly delayed
  - There was no pallor or signs of rickets
  - Kidneys and bladder were not palpable
  - Normal male genitalia

- Estimated oral intake = 930 ml + 200 ml = 1130 ml (BSA ~ 0.30 m^2, 3700 ml/ m^2/day)

- CUE: 1010 / 6.5 / No protein / No sugar / occ WBC

Case 2 contd …

Question 1:

Does he have polydipsia? ---------- YES

Question2:

Is it associated with polyuria / nocturnal polydipsia / FTT ---------- YES

Question 3:

What investigations, if any? ---------- YES

Question 4:

What is the etiology of his Polydipsia?

Case 2 contd …

- Investigations:

- ABG: 7.56 / 56 / 88 / 45

- Electrolytes: 116 / 2.6 / 67 / 43

- Serum creatinine 0.4 mg/dl, blood urea – 45 mg/dl

- Ca / Po4 / ALP were normal

- **Urinary electrolytes**: Na- 96, K – 34, Cl- 112 (High, Salt diuresis)

- Renal USG: Normal (Normal renal size, No Hydronephrosis, No nephrocalcinosis)

Case 2 contd …

- Diagnosis:
  - Bartter's syndrome (SGA preterm infant with h/o polyhydramnios has FTT, polydipsia, polyuria, constipation, hypokalemic, hypochloremic metabolic alkalosis, increased urinary chloride excretion, and hypercalciuria)

- Treatment:
  - Oral salt, Oral KCl, and Ibuprofen

Case 3

- 5 years girl presents with increased urination for the **past 1 month**
- Upon enquiry, drinks 12-15 glasses of water per day, and is voiding urine 1-2 times a hour
- Does urinate 1-2 times at night and usually demands water after urination
- Prior to one month, she was voiding 3-5 times a day, and occasionally at night
- Denies weight loss, vomiting, headache, constipation
- No family h/o kidney disease
- Maternal uncle has Diabetes Mellitus

Case 3 contd …

- O/E:
  - Weight 17 kg, and height 106 cms (50th percentile)
  - BP 100 / 56 mm Hg
  - Euvolemic
  - Fundus is normal, EOM range is complete
  - CUE: 1010 / 5.5 / No protein / No sugar / occ RBC's

Case 3 contd …

- What is the differential diagnosis?
  - Polyuria + Polydipsia: Is it Significant or Not Significant?
  - Well grown, and new onset symptoms: Acute / Chronic (?) condition
    (unlikely inherited / chronic defect)
    - Diabetes mellitus
    - Diabetes insipidus
    - Pyschogenic polydipsia
    - Voiding dysfunction
      (less likely due to presence of polydipsia, and nocturia)

Case 3 contd …

Investigations:

- RBS – 80 mg/dl, Urine sugar is negative : Rules out DM
- Serum electrolytes – 139 / 3.9 / 103 / 23 meq/L
- Blood urea – 22 mg/dl, serum creatinine 0.5 mg/dl
- Serum calcium 9.3 mg/dl, serum phosphorus 4.4 mg/dl
- USG Abdomen – 7.5 / 7.2 cms, No nephrocalcinosis / HN
- Urine electrolytes – Na 15 / K 10 / Cl 18 meq/L

Case 3 contd …

Investigations:

- ✓ Urine electrolytes – Na 15 / K 10 / Cl 18 meq/L
  (Low, Water diuresis)

- ✓ Urine osmolality – 65 mOsm/Kg H_2O

Case 3 contd …

- Diagnosis: Diabetes Insipidus
- Water Deprivation test to differentiate between Central and Nephrogenic: Central DI
- MRI Brain: Craniopharyngioma

Water deprivation test in children

Interpretation of serum and urine osmolality in the differential diagnosis of polyuria and polydipsia after the water deprivation test.

Serum Osmolality (mOsm/kg)	Urine osmolality after deprivation (mOsm/kg)	Urine osmolality after DDAVP (mOsm/kg)	Plasma AVP level	Diagnosis
> 300	< 300	> 750	< 2	Central DI
> 300	< 300	< 300	> 5	Nephrogenic DI
< 290	> 750	> 750	2 - 5	Primary Polydipsia
> 290	300 - 750	< 750	Variable	Partial DI or Primary Polydipsia

DDAVP, desmopressin; AVP, arginine vasopressin (pg/mL); DI, diabetes insipidus.

Baylis P. H., Cheetham T. Diabetes insipidus. *Archives of Disease in Childhood*. 1998;79(1):84–89.

Wong L. M., Man S. S. Water deprivation test in children with polyuria. *Journal of Pediatric Endocrinology and Metabolism*. 2012;25(9-10):869–874.

Case 4

- 2 year baby boy presents with passing urine frequently and drinking plenty of water since early childhood
- H/o occasional vomiting and constipation +
- H/o few episodes of febrile illness
- Antenatal scans were not done

- O/E: Weight 8kg,
  - Mildly dehydrated,
  - Mild pallor
  - No rickets
  - No obvious renal or bladder mass
  - Spine is normal

Case 4

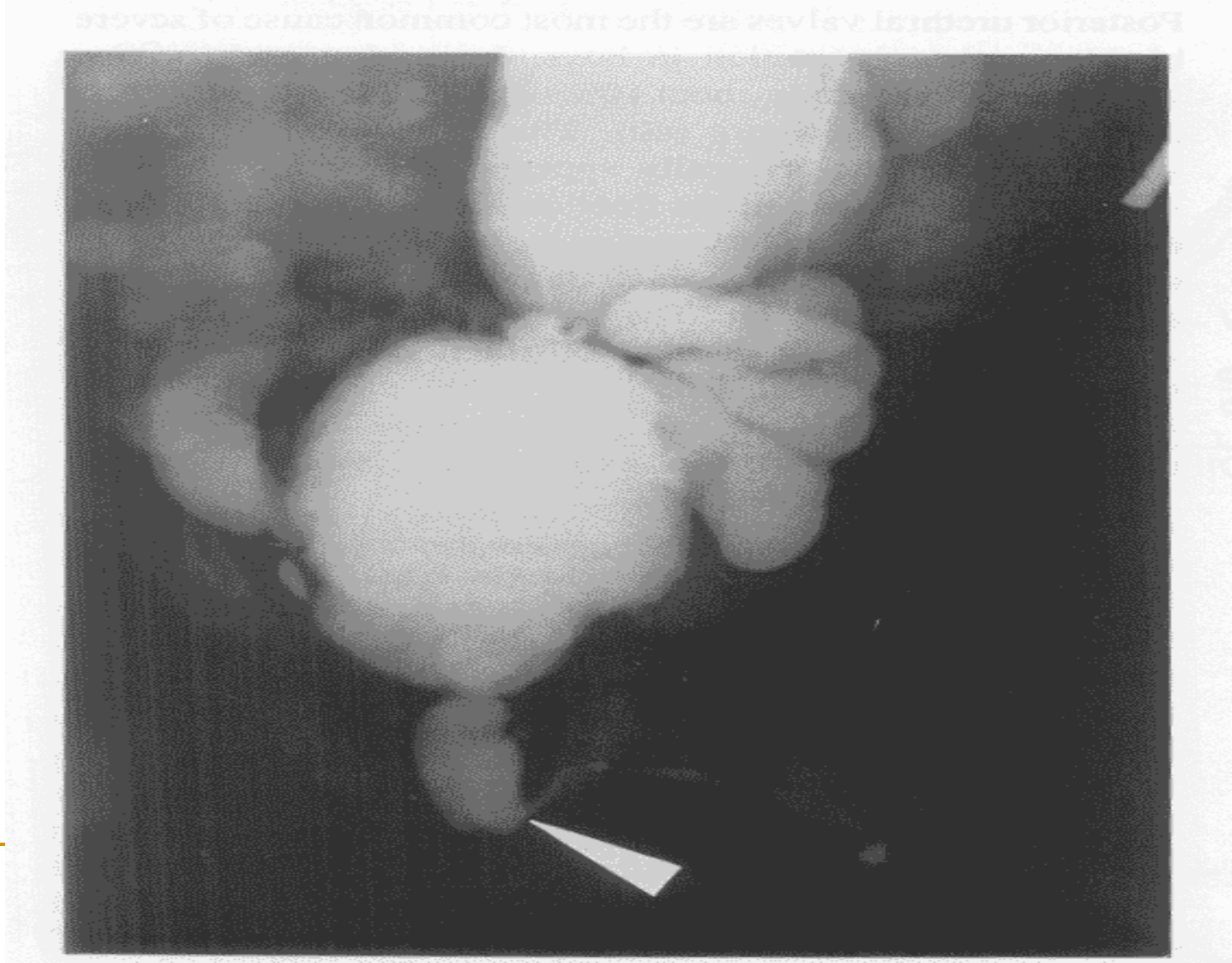
- CUE: 1010 / Trace protein / No sugar / 5-6 WBC's
- Serum electrolytes: 135 / 4.5 / 116 / 16
- VBG: 7.30 / 35 / - / 18
- Serum creatinine: 0.8 mg/dl, Blood urea 35 mg/dl
- USG Abdomen: 5.6 cms / 6.0 cms, No nephrocalcinosis, mild bilateral HN
- Diagnosis: ??

Case 4

What additional investigations:

- Urine pH: 6.0
- Spot urine electrolytes: 60 / 10 / 80
- Urine AGAP: -10
- Any other test ?
  - Clues: Weight, RFT, & Bilateral HN
  - Urinary stream ???

MCUG



Case 5

- 6 years girl
- 1 episode of generalized weakness of 1 day duration
- No vomiting, diarrhea or fever
- Weight 12 kg, Height 99 cms, BP 90/60 mm Hg
- Euvolemic, No rickets, Normal genitalia

Case 5

- Serum electrolytes: 138 / 2.2 / 112 / 18
- CUE: 1010 / 6.5 / no sugar / no protein
- Serum creatinine 0.5 mg/dl
- Diagnosis: Hypokalemic periodic paralysis
- Treatment: IV KCl
- Better in one day and discharged on oral KCl for one week

Case 5

- She came back after 3 months with another episode.

- Why ???
- History of polyuria, polydipsia +
- Growth less than 5th %ile
- VBG: 7.21/24/-/ 15
- USG: medullary nephrocalcinosis

- **Revised Diagnosis:** Hypokalemic periodic paralysis due to distal RTA

Case 6

- 2 years girl
- Polyuria, polydipsia, constipation, vomiting
- Born at term with BW 2.5 kg, AF was adequate
- O/E: weight 7.5 kg, 72 cms, 70-50 mm Hg
- Euvolemic, no rickets, normal genitalia, no abdominal mass

Case 6

- CUE: 1005/6.5/Trace protein/Trace sugar/No RBC
- Serum electrolytes: 142 / 4.8 / 107 / 18
- Blood calcium 8.0, phosphorus 5.5, Alk P 666
- Additional tests: ??
  - VBG: 7.31 / 36 / 18
  - Serum creatinine 2.2, blood urea 76 mg/dl
  - **USG 3.6 / 4.0 cms**
- Diagnosis: **CKD due to hypo-dysplastic kidneys**

Summary

1) Polyuria is a common symptom and often associated with polydipsia

2) Polyuria alone (Adequate growth) – physiological (infants), resolving ATN, behavioral (older children)

3) Polyuria + Polydipsia (Adequate growth) –
Diluted feeds, DM, Central DI in an older child, Resolving ATN

4) Polydipsia + Polyuria + **FTT**
- **CKD, or**
- **obstructive uropathy (PUV)**
- **renal tubulopathy**

5) Evaluation requires step wise approach with detailed history, physical exam, and specific investigations

6) Investigations should include CUE (*including specific gravity & pH*), RFT, serum electrolytes, VBG, and USG Abdomen

7) Children with DI will have normal plasma sodium concentration as long as they have access to free water (intact thirst mechanism)

THANK YOU

Question 1:

- Polyuria is considered when

A] increase in frequency of urination during day

B] increase in frequency of urination during day and night

C] persistent increased volume of urine during 24-hour period

D] Frequency of urination along with dysuria, urgency, and urinary incontinence

Answer 1:

- Polyuria is considered when

C] persistent increased volume of urine during 24-hour period

- > 4 ml/kg/hour or > 100 ml/kg/day in a child

Question 2:

- Polyuria is often associated with

A] Polyphagia

B] Polydipsia

C] Weight gain

D] Diarrhea

Answer 2:

- Polyuria is often always associated with

  B] Polydipsia

- In children, polyuria causes volume depletion / hypernatremia (depending upon etiology) that will stimulate thirst center and cause polydipsia

Question 3:

- Common causes of polyuria in children include all of the below except

A] Chronic kidney disease due to CAKUT

B] Diabetes mellitus

C] Chronic glomerular disease

D] Renal tubulopathy

Answer 3:

- Common causes of polyuria in children include all of the below except

C] chronic glomerular diseases

- These are associated with salt and water retention, edema, hypertension, oliguria

Question 4:

- Besides thorough history and physical examination, initial evaluation of a child with polyuria should include all of the following except

A] Complete urine examination including specific gravity, pH, protein, glucose

B] Renal function tests

C] Venous blood gas and serum electrolytes, serum calcium

D] USG abdomen

E] Urine osmolality

Answer 4:

- Besides thorough history and physical examination, initial evaluation of a child with polyuria should include all of the following except

  E] Urine osmolality

- Urine osmolality is variable depending upon the etiology
  - Low, < 300 mosm/Kg H2) – DI
  - Isosthenuric, 250-300 – CKD due to CAKUT, dRTA
  - Higher than 300 – salt losing renal tubulopathy

  - It should be obtained if DI is suspected after above investigations

Metabolic Acidosis

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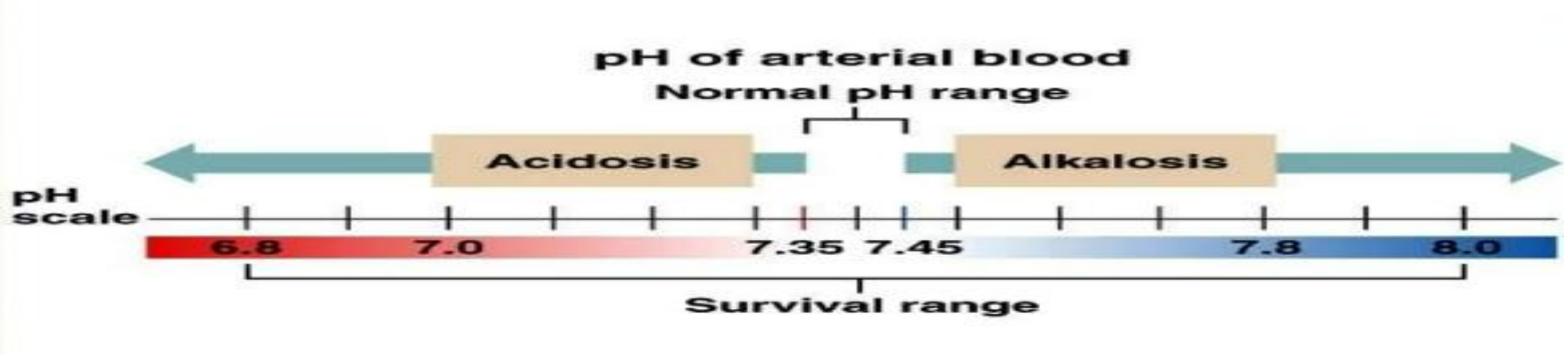
ICH&HC, MMC. Chennai

- How to read an ABG
- Anion gap, delta gap osmolar Gap
- Approach to metabolic acidosis
- scenarios

- “Life is a struggle, not against sin, not against the Money Power, not against malicious animal magnetism, but against hydrogen ions.“

H.L. MENCKEN



Metabolic acidosis-pH<7.35 with low bicarb

- Gain of acids or loss of base
- Addition of fixed acids or exogenous acids
- Anion gap, delta gap, osmolar gap

Read ABG -Is there an abnormality?

- Look at the pH
- Look at the Paco2
- Look at the Hco3

  Abnormal value in any one suggest an abnormality to proceed further analysis

ABG analysis

- **Step 1:** Acidemic, alkalemic, or normal?
- **Step 2:** Is the primary disturbance respiratory or metabolic?
- **Step 3:** For a primary respiratory disturbance, is it acute or chronic?
- **Step 4:** For a respiratory disorder is the compensation ok?
- **Step 5:**For a metabolic disturbance, is the respiratory system compensating OK?
- **Step 6:** For a metabolic acidosis, is there an increased anion gap?
- **Step 7 :** Whether there is any coexistent metabolic disturbances?

Is it acidemic or alkalemic?

- Normal 7.35 -7.45
- Any value below 7.35 acidemic
- Any value above 7.45 alkalemic

Is the primary disturbance respiratory or metabolic?

- Based on the pH
- Look at the Paco2 and Hco3
- For acidosis Paco2 high -respiratory
  Hco3 low - metabolic

- For alkalosis Paco2 low -respiratory
  Hco3 high - metabolic

For a primary respiratory disturbance, is it acute or chronic?

- Acute respiratory acidosis

  0.08 ↓ of pH for every 10 ↑of paco2

- Chronic respiratory acidosis

  0.03 ↓ of pH for every 10 ↑of paco2

- Acute respiratory alkalosis

  0.08 ↑ of pH for every 10 ↓of paco2

- Chronic respiratory alkalosis

  0.03 ↑ of pH for every 10↓ of paco2

For a respiratory disorder is the compensation ok

- Acute respiratory acidosis

  Hco3 ↑ by 1 for every 10 ↑in Paco2

- Acute respiratory alkalosis

  Hco3 ↓ by 2 for every 10 ↓in Paco2

- Chronic respiratory acidosis

  Hco3 ↑ by 3 for every 10 ↑in Paco2

- Chronic respiratory alkalosis

  Hco3 ↓ by 4 for every 10 ↓ in Paco2

Remember 1,2,3,4 begin with resp acidosis

For a metabolic disturbance, is the respiratory compensation OK?

- Metabolic acidosis

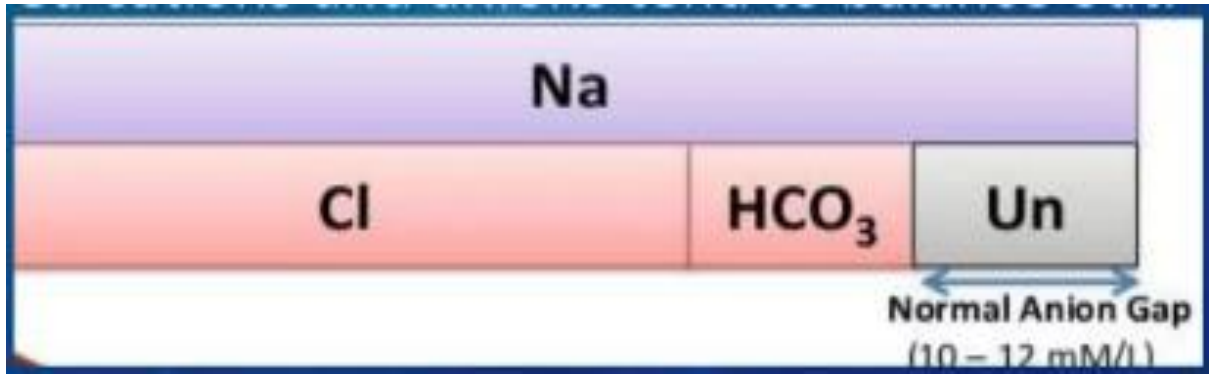
  $Paco_2 = (1.5 \times Hco_3) + 8 \pm 2$

- Metabolic alkalosis

  $Paco_2 \uparrow$ by 7 for every 10 $\uparrow$ in Hco_3

For a metabolic acidosis, is there an increased anion gap?

- Anion gap = Na+K – CL +HCo3 = 15±3



Anion Gap Major cations- anions = 15±3

Gap is due to unmeasured proteins, phosphate sulphate, wk organic acids

Normal AG

- Low bicarb high chlorides
- GI fistula diarrhea
- Renal -RTA
- IV NS

High AG

- Low bicarb normal chlorides
- Fixed acids uremia lactic acid ketoacids
- Exogenous acids
- Salicylates , methanol, ethanol

Urine anion gap

- UAG = Urine (Na +K – Cl) 0- 10mEq/L
- In NAGMA
- Negative anion gap means GI loss of bicarbonate
- Positive anion gap means renal cause

- Normal kidney tries to regenerate bicarb by excreting ammonia which is positively charged and excreted with chloride to maintain electro neutrality. (there are exceptions like volume depletion)

Whether there is any coexistent metabolic disturbances?

- For co existent non anion gap metabolic acidosis or metabolic alkalosis
- Delta Gap measured HCo3+ change in the anion gap = 22-26
- Corrected Hco3 = measured Hco3 +(AG -10) =24

  If >26 think of metabolic alkalosis

  If < 22 think of non anion gap acidosis

Base excess will give a clue

Validity of the ABG report

- H = 24 × Pco2/Hco3
- 80 – H . Should be the PH from the table

or

- last two digits to be subtracted from 7.4
- 7.4-last two digits should be the measured ph
- Eg pH= 6.99 PaCO2= 17.8 Hco3-=5

- 24 X 17.8/5 =85.44
- 0.44
- 7.4-0.44 = 6.96

Delta Ratio- rise in anion gap/fall in HCo3

- Each fixed acid -hydrogen ion and acid anion and the H is buffered by bicarb hence Ratio is one

- < 0.4 normal anion gap
- > 2 resp acidosis
- 0.4- 2 mixed

Osmolar Gap

- Difference between measured and calculated osmolarity
- N <10
- Useful in methanol , ethanol, propylene glycol, mannitol, glycine

Lactic acidosis–Cohen and woods classification.

- Type A in tissue hypoperfusion and hypoxia
- Type B in situations without tissue hypoperfusion
- B1 – acquired conditions-Sepsis, seizures, Diabetes, ARDS,renal failure, malignancy,thyroid storm, post cardio pulmonary byepass(all with excess production) Liver failure (decreased excretion)
- B2 medications - Epinephrine, acetaminophen, isoniazid, nitroprusside.
- B3-IEM related

Limitations of AG

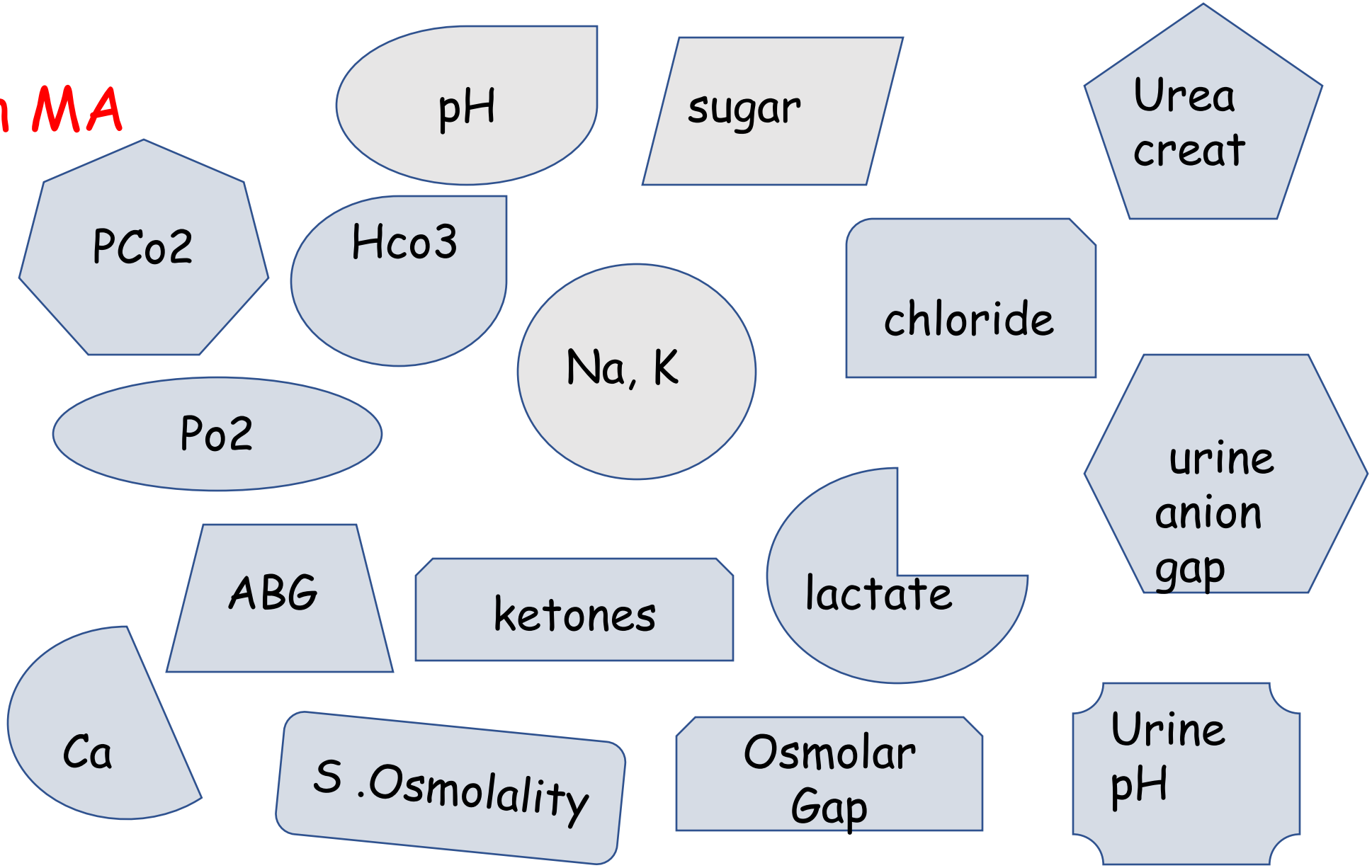
- With normal anion gap of 12-18 still lactate can be high
- Albumin adversely affects AG
- Bicarb accounts only for 60% buffer

- Henderson -Hasselbalch theory $H^+ = 24 \times PaCO_2 / HCO_3$
- Stewart approach is based on the 3 independent variables which control the H^+
- Partial pressure of CO2, the strong-ion difference (SID), and the total amount of weak acids.

- SID is the difference between strong cations and anions.
- (Na+K+Ca+Mg)– (Cl+lactate)
- Normal – 38-42 mEq/L.
- Narrowing is acidosis and widening is alkalosis.

- Weak acids are Albumin and phosphate
- Atot- total concentration of weak acids .
- Increase in ToT is metabolic acidosis and
- Decrease results in metabolic alkalosis

Labs in MA


pH
sugar
Urea
creat
PCo2
Hco3
chloride
Na, K
Po2
urine
anion
gap
ABG
ketones
lactate
Ca
S .Osmolality
Osmolar
Gap
Urine
pH

Metabolic acidosis

- Bicarb buffers
- Non bicarb buffers
- Resp hyperventilation
- Kidneys generate bicarb
- Liver produce bicarb from acid anions
- Exogenous bicarb

- Beware - when ventilating with normal mt vol - kid worsen
- Depressed myocardium
- Symp overactivity
- Catechol resistance
- Arteriolar dilatation
- Venous constriction
- Pul vasoconstriction
- Hyperkalemia

Approach to metabolic acidosis

- History
- Examination for vitals
- Ventilatory support
- Cardiac resuscitation
- Treat hyperkalemia
- Confirm with ABG
- Identify the compensation
- Look for AG delta gap osmolar Gap
- Treat the underlying disorder

Remember

- Treat the patient not the ABG values

Let us work on scenarios

- Get the physiological status
- Interpret the ABG
- Proceed with the evaluation
- Arrive at the management

Primary Hypertension in Children: an underrecognized condition

Priya Pais MD, MSc
Professor & Head, Dept of Pediatric Nephrology
St John's Medical College, Bangalore

Making the case for primary HTN in children

Case: 13 year old boy presents for a mandated school check-up in your OPD.

He has no complaints but his mother is concerned that he is addicted to his mobile phone.

On examination, weight = 54kg, height = 152cm, BMI = 23.4 (90^{th} percentile).

BP = 128/82mmHg and 130/76mmHg

- You must document whether BP is normal is his school form
- How would you classify this child's BP?
- What is your approach?

Defining HTN in children

- AAP 2017

BP Category	Age < 13 years	Ages 13 years & older
Normal	<90th percentile for age, sex, and height	<120/<80 mm Hg
Elevated	90th–<95th percentile for age, sex, and height	120 129/<80 mmHg
Hypertension	≥95th percentile	SBP 130 or more DBP 80 or more

True or False?

- Routine BP measurement in children in not required in primary care settings
- Healthy (asymptomatic) children do not have HTN
- Hospital anxiety typically gives falsely elevated BP readings
- Secondary HTN is more common in children > 13yrs
- Avoiding anti-hypertensive medications for otherwise healthy children is ideal.
- If HTN is detected, pediatricians must refer child to pediatric nephrology centre

Common Misconceptions regarding pediatric HTN

Primary Hypertension is diagnosed when there no evidence of a secondary cause of HTN

1.3 billion adults estimated to have HTN. Only 42% are diagnosed / treated

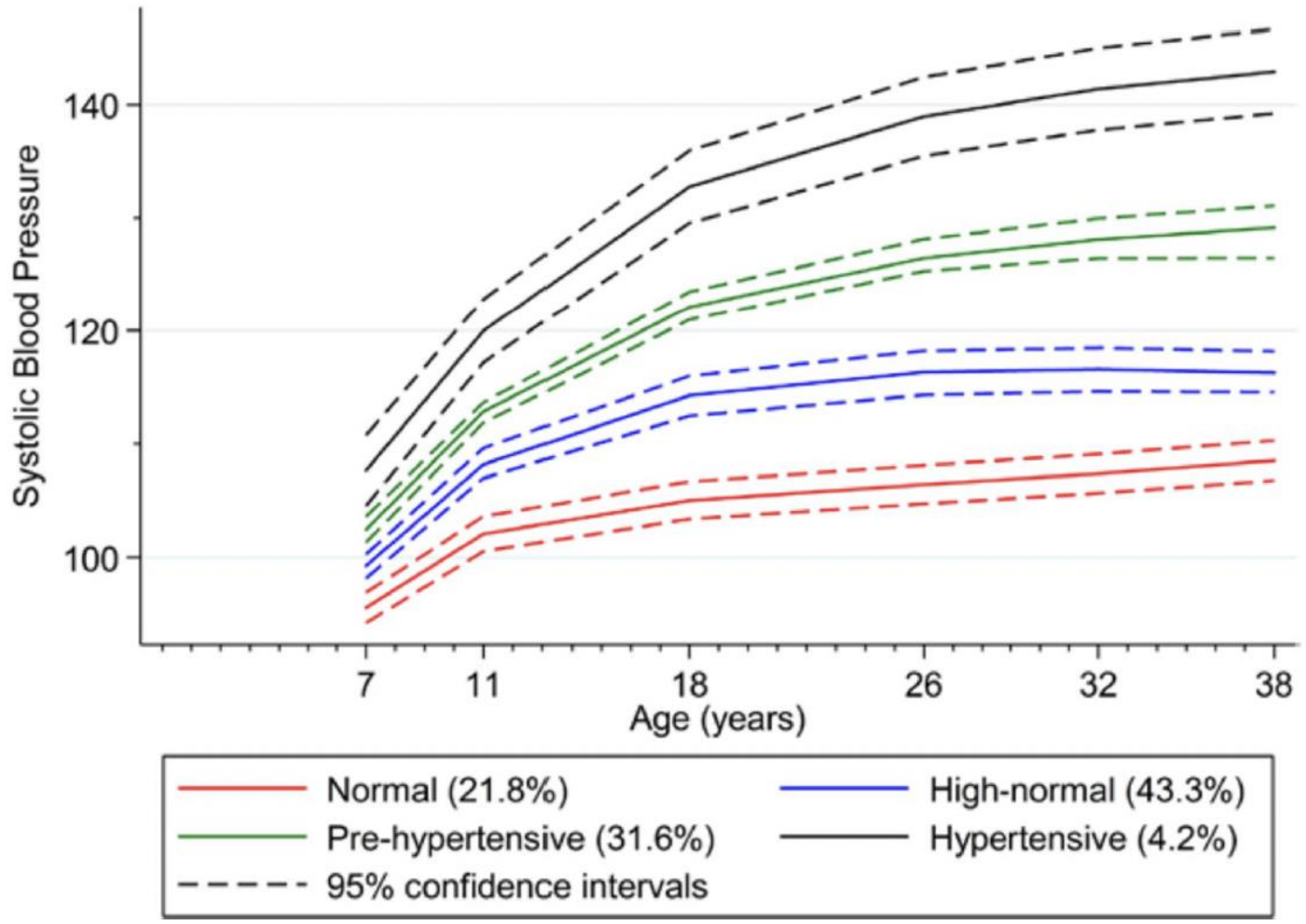
HTN is the greatest modifiable risk factor for cardiovascular death

How does this information apply to pediatricians?

World Health Organization

BP trajectory during life course:

Hypertensive child
→ hypertensive adult



Theodore RF, Hypertension 2015

What is the Prevalence of Childhood HTN?

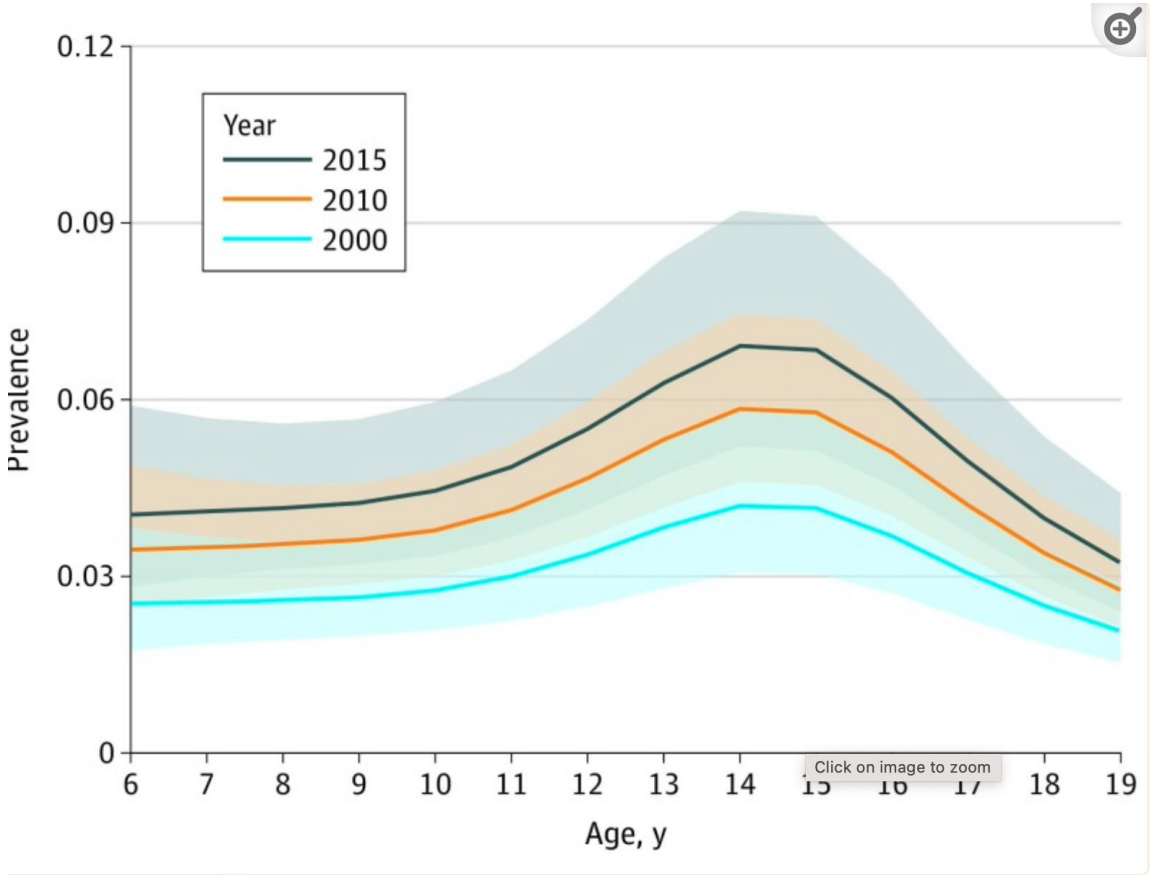
4% at 6 yrs
8% at 14 yrs
15% in obesity

JAMA Pediatrics
View Article

JAMA Pediatr. 2019 Dec; 173(12): 1154–1163.
Published online 2019 Oct 7. doi: 10.1001/jamapediatrics.2019.3310
PMCID: PMC6784751
PMID: 31589252

Global Prevalence of Hypertension in Children

A Systematic Review and Meta-analysis



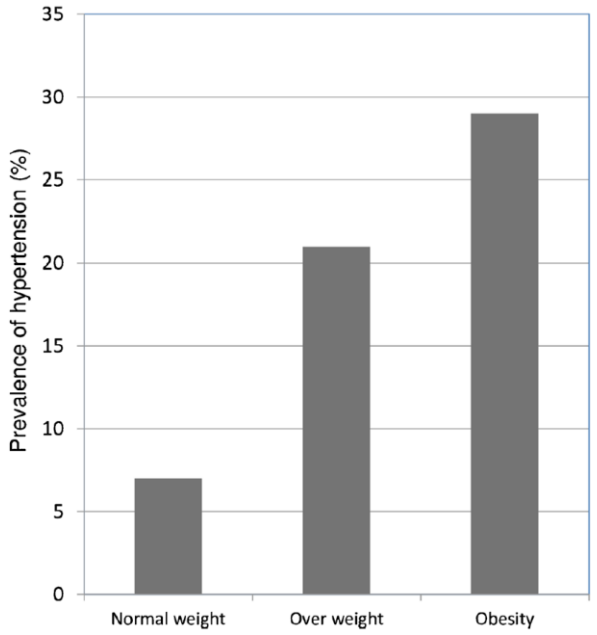
The Indian Journal of Pediatrics
https://doi.org/10.1007/s12098-021-03686-9

ORIGINAL ARTICLE

Prevalence of Hypertension among Children and Adolescents in India: A Systematic Review and Meta-Analysis

Jitendra Meena [1] · Meenu Singh [1] · Amit Agarwal [1] · Anil Chauh

- Based on screening of children in community
- ≥ 3 blood pressure measurements
- Overall pooled prevalence of HTN = 7%
- Higher than global prevalence estimates
- Higher in urban & obese children



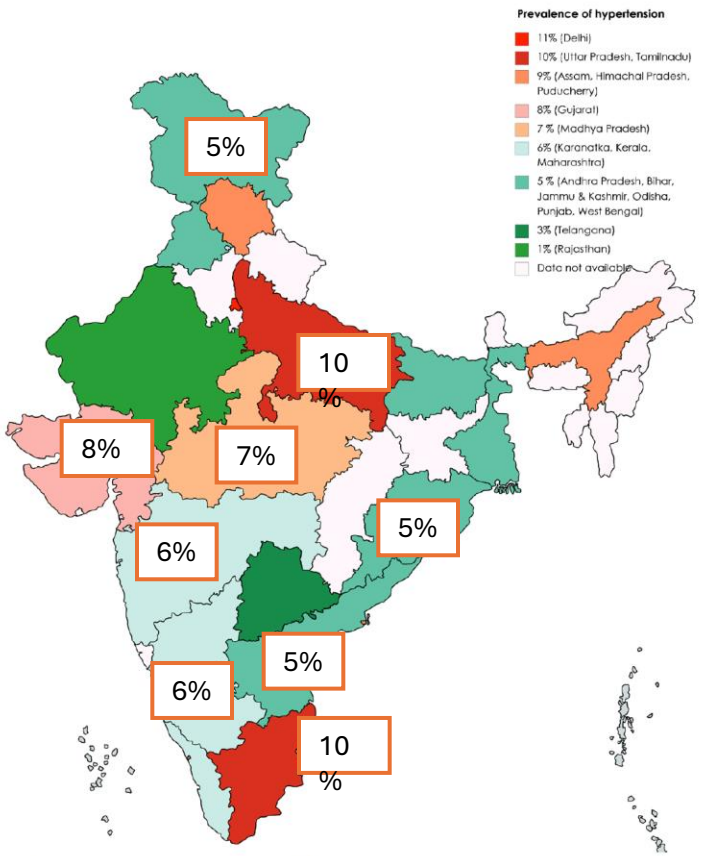


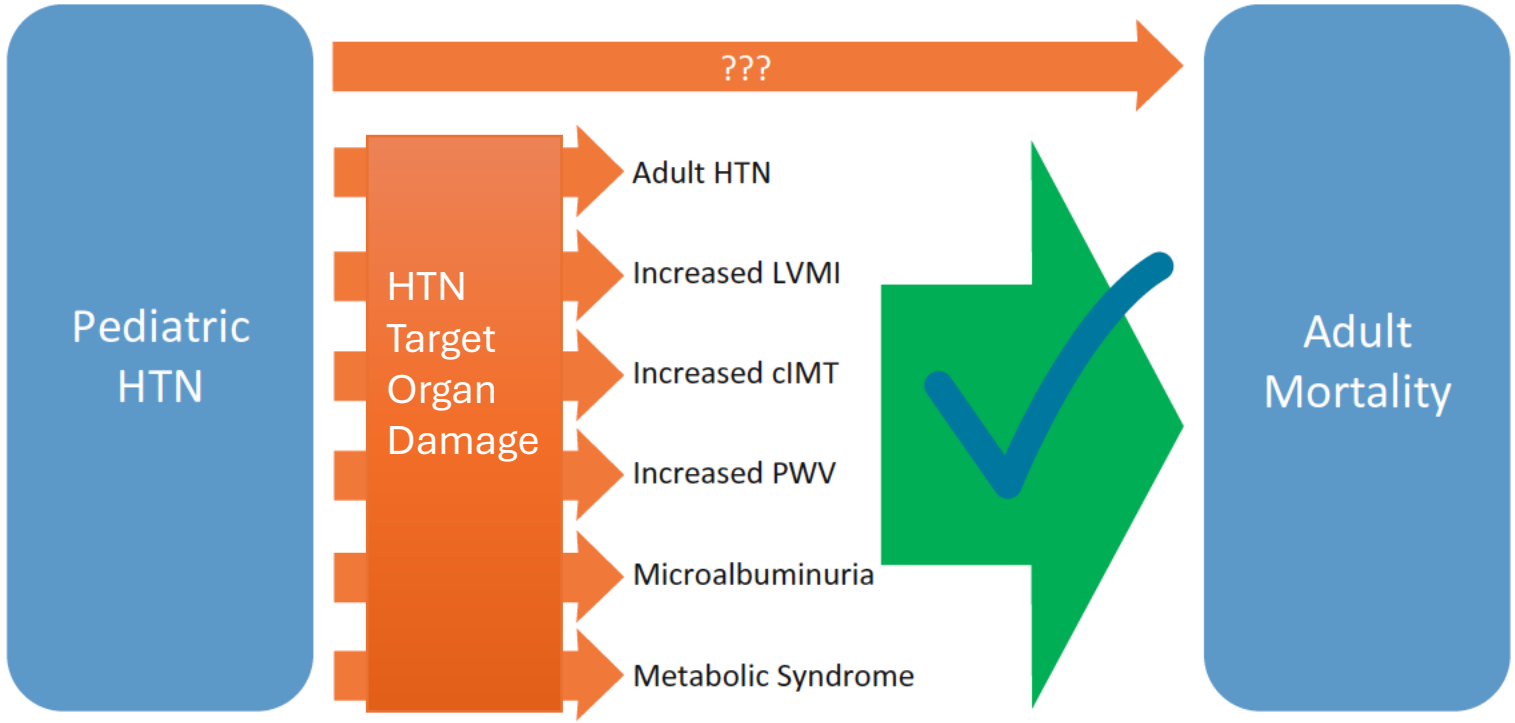
Fig. 3 Pooled prevalence of childhood hypertension across states of India

? Proportion of children with primary (vs secondary) HTN

- Data limited
- Referral clinics always have higher proportion of secondary HTN (>20%)
- In Primary care settings
  - 85% of hypertensive children had primary HTN
  - Only ~ 4% of otherwise healthy children who were evaluated for HTN had secondary cause
- ? Indian data

Yoon et al 2014 Arch of Pediatr & Adol, Nugent F 2022, J Pediatr

Relevance of Pediatric HTN --> Intermediate CV Outcomes → Adult CV Outcomes



Pediatric HTN 5th Ed

Does ***Primary*** HTN in children → Target Organ Damage?

Hypertension

CURRENT ISSUE

RESEARCH ARTICLE | Originally Published 21 February 2023 |

Check for updates

Risk of Target Organ Damage in Children With Primary Ambulatory Hypertension: A Systematic Review and Meta-Analysis

Jason Chung, Cal H. Robinson, Andrew Yu, Abdulaziz A. Bamhraz, Joycelyne E. Ewusie, Stephanie Sanger, Mark Mitsnefes, Rulan S. Parekh, Rupesh Raina, Lehana Thabane, Janis M. Dionne, and Rahul Chanchlani

AUTHOR INFO & AFFILIATIONS

- Compared with normal children, those with primary HTN had
  - More LVH and increased LV mass
  - Increased arterial stiffness
  - Thickening of arteries (early atherosclerosis)

Is Primary HTN under recognized?

- ~ 4% prevalence of HTN in general pediatric population
- But 13 – 18% prevalence of *elevated BP → HTN*
- Prevalence of primary HTN is 10 times > prevalence of secondary HTN
- ?? How many cases of primary HTN have you diagnosed??

If the prevalence of HTN in Indian children is > western children, primary HTN must be going unrecognized

Falkner B et al, AHA Scientific Statement 2023

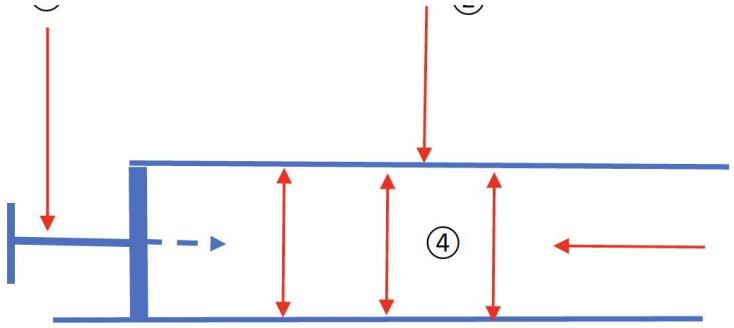
Understanding primary HTN in children: pathophysiology

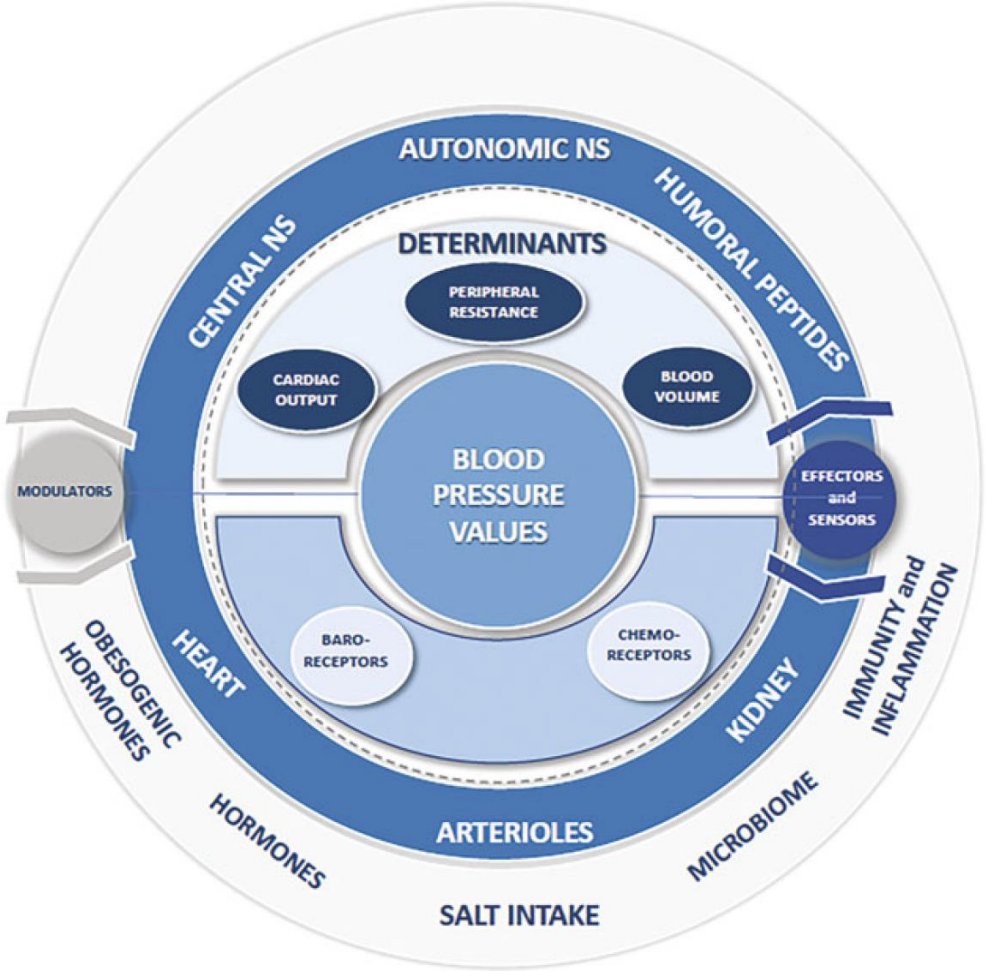
Litwin M, Pediatric Nephrology 2024 https://doi.org/10.1007/s00467-023-06142-2 (free full text)

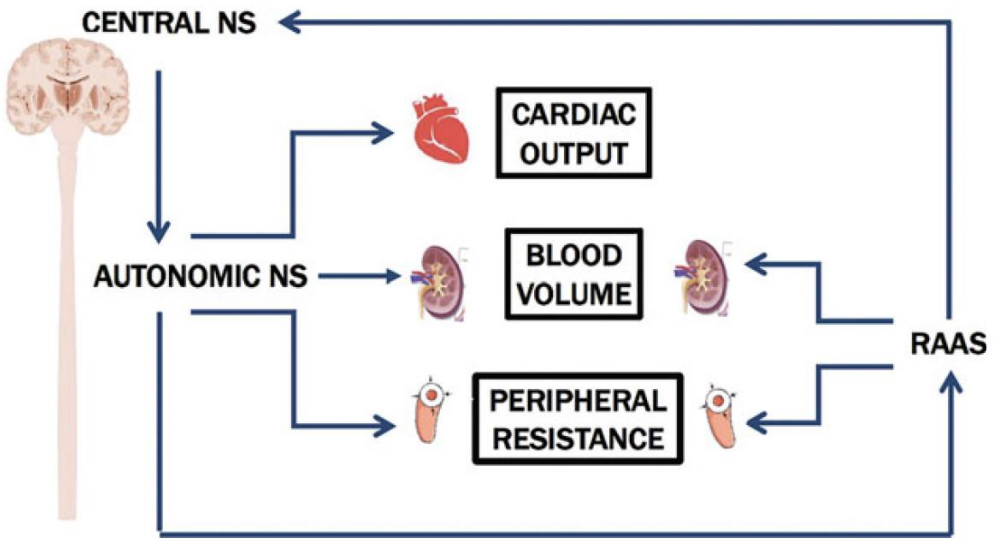
Basic BP Equation: Still the same!

- **BP = Cardiac output X Total peripheral resistance(TPR)**
- Mean arterial pressure = Stroke volume x Heart Rate x TPR
- **Volume** of circulating blood + Contraction force of LV → Stroke Volume
- Determinant of volume is **Salt** + salt/ water homeostasis

Determinants of flow through vessels:
Volume, elasticity of walls, pressure within the vessel



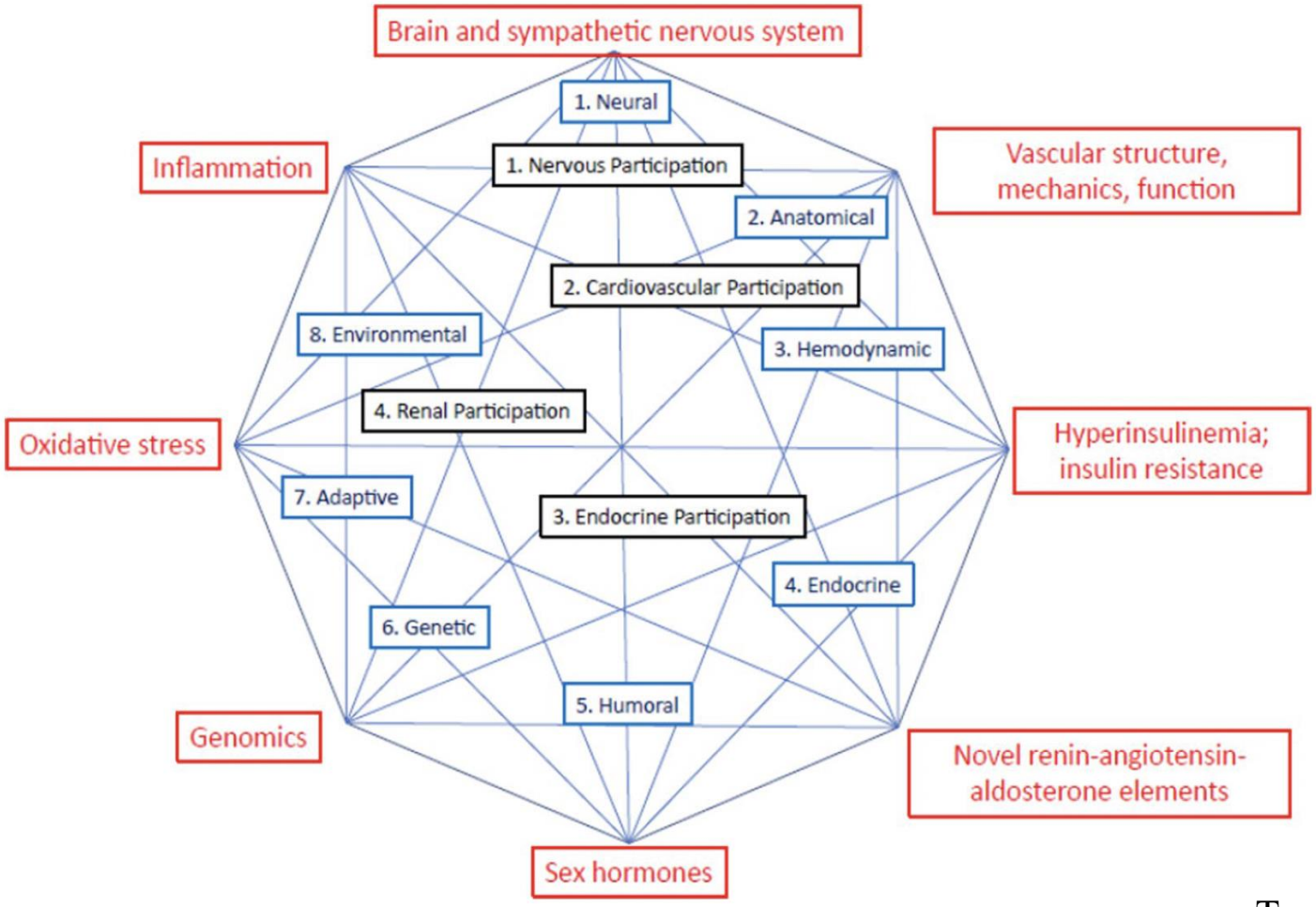




Main Factors Controlling BP
Determinants & Modulators

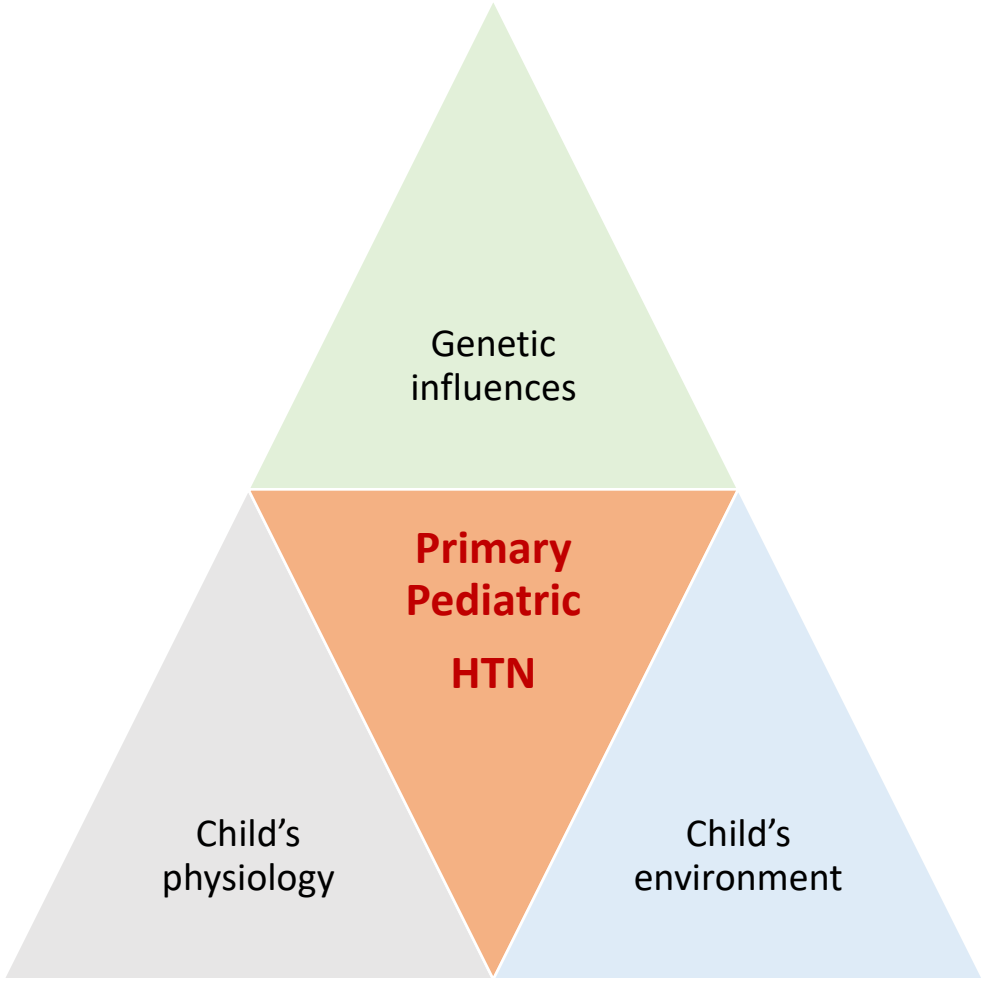
Pediatric HTN 5th Edition

Page's Mosaic: Evolving awareness of Pathogenesis of hypertension

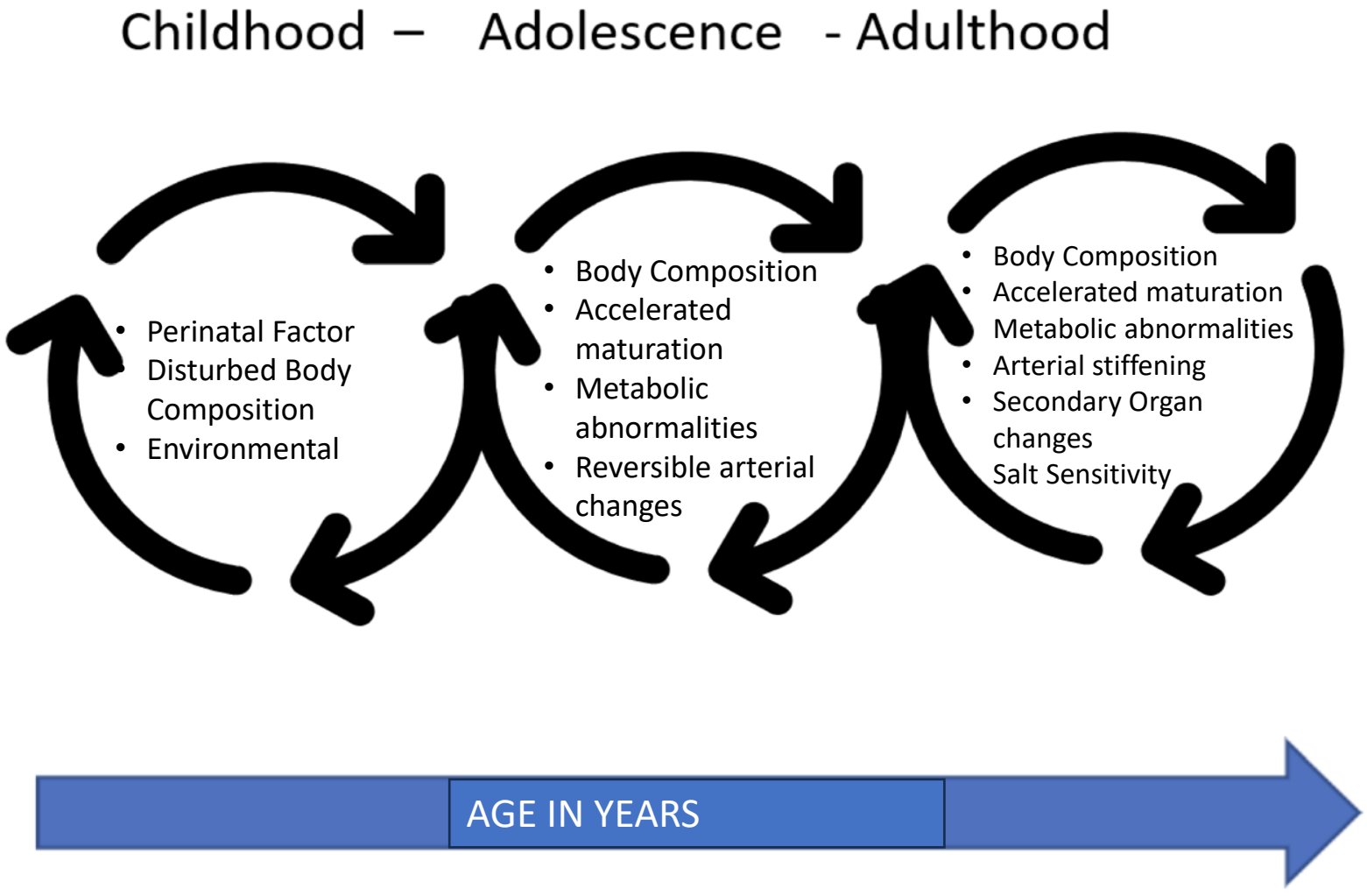


Touyz RM, (2020) Can J Cardiol

Primary HTN is multifactorial



Gradual Development of Hypertension: Risk Factors Accumulate

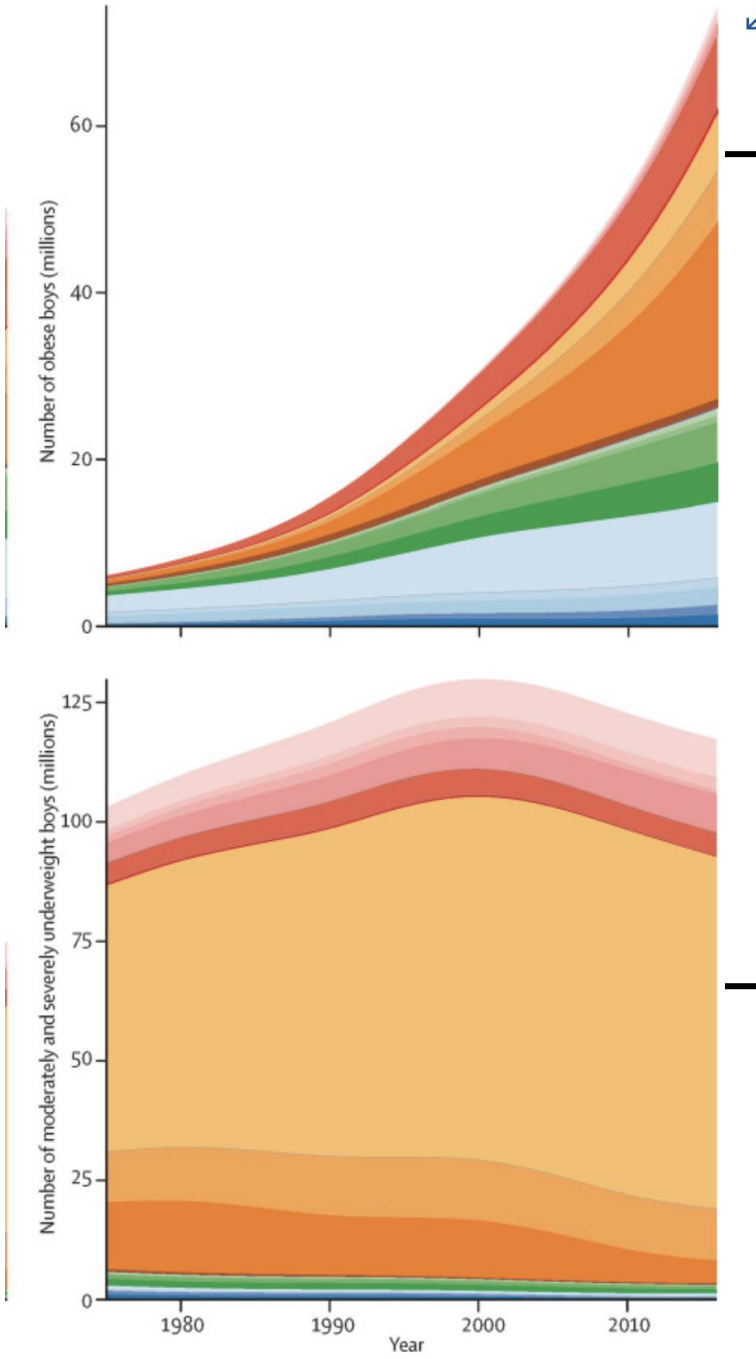


New pathophysiologic mechanisms develop with age and duration of hypertensive disease

Modulators of Primary HTN in Children

- Obesity = visceral adiposity (disturbed body composition)
- Salt sensitivity
- Others
  - Autonomic nervous system abnormalities
  - Metabolic abnormalities
  - Vascular remodeling

Face of ‘Malnutrition’ is changing

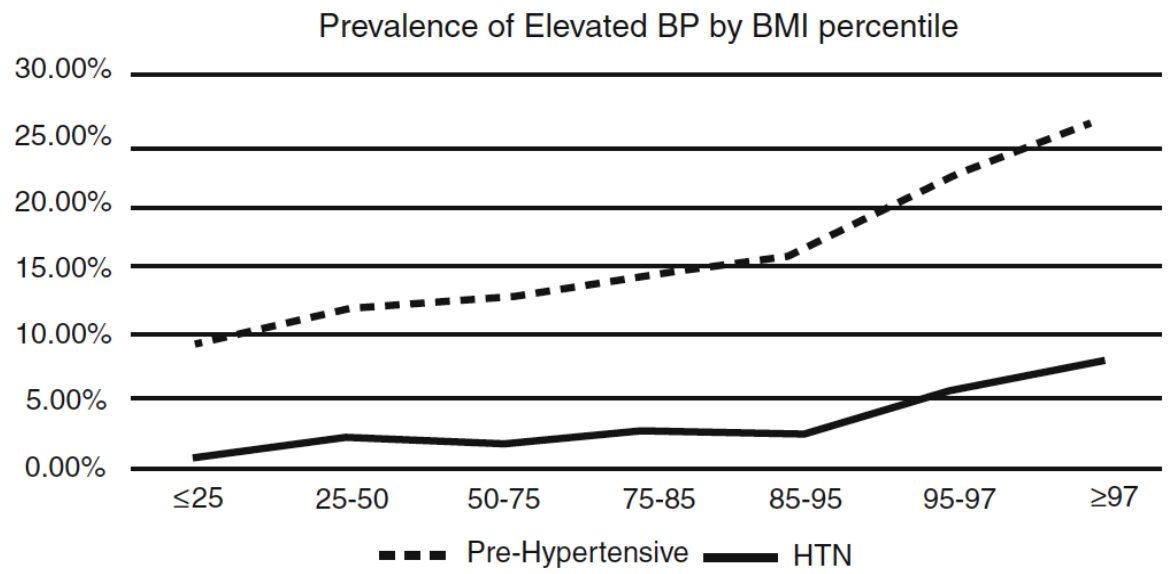


Prevalence of obesity in South Asians

Prevalence of underweight in South Asians

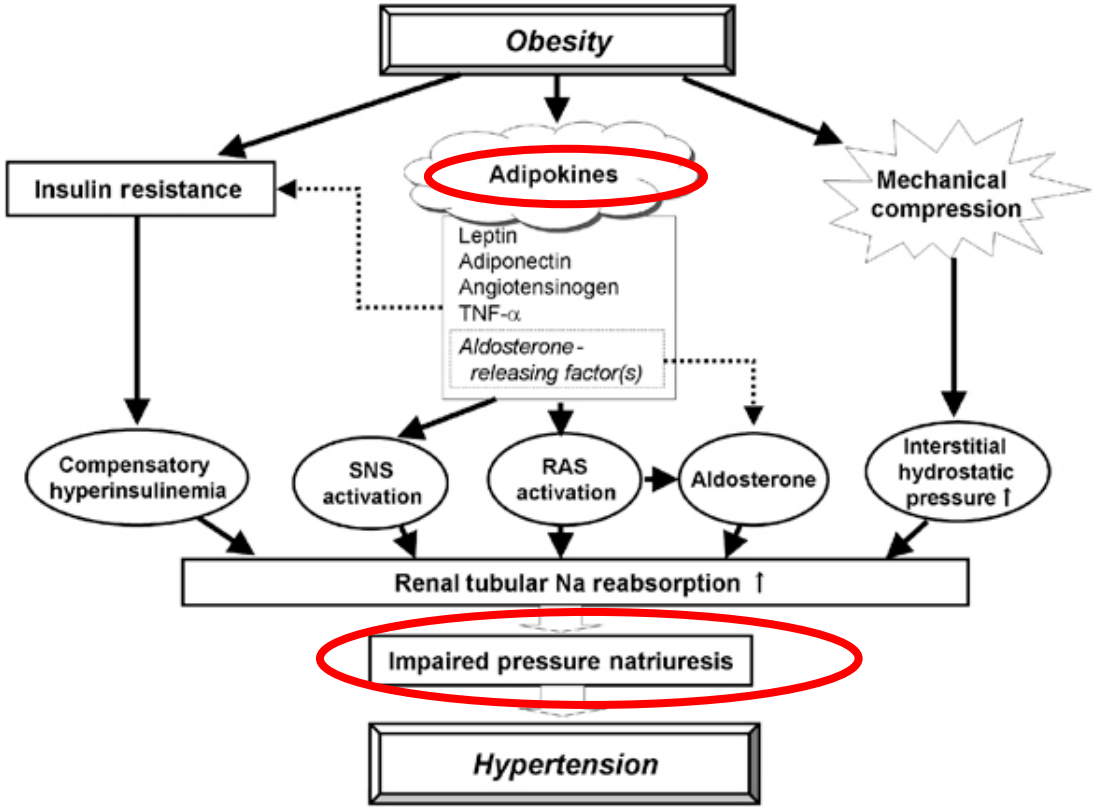
The Lancet, NCD Risk Factor Collaboration 2017

Obesity is a Risk Factor for Primary HTN



McNiece et al 2007 Ped HTN 5th Ed

HTN in Obesity



Mechanisms of HTN in childhood obesity

Insulin resistance and hyperinsulinemia[a] leading to: 1. Sympathetic nervous system activation 2. Renal sodium reabsorption 3. Impaired vasodilatation 4. Vascular smooth muscle proliferation Hyperleptinemia leading to 1. Sympathetic nervous system activation 2. TGF-β synthesis and increased type 1V collagen leading to glomerulosclerosis [a]Unexplained insulin resistance in lean individuals with hypertension has been reported. Mechanisms for increased BP secondary insulin resistance and hyperinsulinemia are hypothesized to be similar to those in obese individuals
Activation of RAAS and elevation of plasma renin
Increased pro-inflammatory cytokines such as TNF-α, IL-6 contributing to insulin resistance
Increased oxidative stress
Direct renal damage 1. Renal compression by perirenal fat leading reduced medullary blood flow, tubular compression leading to increased sodium reabsorption 2. Hyperfiltration injury 3. Increased TGF-β1 expression synthesis
Poor sleep quality and sleep apnea leading to sympathetic nervous system activation
Low vitamin D level

Adapted from Bucher et al. (2013), Yamaguchi and Flynn (2009)

Salt sensitivity

- In a proportion of population changes in dietary sodium intake → exaggerated and parallel changes in BP
- Modulated by ENaC channels present in various organs and blood vessels
- Pathophysiology of SS:
  - Increased volume
  - Also increased stiffness of vessels
- Asians, blacks, obese and small for gestational age birth history = SS

Weinberger M Hypertension, Elliott P BMJ 1996 INTERSALT cooperative research group

› Ann Glob Health. 2016 Mar-Apr;82(2):234-42. doi: 10.1016/j.aogh.2016.02.001.

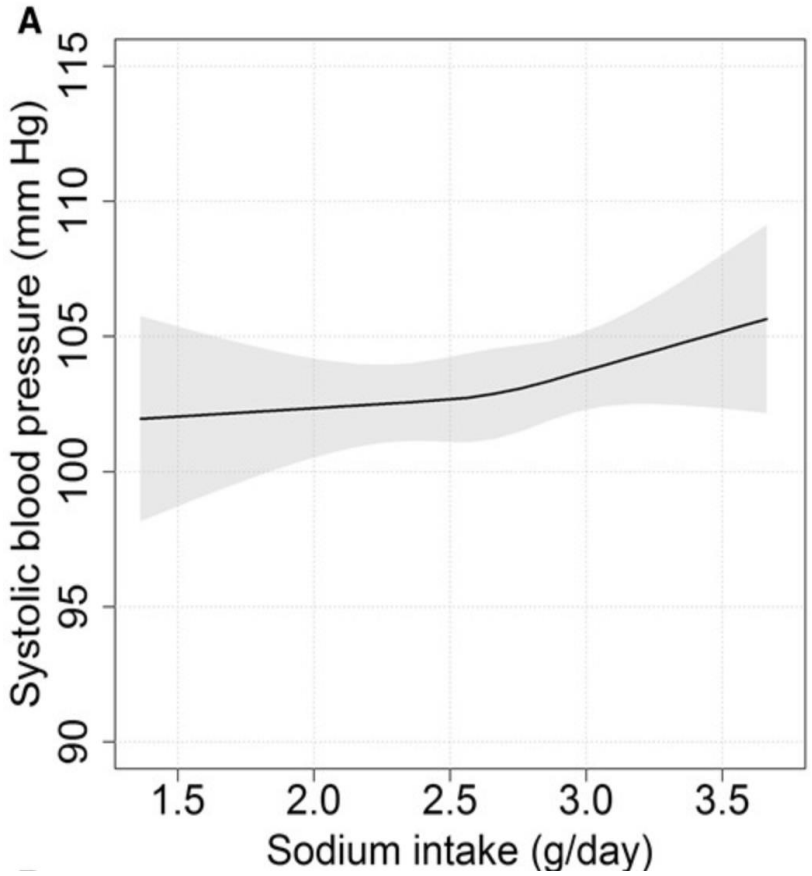
Sodium Intake, Blood Pressure, and Dietary Sources of Sodium in an Adult South Indian Population

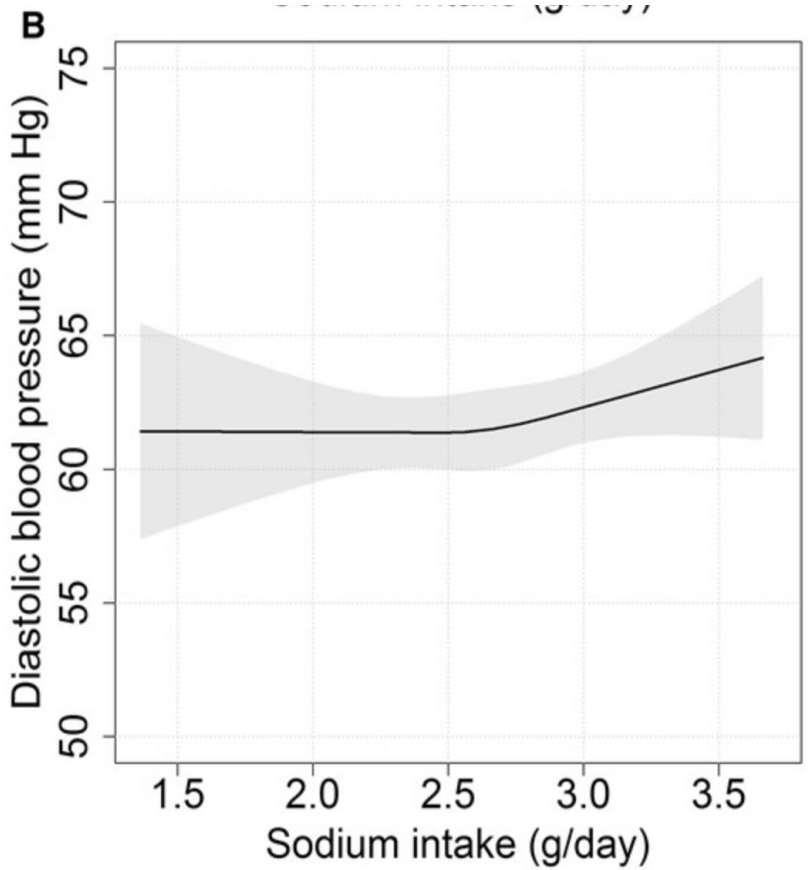
Sripriya Ravi [1], Odilia I Bermudez [2], Vijayakumar Harivanzan [3], Kwan Ho Kenneth Chui [2], Preethi Vasudevan [3], Aviva Must [2], Sadagopan Thanikachalam [3], Mohan Thanikachalam [4]

- 8000 Indians
- Dietary salt intake independently associated with SBP
- Dietary intake was higher than guidelines
- Source of salt homemade foods

Dose response relationship between sodium intake and BP in children

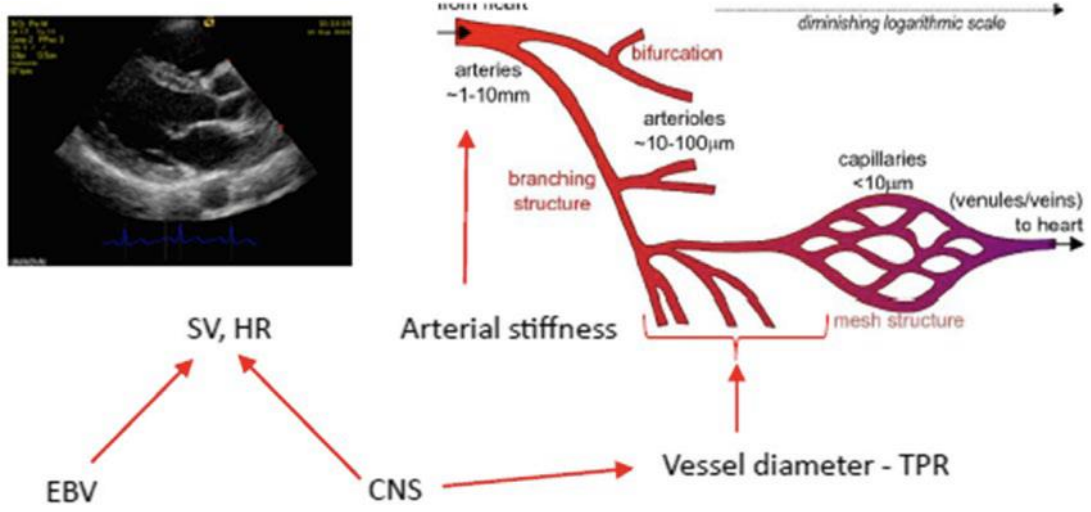
1 gram extra sodium intake = 1 mmHg increase in SBP/DBP





Int J Epidemiol, Volume 47, Issue 6, December 2018, Pages 1796–1810, https://doi.org/10.1093/ije/dyy121

Alteration of macro and microcirculation



- Children with PH have
- Macrocirculation
  - Increased vessel wall thickness & stiffness
  - [increased cIMT/ higher pulse wave velocity/ greater pulse pressure]
- Microcirculation
  - Vasoconstriction of retinal vessels
  - Reduction in perfusion

Autonomic activation & Metabolic abnormalities associated with Primary HTN

- Primordial factors: prematurity, SGA, lower nephron number (Brenner hypothesis

After birth:

- Higher insulin and insulin resistance
- High uric acid levels
- Sympathetic NS activation
- Adipocytokines dysregulation
- Dysregulation gut microbiome (salt intake)

Litwin M, Pediatr Nephrol 2024

Approach to Child with Hypertension

Recognizing Primary HTN

I-SCREAM – an approach for pediatricians

- **I** = pediatrician or primary care physician (no need referral)
- **S** = screen for HTN
- **C** = confirm diagnosis of HTN
- **R** = Risk factor assessment by history [primary + secondary HTN]
- **E** = Evaluate with labs to rule out secondary and risk for primary
- **A** = Assessment for Target Organ Damage (LVH, Fundus examination)
- **M** = Manage with lifestyle modification +/- antihypertensive medications

Screening for HTN

- Healthy children > 3 yrs: Annually
- Children at risk for developing HTN: < 3 years, at every health encounter

TABLE 9 Conditions Under Which Children Younger Than 3 Years Should Have BP Measured

History of prematurity <32 week's gestation or small for gestational age, very low birth weight, other neonatal complications requiring intensive care, umbilical artery line
Congenital heart disease (repaired or unrepaired)
Recurrent urinary tract infections, hematuria, or proteinuria
Known renal disease or urologic malformations
Family history of congenital renal disease
Solid-organ transplant
Malignancy or bone marrow transplant
Treatment with drugs known to raise BP
Other systemic illnesses associated with HTN (neurofibromatosis, tuberous sclerosis, sickle cell disease,[114] etc)
Evidence of elevated intracranial pressure

Adapted from Table 3 in the Fourth Report.[1]

AAP 2017 and ESH

Checking BP – the only way to diagnose HTN!

- HTN defined as **mean (average)** of **replicate BPs** measured on **3 separate occasions**
- **Validity of Automated oscillometric BP measurements+/-**
  - **Good agreement (Araujo Moura 2021)**
  - **Only moderate agreement (Hanevold 2020)**
- **High Oscillometric BPs must be repeated by auscultation**

Repeating BP Measurements

- Isolated Hypertensive Level BP: BP at or > 95% once (or average of 2 readings) during a single visit
  - Bell et al during screening = 13%
  - (higher than actual prevalence of HTN inchildren)
- Persistent HTN: Elevated BP on 2 or more occasions.
- Important to avoid ‘false positives’ by repeated measurements on different occasions

Checklist of Manual / Oscillometric Validated BP devices

http://www.dableducational.org/sphygmomanometers/devices_1_clinical.html#ClinTable

dabl® Educational Trust

Blood Pressure Monitors - Validations, Papers and Reviews

Sphygmomanometers for Clinical Use

The following tables are lists of currently available Mercury, Aneroid and Non-Mercury Manual Sphygmomanometers, Automated Devices for Clinical Use and Finger Devices for Clinical Measurement. Discontinued devices are shown on a separate table. A complete list of all devices is available on our Device Index.

Manual Devices

Printable version>>

Device	Mode	AAMI	BHS	ESH 2002	ESH 2010	ISO 81060-2:2013	ISO 81060-2:2018	Circumstance	Recommendation Ref
A&D UM-101				Pass				Without use of "Mark" button	Recommended 7
				Fail				With use of "Mark" button	Not Recommended 7
A&D UM-102				Pass				A&D UM-101 Equivalence, Without use of "Mark" button	Recommended E137
Accoson Greenlight 300	Electronic Display			Pass				At rest	Recommended 1
Heine Gamma G7	Aneroid			Pass				At rest	Recommended 6
Heine Gamma XXL-LF	Aneroid			Pass				At rest	Recommended 6
Microlife BP 3AS1-2	Electronic			Pass				At rest	Recommended 10
Microlife WatchBP Office	Electronic			Pass				At rest	Recommended 8
Microlife WatchBP Office AFIB	Electronic			Pass				WatchBP Office Equivalence	Recommended E29
Nissei DM-3000	Electronic Display			Pass				2.5 mmHg/s deflation rate	Recommended 12
				Pass				"Blinded mode" with use of "Mark" button	Recommended 12
Pic Solution (Artsana) Pic Indolor (Artsana) Professional Check	Electronic + Osc Help			Pass				At rest	Recommended 11
Plusmed pM-NT 01	Electronic			Pass				Microlife BP3AS1-2 Equivalence	Recommended E125
PMS Mandaus		Pass	A/A					Abstract; Protocol violation	Questionable 2
				Pass				Minor adjustments	Recommended 5
PyMaH Mercury	Hg	Pass	A/A	NA				At rest	Recommended 3

Role of ABPM in Investigating HTN

- Is ABPM superior to clinic BP in making an accurate diagnosis of HTN?
- ABPM better reproducibility: Helpful but not mandatory

Indication	AHA/ ESH
For Diagnosis of HTN	
Confirm HTN in those with 'elevated BP' and Stage 1 HTN prior to evaluation	+
Confirm HTN before starting treatment (if TOD is present)	+
Detect masked HTN in high-risk patients – CKD, Tx, DM, Coarct of A, obesity, OSA	+
During Treatment of HTN	
Assess effectiveness of BP control	+
In CKD to intensify BP control	+
Repeat ABPM regularly to ensure BP control	+
In Clinical Research	
Clinical trials involving HTN	+

Primary vs Secondary HTN

- Secondary HTN: Specific Cause

- Age < 6 years
- Stage 2 HTN
- HTN urgencies & emergencies
- ABPM masked HTN, nocturnal HTN
- Potentially correctable

- Primary HTN

- Diagnosis of exclusion?
- Older children
- Milder HTN
- Overweight/ obese
- Family history of HTN in parents/ Grandparents

Causes of Secondary Hypertension

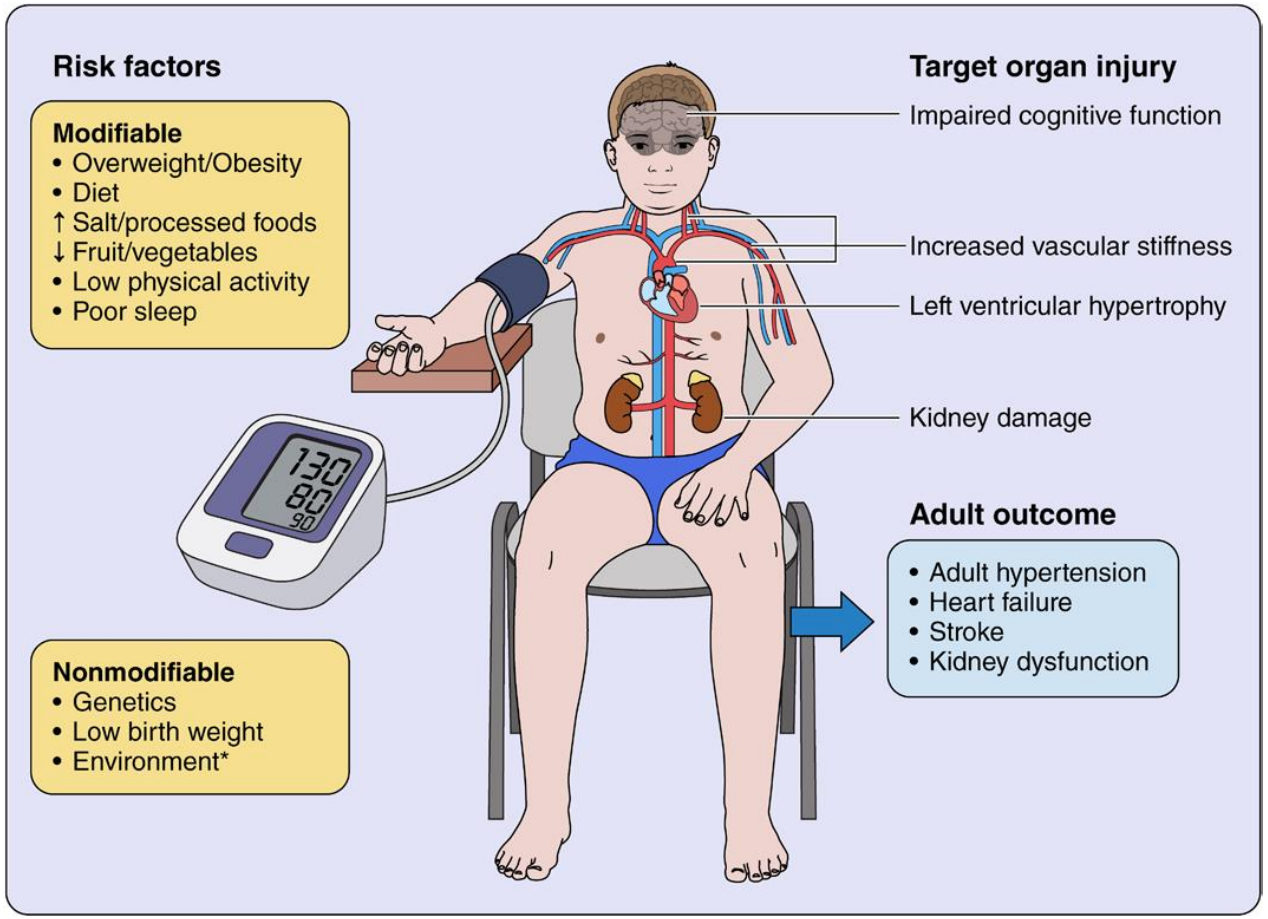
Age Group	Cause
Newborn	**Renal artery thrombosis (UAC)** **Renal vein thrombosis** Polycystic Kidney disease Coarctation of Aorta
1 – 5 years	**Renal Parenchymal** disease – Acute GN, HUS Renal Artery Stenosis Coarctation of Aorta
5 – 10 years	**Renal Parenchymal Disease** **Renal artery stenosis** Endocrine causes
Adolescence	Renal parenchymal disease Primary hypertension Renal artery stenosis

Prevalence of HTN in special pediatric populations

CKD 60 %– 70%
Post Kidney Transplant 60% – 90%
Other Solid Organ Transplants 30%(liver) – 70% (heart)
Coarctation of Aorta 45%
Type I DM 30%
Type II DM 30%
Syndromes with HTN 20% (Turners, NF1 etc)

Avner 8th Edition

Risk Factors to assess for Primary HTN



Examination	What to Look for	Significance
BP measurement	Upper & Lower Extremity BP discrepancy	Coarctation of Aorta/ Mid-Aortic Syndrome
Pulses	Distal Pulses poorly felt	Coarctation of Aorta
Height, Weight	Poor growth Obesity	CKD, chronic HTN Primary HTN
Facies	Cushingoid Elfin Short webbed neck	Steroid induced Williams syndrome Turner's syndrome
General Examination	Pallor Edema Ambiguous Genitalia	CKD, HUS Glomerular Disease, Severe CKD CAH
Severe HTN	Fundus, S/o CHF, Mental Status, Bell's Palsy, Fundus	HTN urgency, Emergency
Abdomen	Bruit	Renovascular Disease
Skin	Café-au-Lait	NF

Basic Screening Evaluation - Labs

Lab Test	What to Look for?	Significance
Urine first	RBCs, RBC casts, proteinuria	Presence of renal parenchymal Disease
CBC	Anemia	Chronic kidney disease
Creatinine	elevated	renal parenchymal disease
Electrolytes	Low or high K, acidosis	? Rare inherited renal tubular disorders→ HTN
Renal Ultrasound	Small kidney (one side) Two small kidneys Large but normal Large with Cysts Hydronephrosis	Scar, Renal artery stenosis Renal dysplasia, bilateral RAS Acute GN Polycystic Kidney Disease VUR, obstructive uropathy

Summary of Recommended Evaluation tests in various HTN Guidelines

Investigations	AAP 2017	European Society of HTN 2023	Indian Society of Pediatric Nephrology (2007)	Canada
Urea, Creatinine, Electrolytes	All Children with HTN	All Children with HTN	All Children with HTN	All Children with HTN
Urinalysis	ALL	ALL	ALL	ALL
Kidney Ultrasound	Only < 6 yrs OR abnormal results from blood/urine	ALL	ALL	ALL
Echo	At start of anti-HTN therapy	ALL	Additional test	ALL
Retina Examination	No recommendation	In severe HTN OR HTN emergency	ALL	ALL
Lipids & Fasting Glucose	ALL	ALL	ALL	ALL
Proteinuria/ Microalbuminuria	Only in CKD pts	ALL	ALL	ALL

LVH Prevalence in Youth with Primary HTN at diagnosis

- Risk of LVH increases with BP values > 90 percentile.
- **Pooled Prevalence of LVH in Primary HTN 31%**
- (Prevalence of LVH in secondary HTN is higher)
- Effective antihypertensive treatment AND weight loss leads to LVH regression

Sinha MD Frontiers in CV med 2022, Litwin M Ped Nephrol 2010

Managing HTN : Prevention

- Address primordial risk factors (**ask** maternal/ birth history)
- Prevent Obesity: **ask** about diet and exercise
- Increase physical activity: **ask** about phone time, type of activity
- Avoid excessive salt intake/ increase fruits/ vegetables (K+) → 36% lower risk of HTN in adulthood

WHO GUIDELINES ON **PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR**

https://www.who.int/publications

CHILDREN AND ADOLESCENTS
(aged 5–17 years)

In children and adolescents, physical activity confers benefits for the following health outcomes: improved physical fitness (cardiorespiratory and muscular fitness), cardiometabolic health (blood pressure, dyslipidaemia, glucose, and insulin resistance), bone health, cognitive outcomes (academic performance, executive function), mental health (reduced symptoms of depression); and reduced adiposity.

At least 60 minutes a day

moderate- to vigorous-intensity physical activity across the week; most of this physical activity should be aerobic.

It is recommended that:

› **Children and adolescents should do at least an average of 60 minutes per day of moderate- to vigorous-intensity, mostly aerobic, physical activity, across the week.**

Strong recommendation, moderate certainty evidence

› **Vigorous-intensity aerobic activities, as well as those that strengthen muscle and bone, should be incorporated at least 3 days a week.**

Strong recommendation, moderate certainty evidence

On at least 3 days a week

vigorous-intensity aerobic activities, as well as those that **strengthen muscle and bone** should be incorporated.

GOOD PRACTICE STATEMENTS

- Doing some physical activity is better than doing none.
- If children and adolescents are not meeting the recommendations, doing some physical activity will benefit their health.
- Children and adolescents should start by doing small amounts of physical activity, and gradually increase the frequency, intensity and duration over time.
- It is important to provide all children and adolescents with safe and equitable opportunities, and encouragement, to participate in physical activities that are enjoyable, offer variety, and are appropriate for their age and ability.

Treatment of Primary Hypertension

- Goal : <90th percentile or <130/80 mm Hg, whichever is lower
- Reduce risk of target organ damage in childhood
- Reduce risk of CV morbidity in adulthood

Non-pharmacologic Treatment (Lifestyle modification

Pharmacologic Treatment (Antihypertensive Rx)

Non-pharmacological therapies

- Weight Loss: Family effort more successful
- Diet: DASH Diet
  - Fruits/ Veg 5 per day
  - Whole grains
  - Low fat milk products 2 or more
  - Meat/ fish/legumes 1-2 per day
  - Sugar and sugary drink not more than 1
  - Dietary sodium < 2.5 gm per day
- Exercise: 40 minutes of moderate, vigorous physican activity → BP reduction by 6mmHg

AAP 2017

Indications for Antihypertensive medications

- Optimal BP level to be achieved with treatment of childhood HTN is <90th percentile or <130/80 mm Hg, whichever is lower
- Use antihypertensive medications if
  - Remain hypertensive despite lifestyle modifications
  - Symptomatic HTN
  - Stage 2 HTN
  - HTN with moderate to severe LVH
- Choice of drug: ACE inhibitors, ARB, Calcium channel blockers

Case: 13 year old boy presents for a mandated school check-up in your OPD. He has no complaints but his mother is concerned that he is addicted to his mobile phone.

On examination, weight = 54kg, height = 152cm, BMI = 23.4 (90^{th} percentile).

BP = 128/82mmHg and 130/76mmHg

- You must document whether BP is normal is his school form
- How would you classify this child's BP? Hypertension
- What is your approach? I-SCREAM

Summary

- HTN is leading modifiable risk factor for CV disease
- Primary HTN in children is underrecognized (misconceptions!)
- Primary HTN is commoner in the outpatient general population than secondary HTN
- I-SCREAM: systematic approach for **I** (pediatricians) to **s**creen, **c**onfirm, ask for **r**isk factors, **e**valuate for cause and target organ damage and **m**anage HTN in children
- Pediatricians are the key!

Thank you!

A 10 year old boy new to your clinic presents with an upper respiratory tract infection. His BMI is 26 (> 95th percentile). His throat is mildly congested but his chest is clear. After prescribing an antihistamine, which of the following is the most appropriate next step in his evaluation.

a) Ask the child to return the following month to measure BP with an auscultatory BP manometer
b) Ask about the perinatal history and for a family history of hypertension
c) Instruct the parents to monitor home BPs for a week to diagnose hypertension
d) Refer the child to a pediatric nephrologist to perform ABPM (ambulatory BP monitoring

Answer b)

You screen the patient's BP using an oscillometric device available in your clinic. His BP is 126/80 mmHg in the right arm which is 5 mm above the > 95th percentile. He has no symptoms of HTN. In addition to obesity, each of the following clinical features is indicative of a diagnosis of **primary** HTN EXCEPT

a) BPs corresponding to Stage 1 HTN without clinical symptoms

b) Family history of HTN and obesity in father and grandfather

c) Presence of acanthosis nigricans on neck and axilla

d) History of 3 episodes of febrile UTI during infancy

Answer d)

Which of the following statements is true regarding the pathophysiology of primary HTN

a) Characterised by salt sensitivity ie, the paradoxical increase in BP after oral salt depletion
b) Increased cIMT measures a form of arterial stiffness associated with primary HTN
c) In constrast to adult, primary HTN in pediatrics is 4 times more likely in girls
d) Reduced blood flow to the kidneys results in Renin Angiotensin system activation and HTN

Answer b)

You diagnose primary HTN based on repeat BPs on 3 occasions consistently > 95% percentile. Screening urinalysis and renal function tests are normal. Echo shows mild concentric LVH. Each of the following strategies for managing primary HTN is correct EXCEPT:

a) Avoid antihypertensive medications unless lifestyle modifications for 6 months fail
b) Weight loss by following a diet high in fruits, vegetables and legumes
c) Moderate to vigorous physical activity 3-5 days per week
d) ACE inhibitors are a good choice for first line antihypertensive medication if indicated

NephKids 2024

HYPONATREMIA

Moderator: Dr Rajakumar PS

Panelists:

Dr Srinivasan

Dr Muthiah

Dr Swathi kiran

HYPONATREMIA

Dr Rajakumar PS

Professor of Paediatrics &

Senior Consultant Paediatric Intensivist,

Sri Ramachandra Institute of Higher Education & Research (SRIHER)

DEFINITIONS

- Hyponatremia

- Mild
- Moderate
- Severe

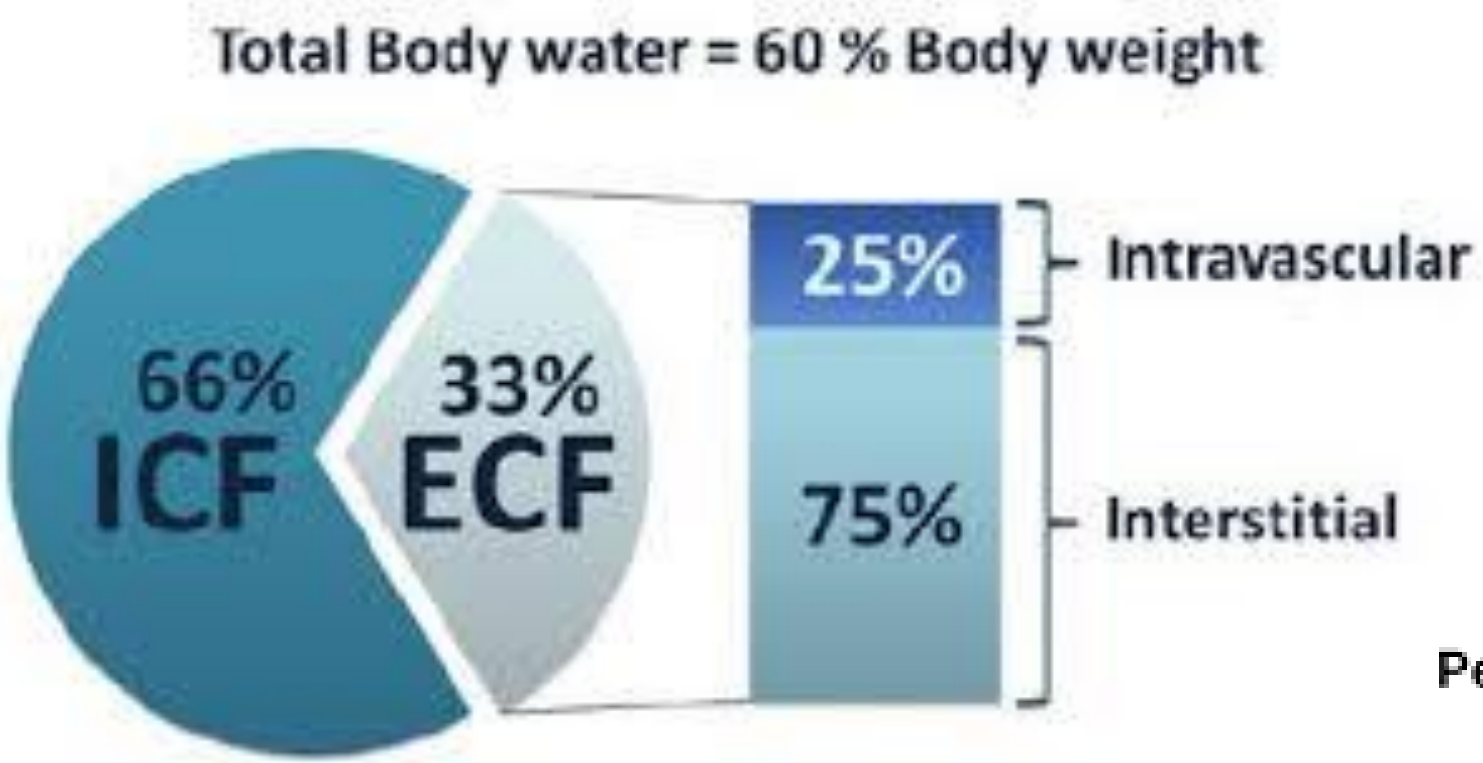
- Acute
- Chronic

DEFINITIONS

- Hyponatremia < 135 meq/L

- Mild 130 - 134
- Moderate 121 - 129
- Severe < 120

- Acute < 48 hrs
- Chronic > 48 hrs



How much is Total Body Water, ICF, ECF, Interstitial, Intravascular volumes?

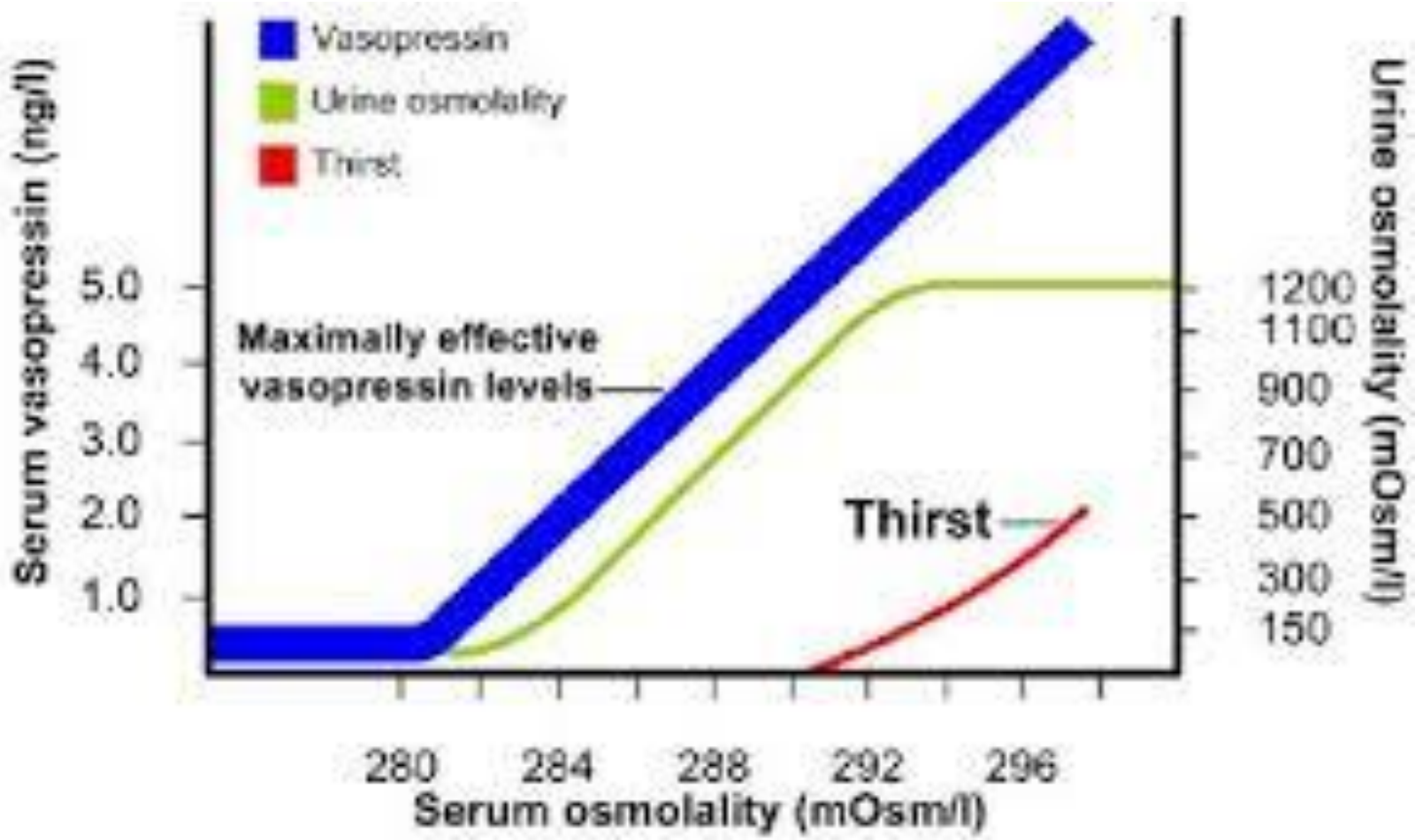
Sodium Correction =

0.6 x Body weight x (Normal - Actual Sodium)

What are the defenses against sodium imbalance ?

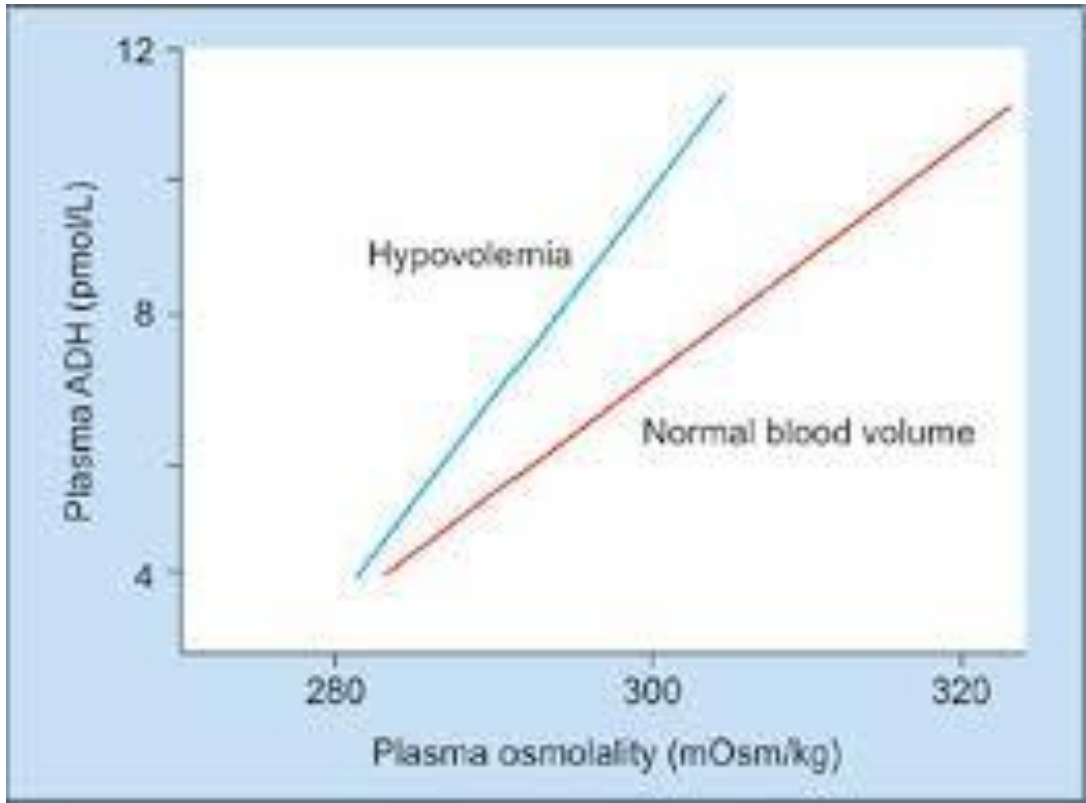
- ADH
- Thirst

- Which one first?

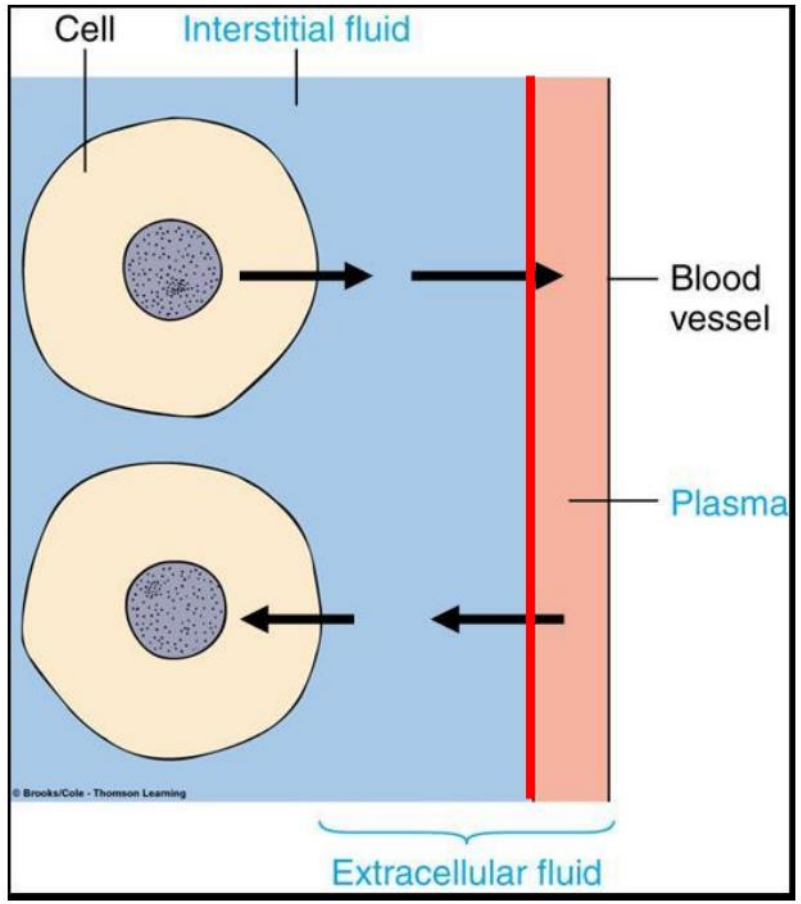


ADH - HYPOVOLEMIA VS OSMOLALITY

- ADH rises in hypovolemia
- If osmolality and plasma volume both are low, what happens?



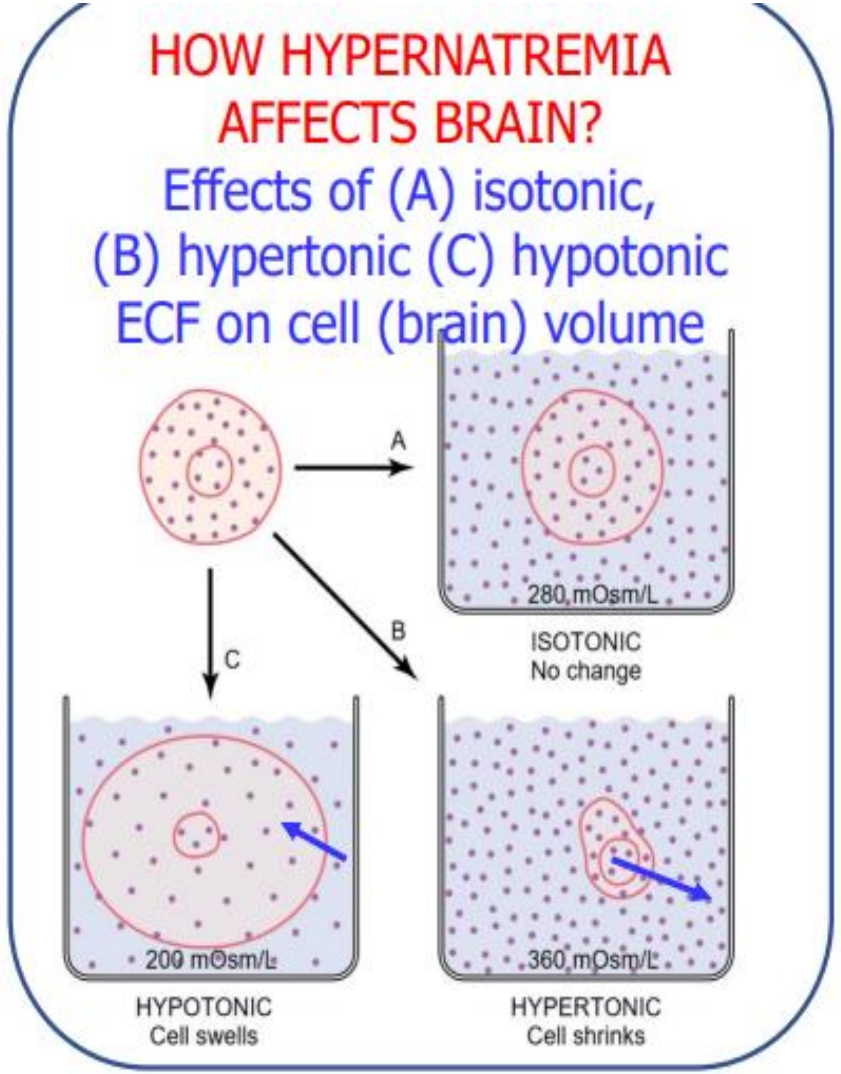
Shift of water



- Cell membrane which allows water only
- Lower tonicity to higher tonicity

What happens in dysnatremia?

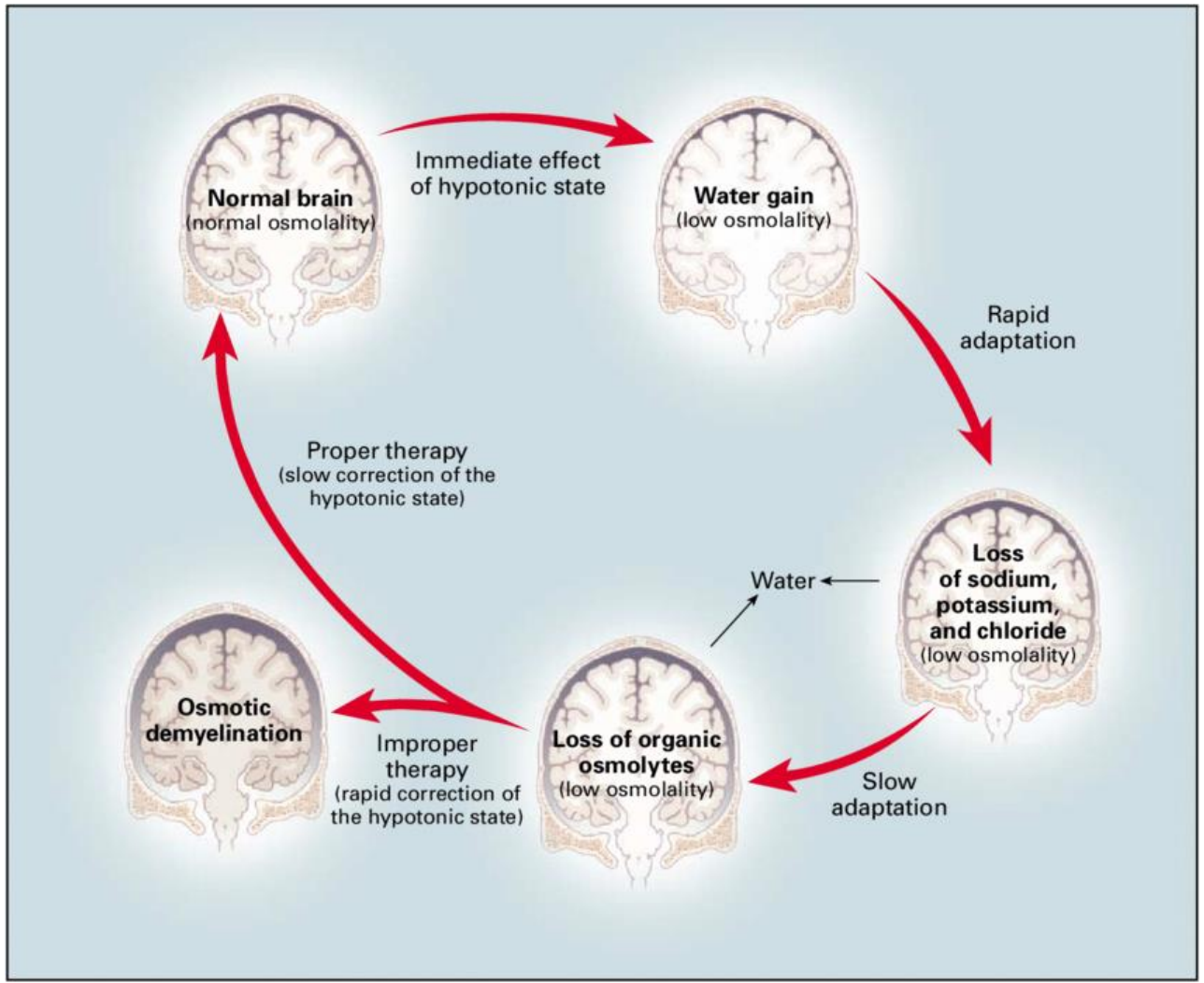
In hyponatremia
Brain swells up



In hypernatremia,
brain shrinks

Courtesy Dr S.Thangavelu

What happens in chronic hyponatremia & rapid correction?



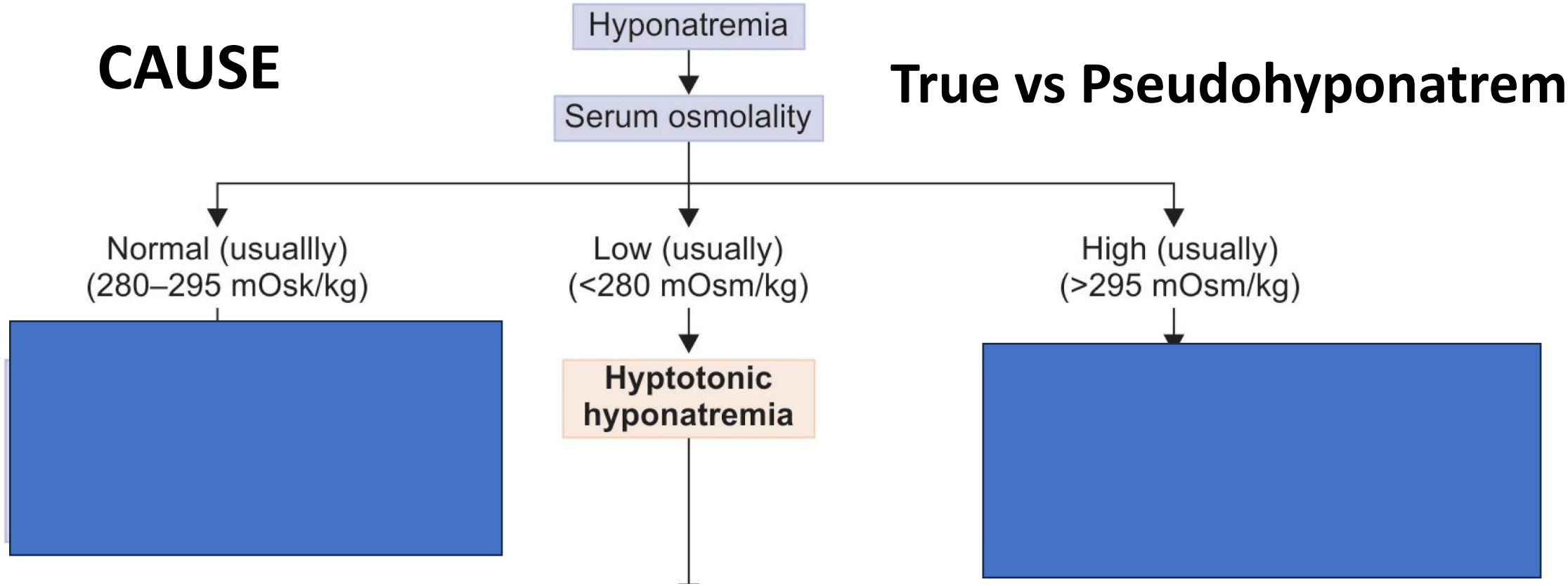
Approach to Hyponatremia
5 Questions to ask

Questions	Why?
1. Does the child have neurologic symptoms?	
2. If asymptomatic, check whether Pseudohyponatremia	
3. Is it acute or chronic?	
4. What is the Volume status?	
5. What is Urine Sodium?	

Approach to Hyponatremia
5 Questions to ask

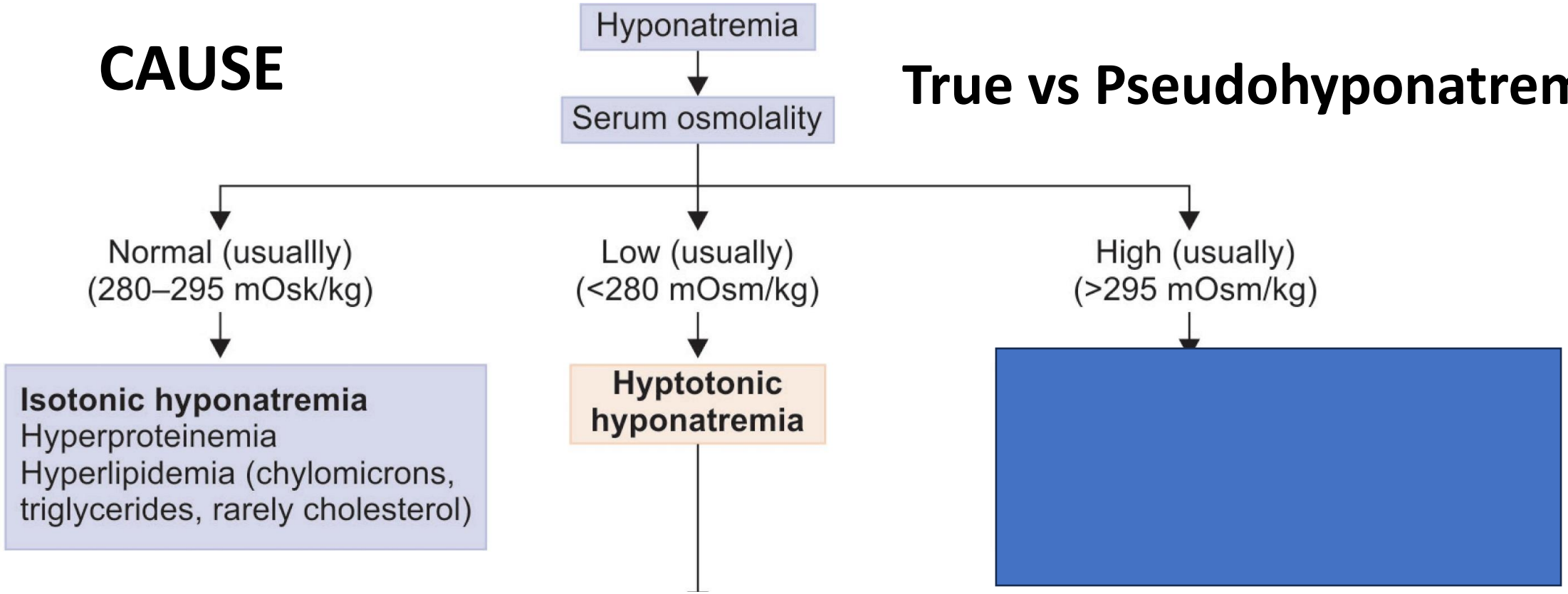
Questions	Why?
1. Does the child have neurologic symptoms?	Treatment varies
2. If asymptomatic, check whether Pseudohyponatremia	No need to treat
3. Is it acute or chronic?	Complications of rapid correction
4. What is the Volume status?	Cause & Treatment
5. What is Urine Sodium?	Cause & Treatment

CAUSE



True vs Pseudohyponatremia

CAUSE



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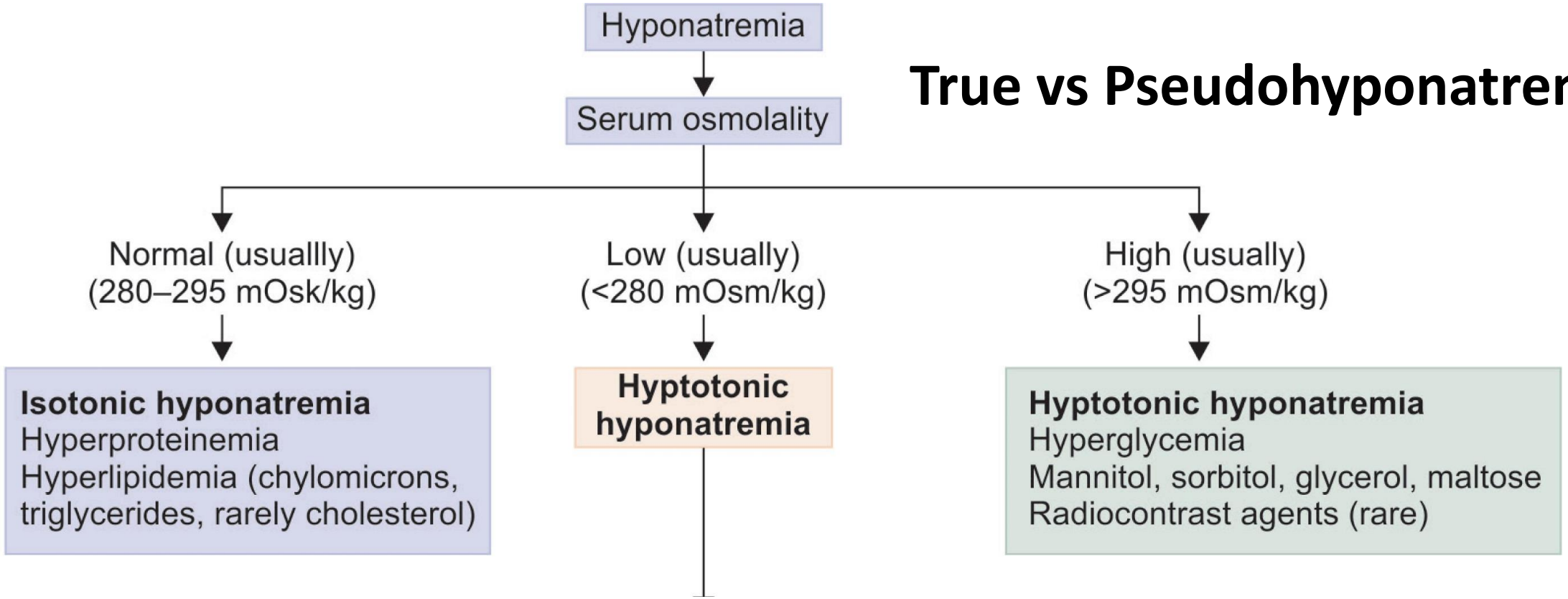
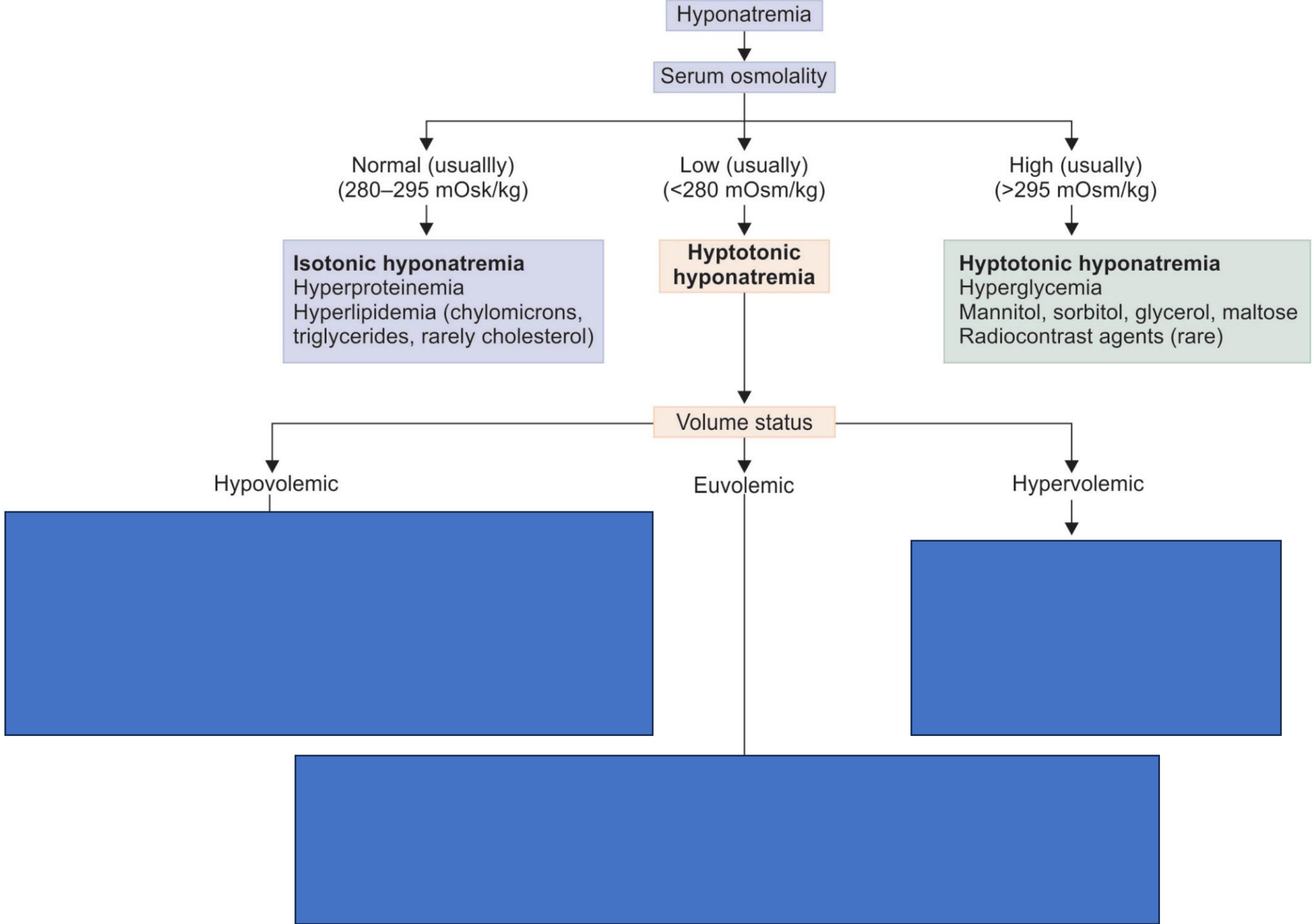
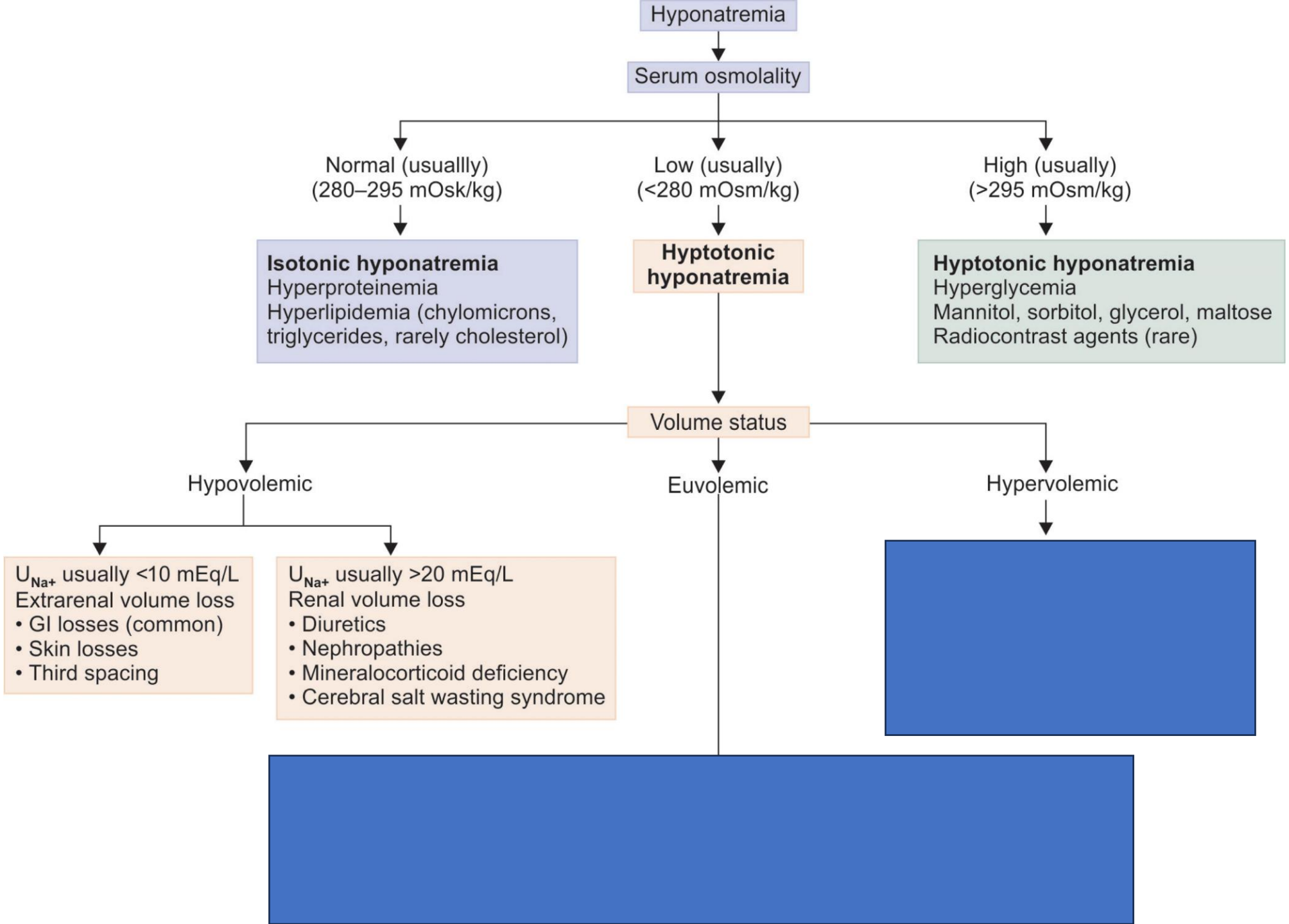



Hyponatremia
Serum osmolality
Normal (usuallly)
(280–295 mOsk/kg)
Low (usually)
(<280 mOsm/kg)
High (usually)
(>295 mOsm/kg)
Isotonic hyponatremia
Hyperproteinemia
Hyperlipidemia (chylomicrons, triglycerides, rarely cholesterol)
Hyptotonic hyponatremia
Hyptotonic hyponatremia
Hyperglycemia
Mannitol, sorbitol, glycerol, maltose
Radiocontrast agents (rare)
Volume status
Hypovolemic
Euvolemic
Hypervolemic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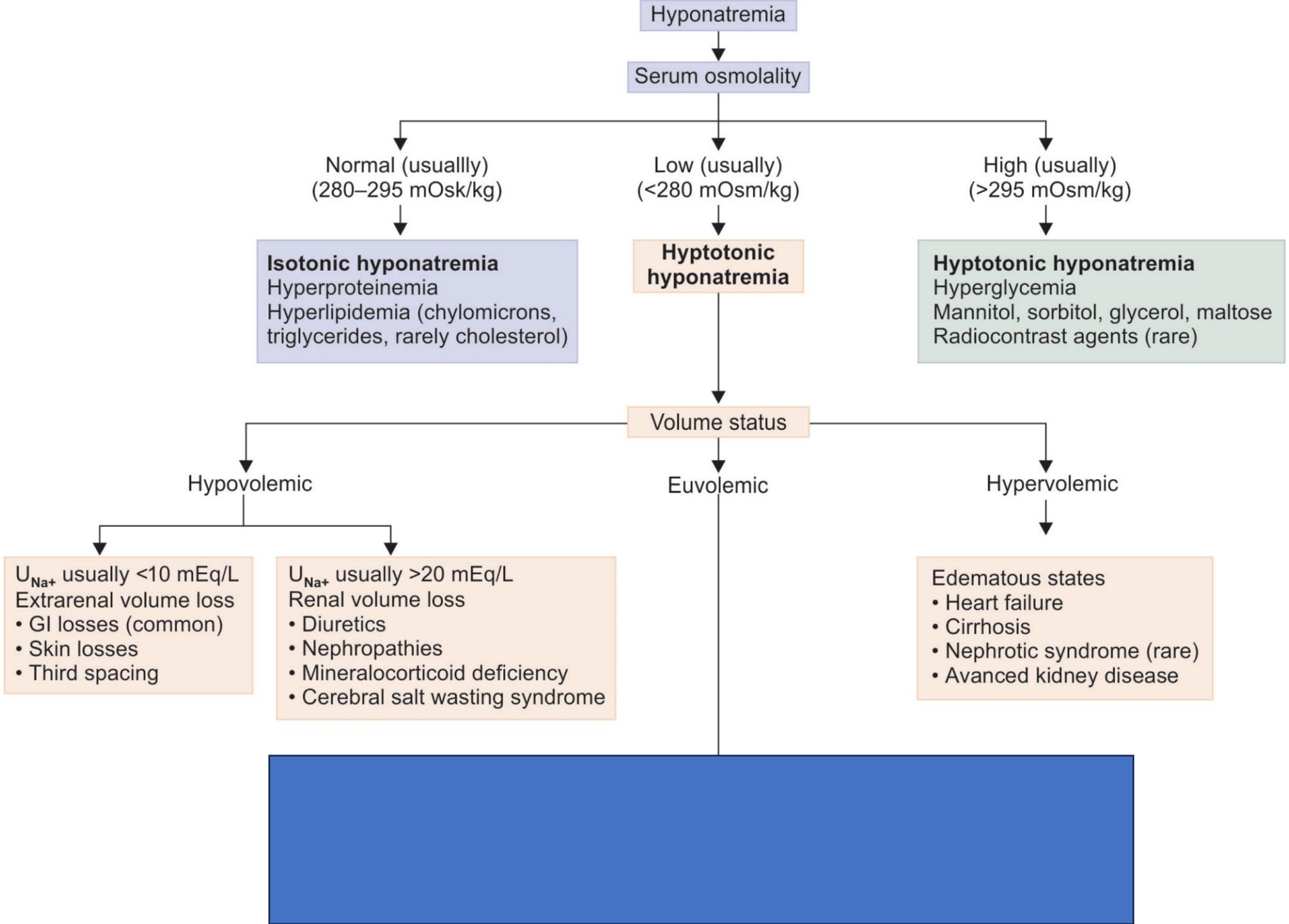
Hypervolemic
U_{Na+} usually <10 mEq/L
Extrarenal volume loss
• GI losses (common)
• Skin losses
• Third spacing
U_{Na+} usually >20 mEq/L
Renal volume loss
• Diuretics
• Nephropathies
• Mineralocorticoid deficiency
• Cerebral salt wasting syndrome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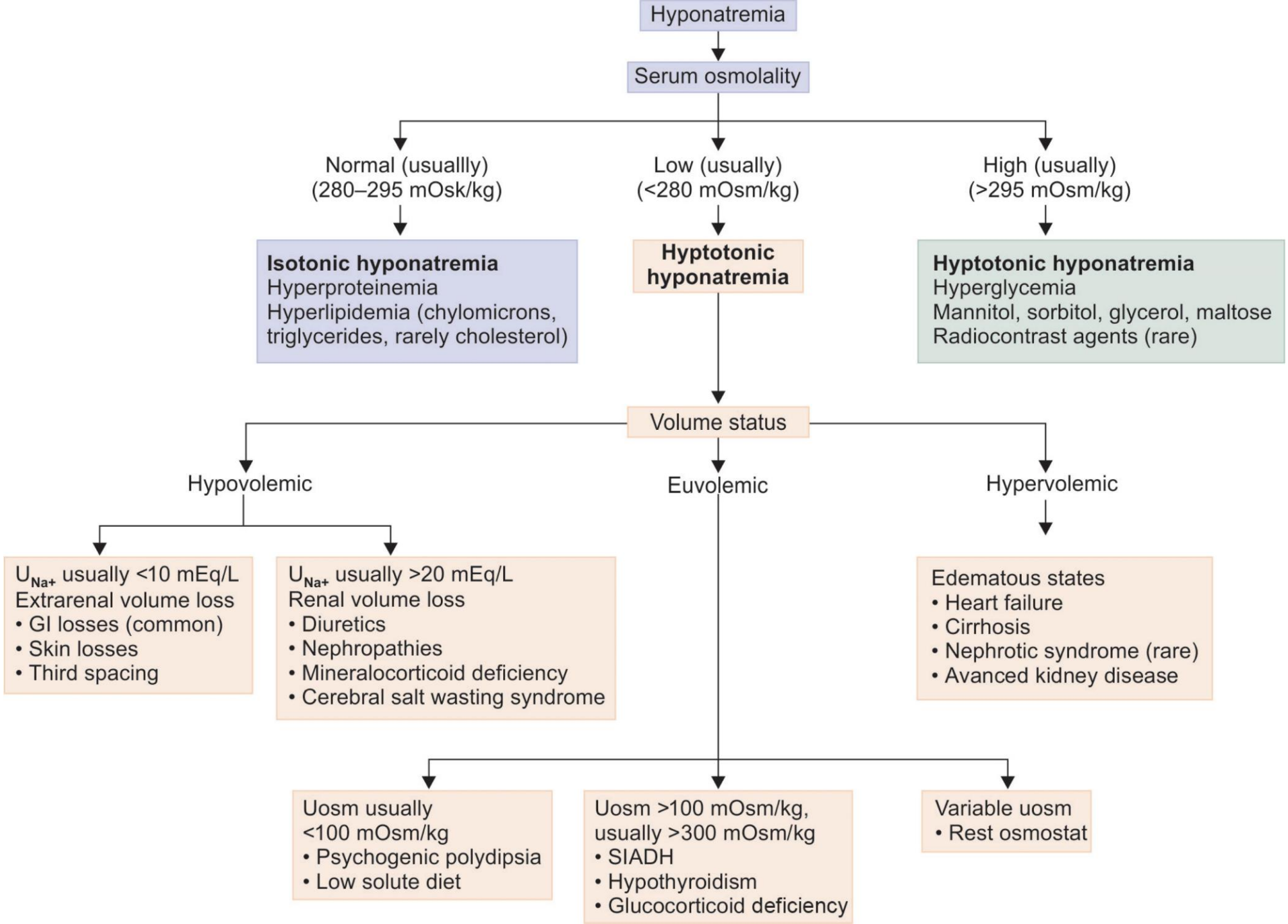
• Cerebral salt wasting syndrome
Edematous states
• Heart failure
• Cirrhosis
• Nephrotic syndrome (rare)
• Avanced kidney disease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• Heart failure
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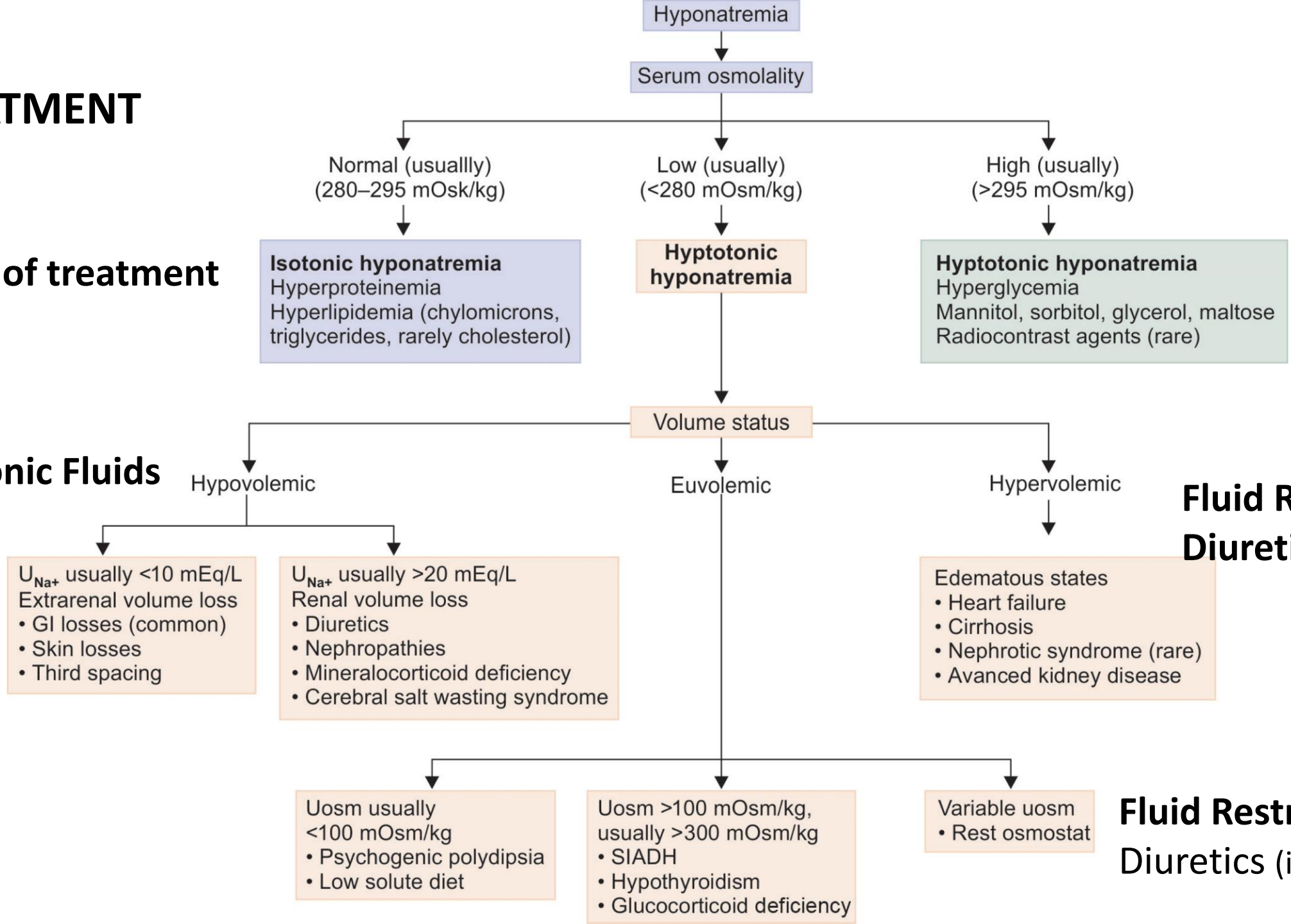
• Nephrotic syndrome (rare)
• Avanced kidney disease
Uosm usually
<100 mOsm/kg
• Psychogenic polydipsia
• Low solute diet
Uosm >100 mOsm/kg,
usually >300 mOsm/kg
• SIADH
• Hypothyroidism
• Glucocorticoid deficiency
Variable uosm
• Rest osmostat

TREATMENT



No need of treatment

Isotonic Fluids

Fluid Restriction
Diuretics

Fluid Restriction
Diuretics (if needed)

TAKE HOME MESSAGE
Approach to Hyponatremia - 5 Questions

Questions	Why?
1. Does the child have neurologic symptoms?	Treatment varies
2. If asymptomatic, check whether Pseudohyponatremia	No need to treat
3. Is it acute or chronic?	Complications of rapid correction
4. What is the Volume status?	Cause & Treatment
5. What is Urine Sodium?	Cause & Treatment

CHENNAI

PEDICRITICON 2024

EMBRACE, ENHANCE, EMPOWER

26th National Conference of IAP - Intensive Care Chapter

Workshops - 11th and 12th December 2024.

Conference - 13th, 14th and 15th December 2024.

Register 2 Workshop Get Discount RS.1000/-

WORKSHOPS DAY 1 - 11.12.2024	
Point of Care Ultrasound (POCUS)	Transplant & Oncology Critical Care
Pediatric Critical Care Nursing Workshop	Clinical Research Methodology: Clinican to Clinical Researcher

WORKSHOPS DAY 2 - 12.12.2024		
PICU Liberation	Advanced Ventilation	ECMO
NIV	SLEDD & CRRT in PICU	Pediatric Bronchoscopy
SONIC-Advanced USG Training	Pediatric Critical Care Nursing Workshop	SIM-BPICC (Simulation based Basic Pediatric Intensive Care Course)
RESUS (Redefining Emergency Skill and Scenario training Using Simulation)		

Hypovolemic Hyponatremia

Dr.Srinivasan

Asst. Prof of Pediatrics, KMC

Case scenario

- One year old boy admitted for diarrhea.Several episodes since yesterday.Mother gave plain water & dhal water . Child irritable ,tongue dry, AF depressed, last voided urine 6 hours ago, skin turgor reduced , HR 128 Peripheral pulses palpable .RR-34. BP 90/60 . Basic investigations were essentially normal except low sodium
- Na- 124 meq/l

How to approach this patient?

Clinical assessment of dehydration

Table 75.1	Clinical Evaluation of Dehydration

Mild dehydration (<5% in an infant; <3% in an older child or adult): Normal or increased pulse; decreased urine output; thirsty; normal physical findings

Moderate dehydration (5–10% in an infant; 3–6% in an older child or adult): Tachycardia; little or no urine output; irritable/lethargic; sunken eyes and fontanel; decreased tears; dry mucous membranes; mild delay in elasticity (skin turgor); delayed capillary refill (>1.5 sec); cool and pale

Severe dehydration (>10% in an infant; >6% in an older child or adult): Peripheral pulses either rapid and weak or absent; decreased blood pressure; no urine output; very sunken eyes and fontanel; no tears; parched mucous membranes; delayed elasticity (poor skin turgor); very delayed capillary refill (>3 sec); cold and mottled; limp, depressed consciousness

Assessment of degree of dehydration based on weight loss

- Pre illness weight-10
- Present weight-9.4

600 gm lost after the diarrhoeal episode- 6% dehydration.

If pre illness weight is not known, use this formula

$$\frac{pre-illness\,weight(kg)}{current weight(kg)} = \frac{100}{100-\%dehydration}$$

Diagnosis

- **AWD / moderate dehydration/ Hypovolemic hyponatremia**
- The volume depletion stimulates synthesis of ADH, resulting in reduced renal water excretion.
- The body's usual mechanism for preventing hyponatremia,renal water excretion, is blocked.
- **More than the Na loss, it's predominantly the water retention that causes hyponatremia in a diarrhoeal setting.**

In general the amount of Na lost in a diarrhoeal stool is very less.

(avg 50 meq/l except in cholera where sodium loss can be high)

Steps in evaluation

- 1. Any neurological symptoms? No
- 2. True or pseudo? Sample appropriate, Glucose (CBG) 107 mg, Sample not lipemic. True
- 3. Volume status? Moderately dehydrated , Hypovolemic. No shock.
- 4. Acute or chronic? Acute -
- 5. Urine sodium levels? Not done - Primarily used to differentiate renal / non renal losses. Here the cause is obvious. So not a must.

Step wise correction of dehydration

- Calculate volume needed:
- Deficit = Here 6% dehydration =60 ml/kg of fluid loss.
- % dehydration × weight = 60×10=600 ml
- Deficit + Maintenance =600 + 1000 =1600 mL
- Replace as D5 NS with appropriate maintenance K
- Give half of total fluid (800ml) in 8 hrs and second half (800ml) in the. next 16 hrs .

Ongoing losses to be replaced ml per ml.

Add KCl if hypokalemic & once the urine output is well established.

- **Correct the dehydration, hyponatremia will get corrected by itself Clinically monitor, repeat electrolytes after 24 hrs.**
- **If any new symptoms occur ,repeat Na at that point.**

Table 75.2	Fluid Management of Dehydration

1. Restore intravascular volume
   Isotonic fluid (NS or LR): 20 mL/kg over 20 min
   Repeat as needed
2. Calculate 24 hr fluid needs: maintenance + deficit volume
3. Subtract isotonic fluid already administered from 24 hr fluid needs
4. Administer remaining volume over 24 hr using 5% dextrose NS + 20 mEq/L KCl
5. Replace ongoing losses as they occur

LR, Ringer lactate; NS, normal saline.

The older method of correcting the Na deficit is not needed. Correct dehydration/ volume with isotonic fluids. Hyponatremia will get corrected by itself.

	Water in ml	Na in mmol/L (3 mmol/kg)
Maintenance	1000	30
Deficit	500	72
Total	1500	102

Correct Na and water deficit together, not separately

Infuse 1500 mL of D5 NS for 24 - 36 hrs

Scenario 2

- The same child was managed in a district hospital. Initial sodium was 124. As the child developed an episode of seizure, it was referred to a tertiary care center where serum Na was 116 meq/l on arrival.How to manage now?

Management

- Target is to increase serum Na by +5 mEq/L to bring down the cerebral edema
- Which fluid? **3% saline 5 mL/Kg or NS 20 mL/kg ?**
- For 10 kg child, 3%Saline 5 ml/kg= 50 mL. (1 ml- 0.5 meq of Na. So 50 mL = 25 meq of Na)
- If NS 20 ml/ kg is given , it provides approx 30 meq in 200 mL.(100 ml= 15.4 meq of Na)
- Both 5ml/kg of 3% saline & 20ml/kg of NS provide around 25-30 mEq of sodium.
- NS bolus (20ml/ kg)is preferred as it corrects hypovolemia as well as sodium deficit. 3% saline may not be the right choice if the child is volume depleted.

Carry home messages

- The initial goal in treating hyponatremia in diarrhoeal patients is restoration of intra- vascular volume with isotonic fluids.
- NS 20 ml/ kg bolus is preferred over 3% saline in volume depleted hyponatremic patients with neurological symptoms.

Scenario 3

A known case of Nephrotic syndrome on follow up . No complaints at present. No clinical edema & urine output is good. Since parents were anxious & wanted to repeat all investigations to ensure that everything is normal, basic investigations were sent. While drawing sample the intern noticed that it looked like how it's depicted in the picture. Na values were reported as 127 meq/l. Comment?

Diagnosis:Pseudohyponatremia

- The child is otherwise clinically normal & the serum looks lipemic.
- In hyperlipedemic / hyperprotenemic states/ IVIG infusions , this happens if the lab uses FEP methods (Flame emission photometry).
- In FEP method, the sodium is measured in relation to the total serum. (Solids + aqueous component). When the solid component rises as in hyperlipidemia/ hyperprotenemia, it gives falsely low sodium values.
- The modern analyzers / ABG analyzers uses ion sensitive electrodes that measure the exact number of Na ions in the serum.
- So when we doubt pseudohyponatremia , counter check with ABG analyzers.

Scenario-4

- 6 yr old Subhadra presented with excessive thirst & tiredness, frequent urination & significant loss of weight in the last one month. Since morning she is breathing fast .
- Her blood sugar was 618 mg/dl, urine sugar 2+, ketones 3+ .ABG- Metabolic acidosis with resp alkalosis.
- Na-127 meq/l K- 3.4 meq/l.
- Comment?

Diagnosis: DKA / Factitious or translocational hyponatremia

Associated with hyperosmolar agents like Mannitol, Glucose, Radio contrast agents etc which causes fluid shifts into ECS because of high osmolality.

- For every 100 mg /dl rise in sugar levels, Na falls by 1.6 meq/l. Once the sugar levels normalizes, the hyponatremia gets corrected on its own. So no need to correct the hyponatremia.
- Neurological symptoms in hyponatremia are due to reduced serum Osmolality.

Thank you

Step 3: If asymptomatic, categorize them according to the volume status: a) Hypovolemic hyponatremia b) Isovolemic hyponatremia c) Hypervolemic hyponatremia (Table I).

Step 1 *True hyponatremia:* First step in the treatment is to confirm whether hyponatremia is true or false. Usually true hyponatremia is associated with hypo-osmolaerity. In pseudo hyponatremia serum osmolality will be normal or high. When facility to test the serum osmolality is available this is easier. If this facility is not available, or cannot be determined, decision should be based on clinical situations. Exclusion of pseudohyponatremia is straight forward once blood glucose is checked and found to be normal, the serum sample is not found to be lipemic and if the sample is taken in right manner.

Step 2 Development of neurological symptoms depends on the severity of hyponatremia as well as the rapidity of its evolution. Treatment of symptomatic hyponatremia: Management is common in all children with hyponatremia and neurological symptoms, irrespective of the category. If the child develops seizures or irritability or altered level of consciousness, serum sodium level has to be raised quickly by at least 5 mEq/L.[4,5] This can be done by giving 6 mL/kg of 3% saline over 30 min to 1 hour through peripheral line and this will be enough to tide over the crisis, irrespective of serum sodium level. One mL/kg of 3% saline will raise the serum sodium level by 0.8 mEq/L. Further management is as for an asymptomatic child. This crisis management is common for all three categories when the child displays neurological symptoms. In general, all calculations and equations cannot replace meticulous clinical and frequent biochemical monitoring, because they do not take into consideration the effects of added solutes and water and presume that there is no ongoing loss. It is also impossible to give precise recommendation for every situation, and it is individualized based on repeated monitoring. Hypertonic saline also reduces ICP by promoting water movement from ICF to intravascular space.

Step 3 If the child has hyponatremia, but does not have seizures or other CNS symptoms, here management based on volume status. In hypovolemic hyponatremia treatment is replacement of salt and water, isovolemic hyponatremia needs water restriction and in hypervolemic hypernatremia, both sodium and water has to be restricted.

1. Treatment of hypovolemic hyponatremia: Calculate the degree of dehydration and correct the deficit using normal saline or ringer lactate. This will correct both dehydration and hyponatremia. This can be done by one of the two methods.

For example, one year old weighing 10 kg moderately dehydrated, no seizures, neurological status normal.

Three phase correction: Deficit 10 x 60 = 600 mL. This has to be given over a period of 6 hrs. Phase 1: In the first hour 20 mL/kg of NS (0–1 hour 200 mL) is given over one hour for rapid deficit correction and in the phase 2 (i.e., 1–6 hrs), the rest of 400 mL of NS can be given over 5 hours. This is followed by Phase 3,where maintenance fluid for 7–24 hrs as 1000 mL of ½ GNS is given. Serum sodium has to be rechecked after 12 hrs after dehydration correction to ensure that serum sodium level is returned to normal (Table II).

Two phase correction: E.g. deficit correction is 600 mL and maintenance fluid is 1000 mL with a total of 1600 mL. Phase 1 : 200 mL in the first hour; rest (1400 mL) is given over 1-24 hrs (Table III).

Table II. Three phase dehydration correction[6]

0–1 hr	1–6 hrs	7–24 hrs
Rapid restoration of intravascular volume (20 mL/kg) 200 mL over one hr (NS/RL)	Deficit correction: Rest of 40 mL/Kg) 400 mL over 5 hrs (NS/RL)	Maintenance + replacement of ongoing losses 1000 mL G5 ½ NS with K 20 mEq/L

Table III. Two phase dehydration correction

0–1 hr	1–24 hrs
Rapid restoration of Intravascular volume (20 mL/kg) 200 mL over one hr (NS/RL)	**Deficit correction** + Maintenance 400 + 1000 mL = 1400 mL over1- 24 hrs (G5 ½ NS + K 20 mEq/L) 0-8 hrs: 700 mL; 9-24 hrs: 700 mL

2. Isovolemic hyponatremia: Here there is a subtle increase in water and that leads to hyponatremia. Restriction of water will raise the serum sodium level. Usually in normovolemic individuals, water retention and resultant fall in tonicity suppresses ADH release. Two appropriate stimuli for ADH release are increase in osmolarity or fall in effective plasma volume. But in SIADH, despite falling tonicity, ADH secretion continues which is inappropriate. Inappropriate stimuli in this situation are certain clinical

appropriately.

HYPONATREMIC DEHYDRATION

The pathogenesis of hyponatremic dehydration usually involves a combination of sodium and water loss and water retention to compensate for the volume depletion. The patient has a pathologic increase in fluid loss, and the lost fluid contains sodium. Most fluid that is lost has a lower sodium concentration, so patients with only fluid loss would have hypernatremia. Diarrhea has, on average, a sodium concentration of 50 mEq/L. Replacing diarrheal fluid with water, which has almost no sodium, causes a reduction in the serum [Na^+] (see Chapter 74). The volume depletion stimulates synthesis of antidiuretic hormone, resulting in reduced renal water excretion. Therefore the body's usual mechanism for preventing hyponatremia, renal water excretion, is blocked. The risk of hyponatremia is further increased if the volume depletion is a result of loss of fluid with a higher sodium concentration, as may occur with renal salt wasting, third space losses, or diarrhea with high sodium content (cholera).

The initial goal in treating hyponatremia is correction of intravascular volume depletion with isotonic fluid. An overly rapid (>8-10 mEq/L over the first 24 hours) or overcorrection in the serum [Na^+] (>135 mEq/L) is associated with an increased risk of **osmotic demyelination syndrome** (formerly *central pontine myelinolysis*) (see Chapter 73). Most patients with hyponatremic dehydration

hyponatremia and severe symptoms needs treatment that will quickly reduce cerebral edema. This goal is best accomplished by increasing the extracellular osmolality so that water moves down its osmolar gradient from the ICS to the ECS.

Intravenous hypertonic saline rapidly increases serum [Na^+], and the effect on serum osmolality leads to a decrease in brain edema. Each mL/kg of 3% NaCl increases the serum [Na^+] by approximately 1 mEq/L. A child with active symptoms often improves after receiving 4-6 mL/kg of 3% NaCl.

The child with **hypovolemic hyponatremia** has a deficiency in Na^+ and may have a deficiency in water. The cornerstone of therapy is to replace the Na^+ deficit and any water deficit present. The first step in treating any dehydrated patient is to restore the intravascular volume with isotonic saline. Ultimately, complete restoration of intravascular volume suppresses ADH production, thereby permitting excretion of the excess water. Chapter 75 discusses the management of hyponatremic dehydration.

The management of **hypervolemic hyponatremia** is difficult; patients have an excess of both water and Na^+. Administration of Na^+ leads to worsening volume overload and edema. In addition, patients are retaining water and Na^+ because of their ineffective intravascular volume or renal insufficiency. The cornerstone of therapy is water and Na^+ restriction, because patients have volume overload. Diuretics may help by causing excretion of both Na^+ and water. Vasopressin receptor antagonists (**vaptans**), by blocking the action of ADH and causing a water diuresis, are effective in correct-

[Na+], but avoid
The most impor-
ernatremia is fre-
luid therapy can
oo slow nor too
condary to rapid
be stopped. An
[Na+], reversing

d with hyperna-
ally secondary to
ly with 5% dex-
not had time to
d mortality rates
erly rapid correc-
sodium intoxi-
water to correct
olume overload.
excess Na+, with
sis. In less severe
emoval of excess
. With Na+ over-
venous (IV) fluid

y a problem and

glycemia in diabetes mellitus, water moves back into the cells, and the [Na+] rises to its "true" value. Mannitol or sucrose, a component of IVIG preparations, may cause hyponatremia because of hyperosmolality.

Classification of hyponatremia is based on the patient's volume status. In **hypovolemic hyponatremia,** the child has lost Na^+ from the body. The water balance may be positive or negative, but Na^+ loss has been higher than water loss. The pathogenesis of the hyponatremia is usually a combination of Na^+ loss and water retention to compensate for the volume depletion. The patient has a pathologic increase in fluid loss, and this fluid contains Na^+. Most fluid that is lost has a lower [Na^+] than that of plasma. Viral diarrhea fluid has an average [Na^+] of 50 mEq/L. Replacing diarrhea fluid, which has [Na^+] of 50 mEq/L, with formula, which has only approximately 7-10 mEq/L of Na^+, reduces the serum [Na^+]. Intravascular volume depletion interferes with renal water excretion, the body's usual mechanism for preventing hyponatremia. The volume depletion stimulates ADH synthesis, resulting in renal water retention. Volume depletion also decreases the GFR and enhances water resorption in the proximal tubule, thereby reducing water delivery to the collecting duct.

Diarrhea as a result of gastroenteritis is the most common cause of hypovolemic hyponatremia in children. Emesis causes hyponatremia if the patient takes in hypotonic fluid, either IV or enterally, despite the emesis. Most patients with emesis have either a normal

Case scenarios

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Case scenario 1

- A 1-year-old developmentally normal, previously healthy baby boy is admitted with Lobar Pneumonia with fever, cough and tachypnea. Baby is started on IV Ceftriaxone and IV maintenance fluids.
- On day 2 of admission, baby has decreased urine output (0.4 ml/kg/hr) for last 24 hours.

- Clinically perfusion is normal with no signs of dehydration and no h/o of vomiting/ diarrhea. There is no edema/ hypertension. Urinary bladder is not distended.
- Rest of the examination is unremarkable apart from respiratory signs of Pneumonia. He has normal sensorium with no neurological deficit.

Lab reports

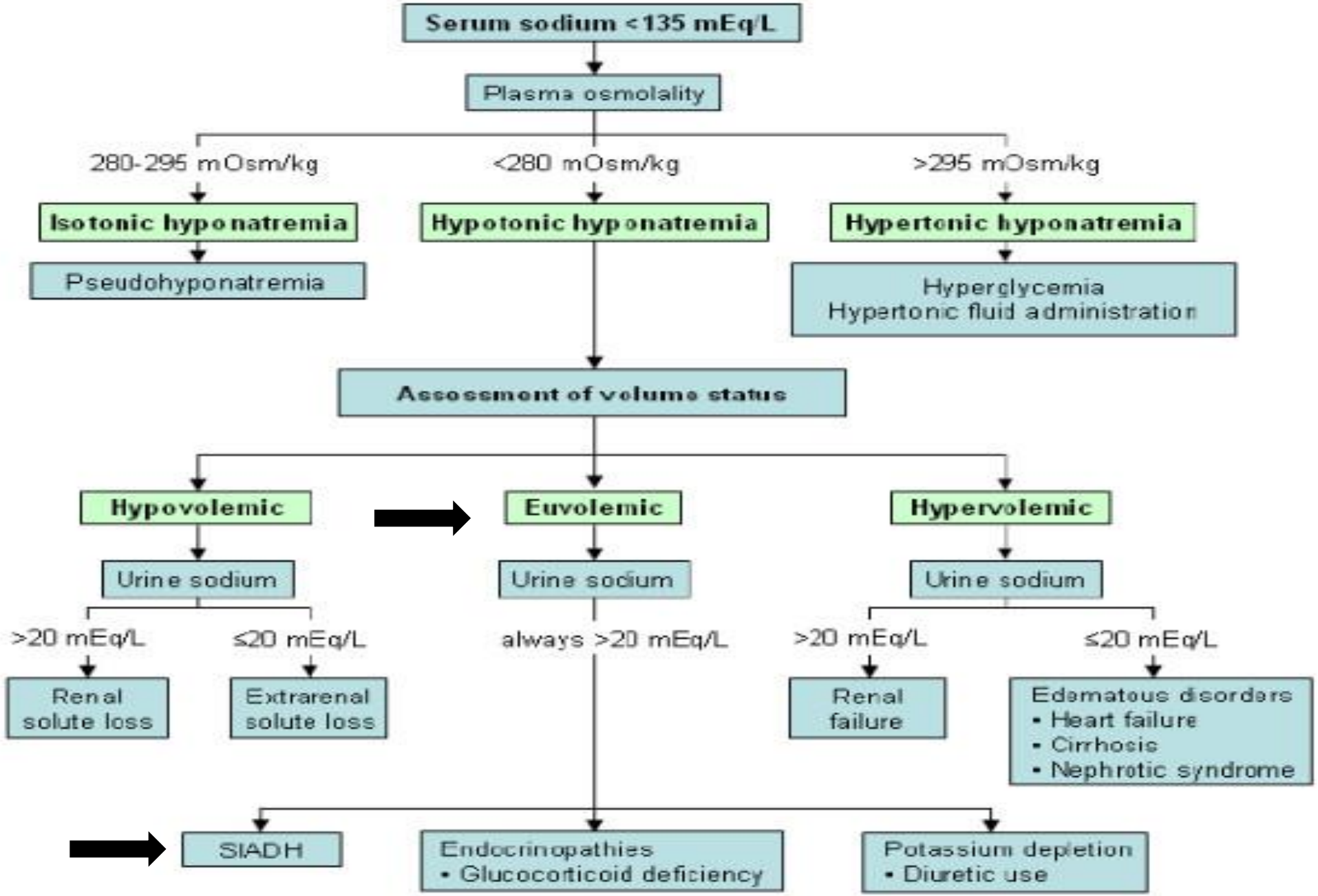
- **Na 126 meq/L**
- K 3.7 meq/L
- Cl 98 meq/L
- HCo3 25 meq/L
- BUN 4 mg/dL
- Creatinine 0.4 mg/dL
- **Glucose 129 mg/dL**
- **Urine Studies Specific gravity 1.035**
- USG KUB normal

- 1. What is the likely cause of oliguria and hyponatremia?

  Probable SIADH
- 2. What test will you do to confirm the diagnosis?

  URINE Sodium, Urine SG, Urine and serum Osmolality
- 3. How will you manage the child further?

  Restrict fluids , treat the cause


Serum sodium <135 mEq/L
Plasma osmolality
280-295 mOsm/kg
<280 mOsm/kg
>295 mOsm/kg
Isotonic hyponatremia
Hypotonic hyponatremia
Hypertonic hyponatremia
Pseudohyponatremia
Hyperglycemia
Hypertonic fluid administration
Assessment of volume status
Hypovolemic
Euvolemic
Hypervolemic
Urine sodium
Urine sodium
Urine sodium
>20 mEq/L
≤20 mEq/L
always >20 mEq/L
>20 mEq/L
≤20 mEq/L
Renal solute loss
Extrarenal solute loss
Renal failure
Edematous disorders
• Heart failure
• Cirrhosis
• Nephrotic syndrome
SIADH
Endocrinopathies
• Glucocorticoid deficiency
Potassium depletion
• Diuretic use

SIADH

Definition:

- Nonphysiologic release of AVP

Etiology:

1. Central lesions
2. Pulmonary diseases
3. Malignancies
4. Drugs
5. Metabolic diseases

SIADH: Diagnostic criteria

Essential

Plasma osmolality <275 mosm/kg

- Urine osmolality >100 with normal RF
- Euvolemia
- Increased urinary sodium
- No endocrinal problem/diuretic use

Supplemental

- Abnormal water load test
- Elevated AVP
- Improvement with fluid restriction

Management of SIADH

- Restrict fluids to 60 to 70% maintenance
- Avoid hypotonic fluids
- Monitor sodium (2 times daily if ≤120 meq/L)
- If resistant can use 3% NS infusion or furosemide infusion (desalination)
- VAPTANS are V2 receptor antagonists (promote free water aquaresis) rarely used in children (Anticipate rapid fall, more useful in hypervolemic hyponatremia)
- If resistant to therapies think of **alternate diagnosis**

- In spite of starting the correct management, baby develops generalised tonic clonic seizures refractory to IV Lorazepam and IV Phenytoin. ABG done shows **Sodium of 116**.
- 4. What will be your immediate management?

  3% NS infusion 4 to 6 ml/kg iv over 15 to 20 min
- 5. How will you manage the baby further after seizure stops?
- 6. What will you monitor (clinical and lab)?

Continue all neuroprotective measures, monitor urine output , sensorium (GCS), limb movements, pupillary response, repeat sodium in 4 hours to titrate fluids.

- What are the clinical features of the dreaded complication that can happen if you correct very fast?

  Osmotic disequilibrium syndrome/Central pontine myelinolysis- altered level of consciousness, quadriparesis, pseudobulbar palsy

Case scenario 2

- 3 year old female, weighing 10kg was brought with fever for 3 weeks associated with bifrontal headache and GTCS refractory to lorazepam and levetiracetam and fosphenytoin, hence she was intubated and mechanically ventilated. CSF study and MRI was suggestive of Tubercular Meningitis. Antituberculosis treatment (ATT) along with intravenous steroids were started. Ventriculoperitoneal (VP) shunt was placed in view of obstructive hydrocephalus. Her admission serum sodium -132. **On day 2 serum sodium -121meq/l)**. vitals HR-100/min, Spo2-99%, ABP-100/76 mmHg, UO-2.8ml/kg/hr.
- 1. How will you approach this low sodium? What is your immediate management?

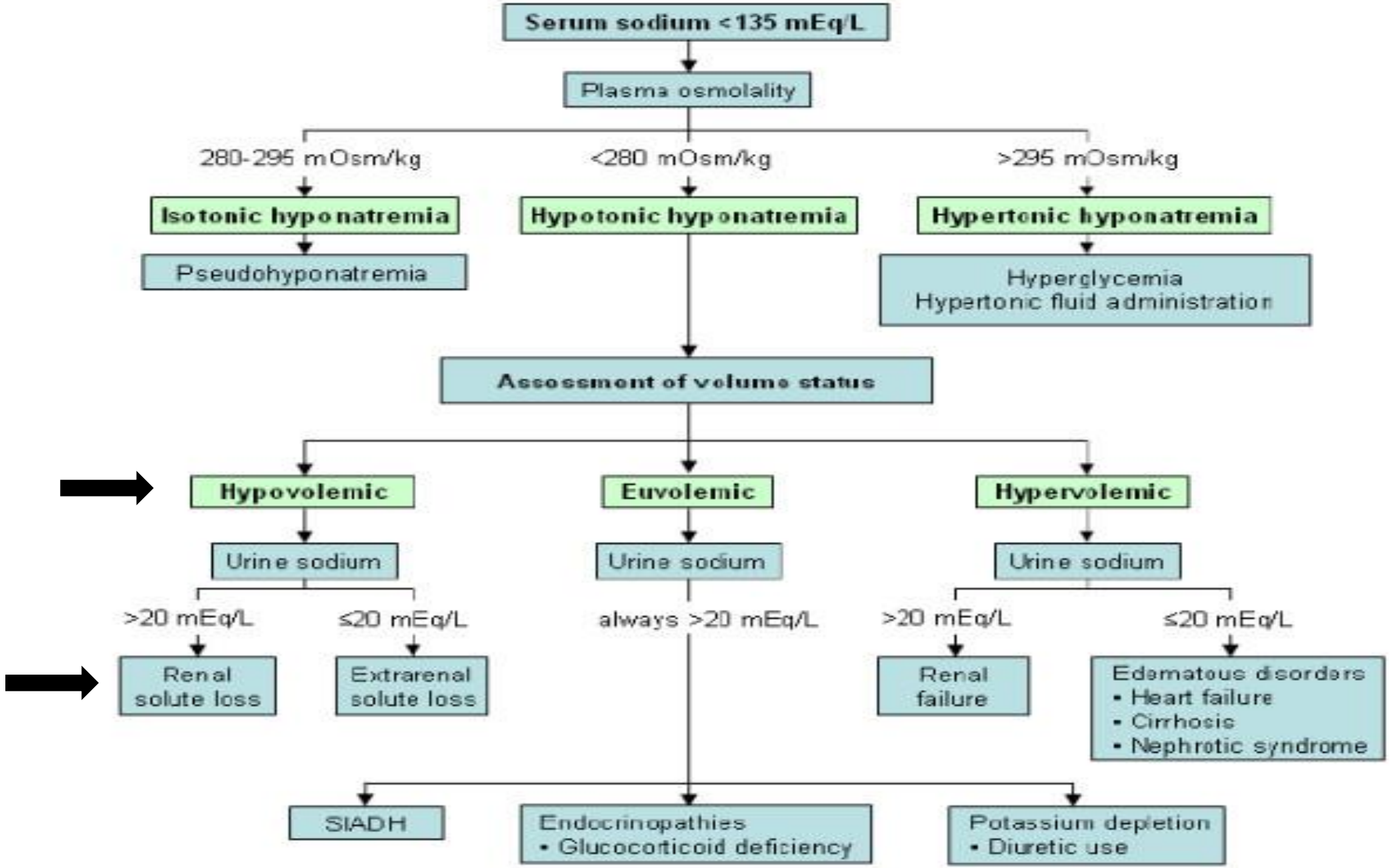
Last 48 hours intake output status, hydration status, assess change in sensorium, restrict fluids and treat the TBM and other supportive measures.

Case scenario progresses:

- Fluid restriction was done to 2/3rd maintenance and 3% saline was continued at 1ml/kg/hr

- EEG monitoring revealed no seizures.
- Serum sodium was monitored 6hrly and Na transiently improved to 125 meq/l, but subsequently by day 4, the serum sodium gradually reduced to **123, 121 and 119 meq/l**

- 1. What is the reason for hyponatremia despite 3% saline? What additional test will you do to confirm your diagnosis?
  CSW/ RSW syndrome , hydration status, urine output, very high urine osmolality, high urine sodium, fractional excretion of urate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Plasma osmolality
280-295 mOsm/kg
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>295 mOsm/kg
Isotonic hyponatremia
Hypotonic hyponatremia
Hypertonic hyponatremia
Pseudohyponatremia
Hyperglycemia
Hypertonic fluid administration
Assessment of volume status
Hypovolemic
Euvolemic
Hypervolemic
Urine sodium
Urine sodium
Urine sodium
>20 mEq/L
≤20 mEq/L
always >20 mEq/L
>20 mEq/L
≤20 mEq/L
Renal solute loss
Extrarenal solute loss
Renal failure
Edematous disorders
• Heart failure
• Cirrhosis
• Nephrotic syndrome
SIADH
Endocrinopathies
• Glucocorticoid deficiency
Potassium depletion
• Diuretic use

Cerebral salt wasting: etiology

- Head Injury
- Infections
- Brain Tumours
- Neuro Surgery
- Subarachnoid Haemorrhage

Cerebral salt wasting: presentation

- Progressive Natriuresis
- Concomitant Diuresis
- Volume (ECF) depletion
- Hyponatremia

Cerebral salt wasting

Main biochemical findings-

- low plasma osmolality
- high urine osmolality (inappropriate)
- normal/high Haematocrit
- hyponatremia
- urine sodium > 100 mmol/L

- 2. Based on reports, How will you calculate fluid prescription for this child weighing 10kg to correct hyponatremia?

  Replenish intravascular volume with 120% maintenance fluids isotonic saline
- 3: What will you need to monitor?

  Sodium levels, hydration status, urine output, sensorium
- 4. She continued to have persistent hyponatremia with polyuria despite sodium replacement. How will you manage refractory hyponatremia in this specific scenario?

  Fludrocortisone 5 to 10 µcg/kg/day
- After 10 days of hospitalization, polyuria improved though serum sodium levels showed fluctuations requiring further fluid and medication adjustment. The child finally improved after 24days of treatment and got discharged.

Characteristics of SIADH and RSW/CSW

Both characterized by:

- Association with intracranial diseases
- Hyponatremia
- Concentrated urine
- Urinary [Na] usually > 30 mEq/L
- Normal renal/adrenal/thyroid function
- Non-edematous
- Hypouricemia <4 , Increased Feurate >10%
- **Only difference is volume status and urine output**

	DI	SIADH	CSW
Urine Output	High	Low	High
Serum Na	High	Low	Low
Urine Na	Low	High	High
Serum Osm	High	Low	Low
Urine Osm	Low	High	High
Volume Status	Normal to low	High	Low

Fe Urate corrected to <10% with water restriction in SIADH and persist to be high in CSW

NephKids 2024

Fluid and electrolyte workshop:

Hyponatremia

Presenter: Dr Swathi Kiran Shiri

MD (Pediatrics), DM (Pediatric Nephrology)

Assistant Professor

Department of Pediatric Nephrology

CMC Vellore

Case 1

- 5 year old female child, known case of steroid dependent nephrotic syndrome on MMF for the last 6 months, presented with
- Generalized edema, pain abdomen and reduced urine output for 6 days.
- Stopped all medications 1 month back.
- Received few doses of oral diuretics for 2 days.

Examination

- Generalised edema present. Alert conscious.
- **Vitals:** PR: 74/min, all peripheral pulses well felt.

  RR: 33/min

  BP: 100/60 mmHg

  SpO2: 99% RA

Anthropometry: Weight: 27 kg (pre- edema weight: 23kg)

Height: 108 cm

Systemic examination: Respiratory system: reduced air entry in right infrascapular area

Per-abdomen: shifting dullness present. No organomegaly.

Investigations

PARAMETER	VALUE
S. Creatinine	0.4mg/dl
B urea	23mg/dl
S. Sodium	***128meq/L***
S. Potassium	***5.8meq/L***
S. Chloride	98meq/L
S. Bicarbonate	22meq/L
S albumin	***2.1 g/dl***
Urine PCR	***14.4 mg/mg***
S. cholesterol	343 mg/dl
Hemoglobin	***15.5g/dl***
TC	8,900/mm3
Platelet	5.5 lakh/mm3

Question 1

What is the metabolic abnormality and its cause?

Ans: ***Hyponatremia:*** Multifactorial causes

Causes of hyponatremia in NS

Hyponatremia

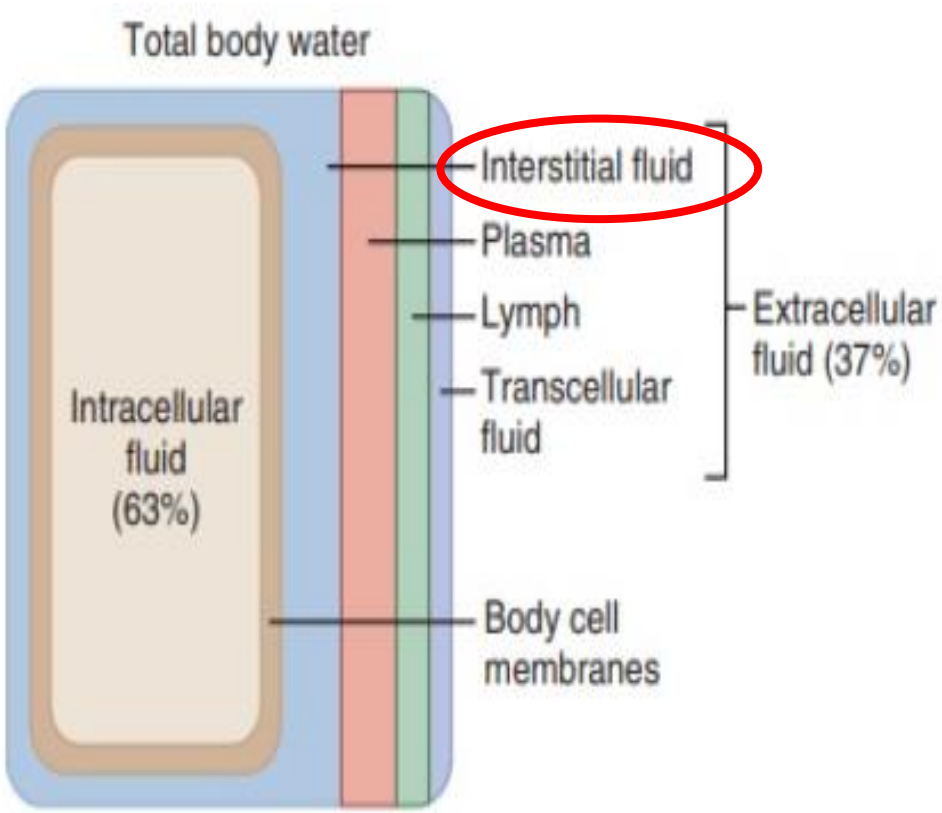
Hypovolemia:
severe edema; 4 kg above pre edema weight 17.3%
Hemoconcentration

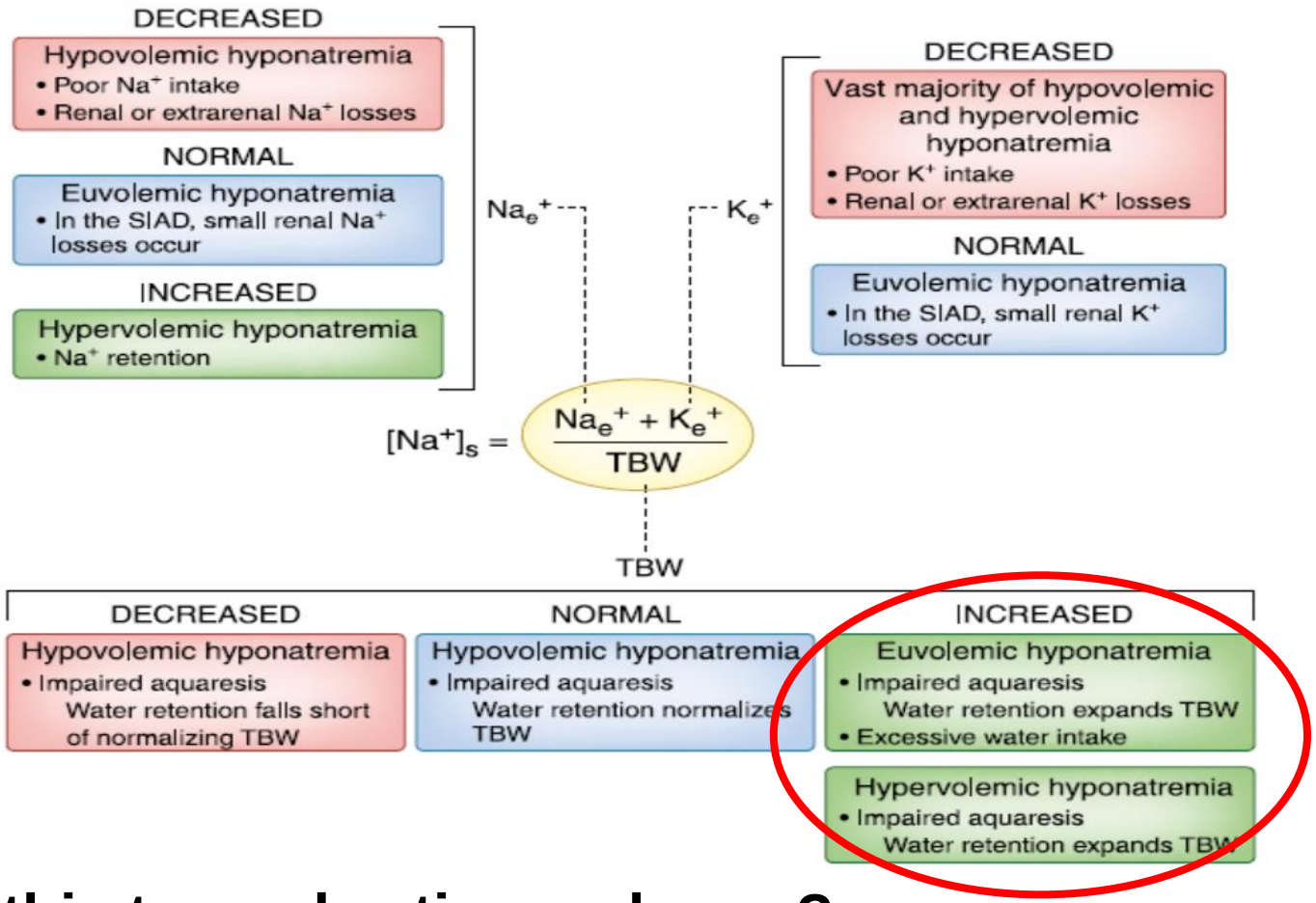
Diuretics induced Na wasting

Dilutional component:
Underfill theory

Correction factor for hyperlipidemia

Physiological approach to hyponatremia





How do we apply this to nephrotic syndrome?

JASN 2016

Hypovolemia in NS

Hypovolemia in NS

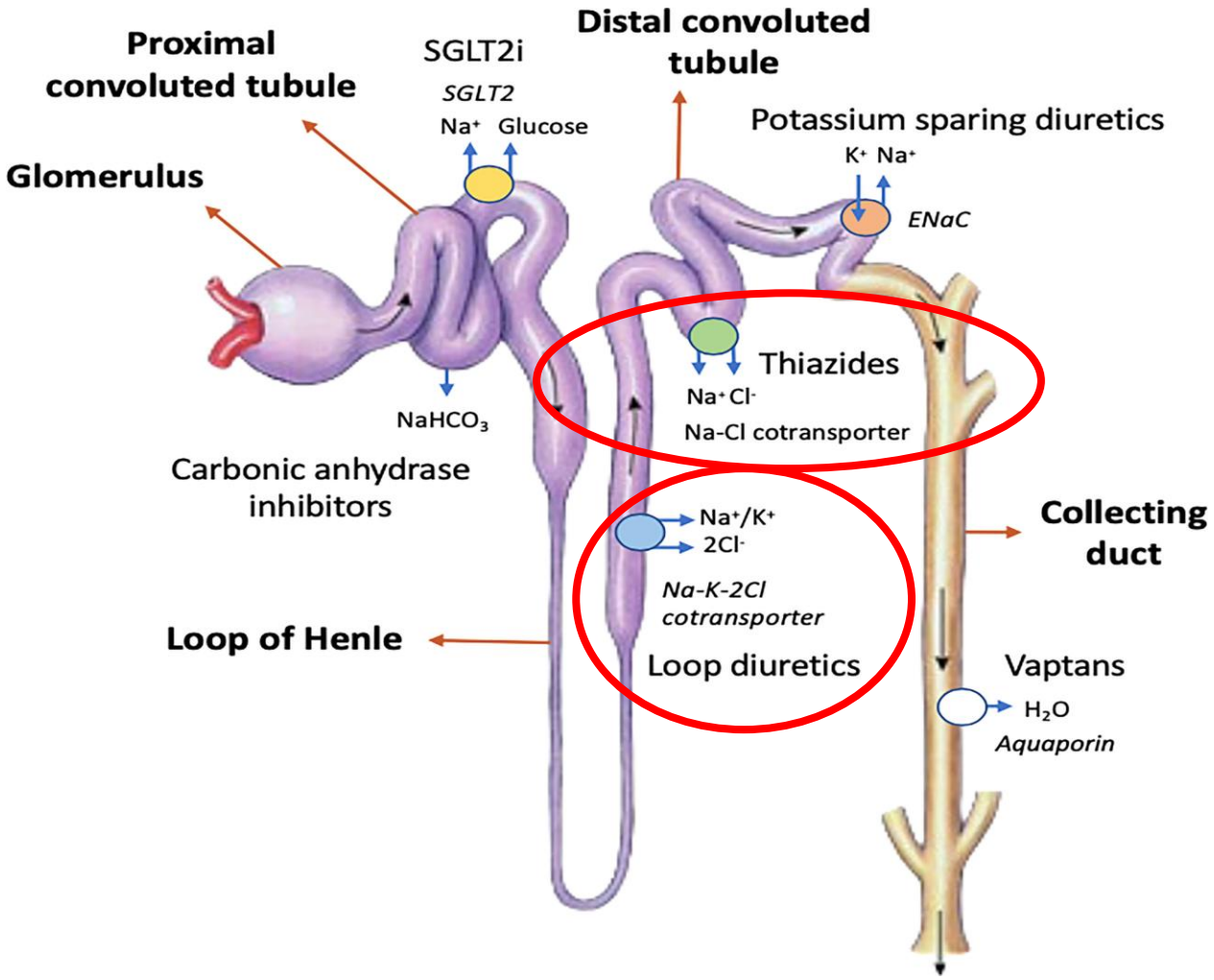
Clinical features: Abdominal pain, lethargy, prolonged CRT, tachycardia, postural hypotension

Laboratory features: elevated hematocrit
Blood urea/ creatinine >100
FeNa <0.5%
Urine K index >0.6
USG: Decreased IVC diameter and collapsibility

Hypovolemia on its own may not cause hyponatremia; unless associated with diuretics or acute kidney injury

Diuretics induced Na+ wasting

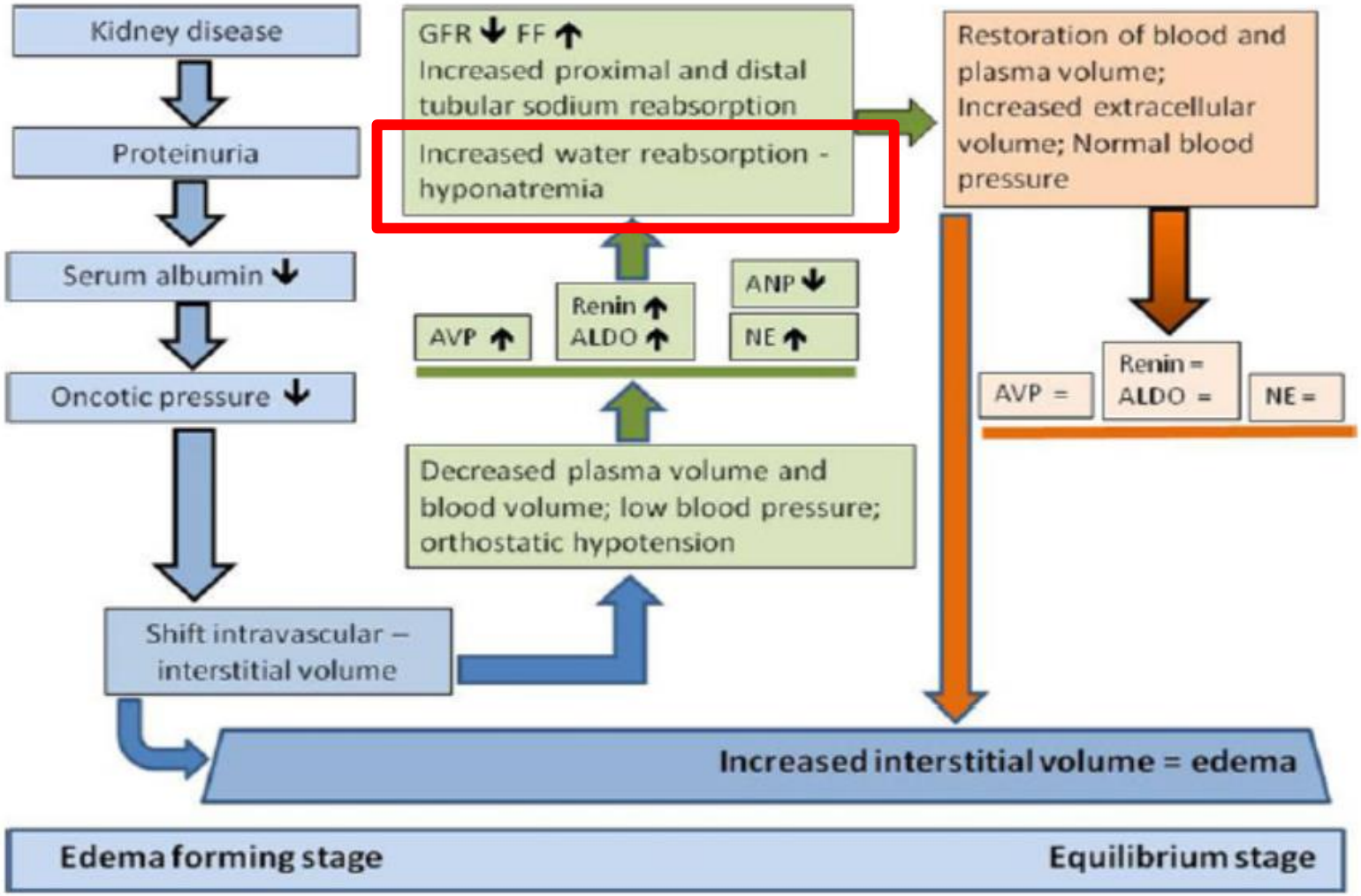
- Thiazide >> Loop
- Associated hypovolemia
- Metabolic alkalosis
- Hypokalemia
- Hypochloremia



AJKD 2021

Dilutional hyponatremia

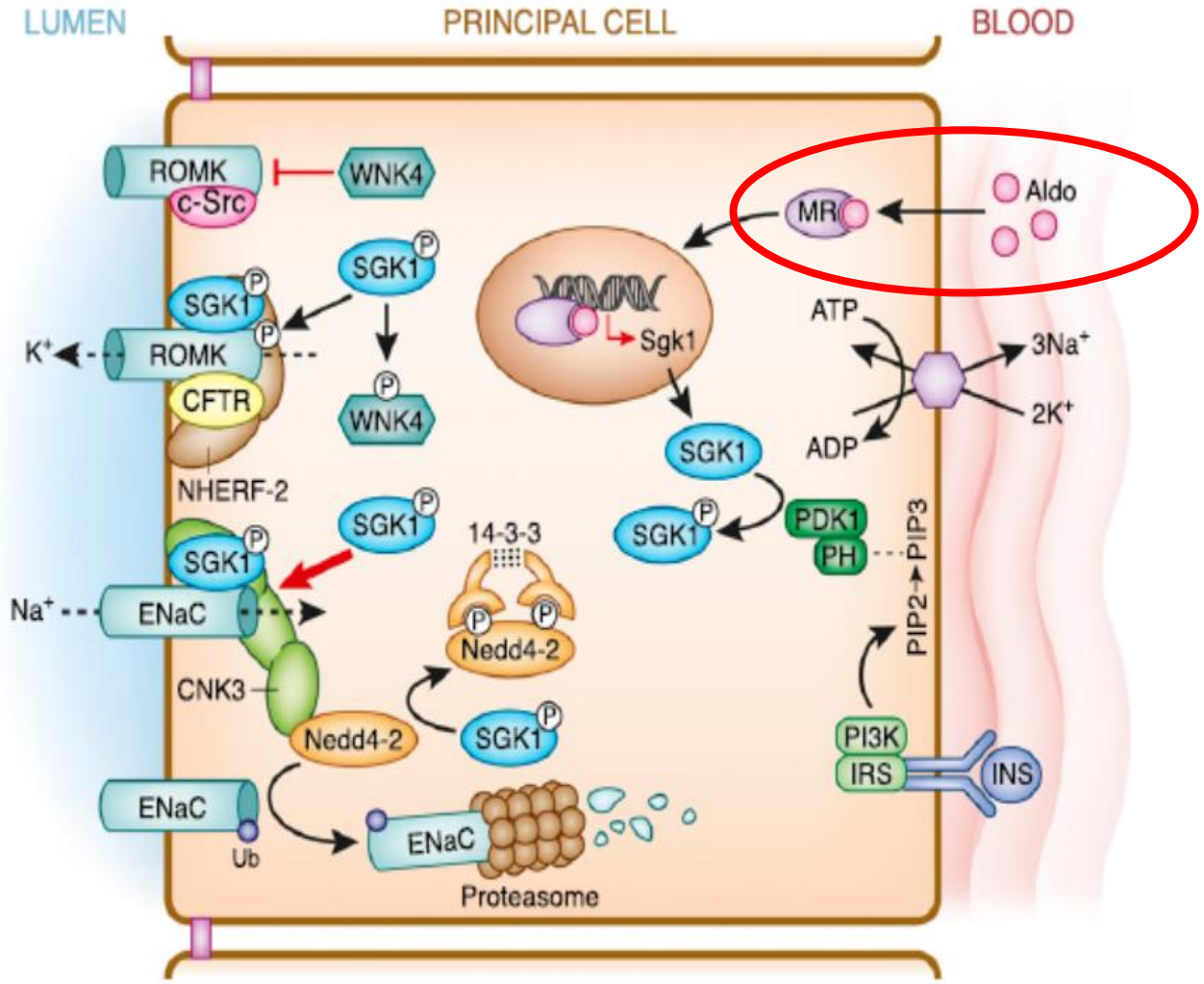
- Underfill hypothesis
- AVP and RAAS activation
- Water retention>Na reabsorption
- Decreased atrial natriuretic peptide
- Not a definitive theory



Pediatr Nephrol 2018

Acute adrenal insufficiency

- Long term corticosteroids
- HPA axis suppression
- 2mg/kg/day for 2 weeks or 0.75-1mg/kg alternate day for more than 6 to 8 weeks
- In last 6 months to 1 year
- Acute crisis or sudden withdrawal of steroids
- Hyponatremia, hyperkalemia and metabolic acidosis



CJASN 2016

Question 2

What additional investigations will you order?

Evaluation of hyponatremia in NS

- Complete blood count: Focus on hemoglobin and hematocrit
- Serum albumin: <2g/dl has higher risk of volume contraction
- Serum creatinine, serum sodium, potassium, chloride and bicarbonate
- Serum osmolarity, urine spot osmolarity, urine spot Na, K, Creatinine
- All samples should be when child is not on IV fluids, diuretics, ACEI or ARB or salt supplementation

Question 3

How will you manage this case?

Management strategies of hyponatremia in NS

Step 1: Rule out pseudohyponatremia and correct Na+ for the total cholesterol (0.002 x cholesterol (mg/dl))

Step 2: Classify the severity and duration of hyponatremia:

Mild/mod/severe and acute versus chronic

Step 3: Assess for clinical features of hypovolemia and use of diuretics

Step 4: Categorise the extent of edema

Mild to moderate (<7%) and severe (>7%)

Step 5: Spot samples

Managing hyponatremia in NS

- Severe symptomatic hyponatremia: IV 3% Nacl correction
- Outweigh the risk and benefits with 3% Nacl correction
- Hypovolemia: IV or oral hydration based on the severity
- Stop diuretics for 24 to 48 hours
- Add maintenance salt in the diet (1g of common salt:17meq sodium)
- Restrict excessive free water.
- 20% albumin infusion: persistent hypovolemia, no AKI and no active focus of infection (12meq Na in 100 ml)
- Stress dose steroids (0.5 to 0.75 mg/kg/day of prednisolone) if any acute infection.

Question 4

How will you interpret urine sodium, urine osmolarity and serum osmolarity in nephrotic syndrome?

Serum and urinary indices in NS

- Calculated S. osmolarity: $2\,[Na^+] + \frac{glucose(mg/dl)}{18} + \frac{BUN\ (mg/dl)}{2.8}$
- Urine indices : **FeNa:** $\frac{S_{cr} \times U_{Na} \times 100}{S_{Na} \times U_{cr}}$ < 0.2 ± 0.2% in volume contraction(VC)
- **Urine potassium index**: $\frac{U_K}{U_{Na} \times U_K}$ >0.6 or 60% in VC
- Blood urea nitrogen: elevated in VC
- BUN/ serum creatinine ratio: >100 in VC
- Mean **hemoglobin/ hematocrit: elevated**
- Urine osmolarity: normal / increased /low
- Urine osmolarity / serum osmolarity: increased in volume contraction

In case of relapse in NS FeNa can be less than 0.5%

IJN 2014

THANK YOU

Hypomagnesemia

14.9.24

Nephkid electrolyte workshop 2024

Physiology

- Third most common intracellular cation
- Most intracellular Mg is present in muscle and liver.
- 50-60% is in bone
- Only 1% is extracellular(60%ionized,15%complexed,25% protein bound

Physiology

- 30-50% of dietary Mg is absorbed.

- Renal excretion is the principal regulator of Mg balance.

Physiology

- Magnesium absorption and excretion are influenced by different hormones
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- Estrogens are known to stimulate TRPM6 expression
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Functions

- A co-factor in many biochemical reactions
- Cellular function and nerve conduction.
- Membrane stabilization
- Affects the electrical activity of the myocardium and vascular tone

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History

- Intake
- Malabsorption
- Chronic diarrhea
- Renal disease
- Drugs

Clinical features

- Most cases are asymptomatic
- Neuromuscular irritability: tremors, tetany(Chvostek sign, Trousseau sign) hyperreflexia, seizures
- CNS : Irritability and combativeness ,disorientation ,psychosis, ataxia, nystagmus vertigo
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Family history	Interstitial nephritis, GN, post –obstructive diuresis
Chronic renal disease	Hungry bone syndrome
Thyroid surgery, parathyroidectomy	

Consider hypomagnesemia

- In any child with refractory hypocalcemia or hypokalemia.

Hypomagnesemia in critically ill children

- 40-50%
- In critically ill children (often associated with other electrolyte abnormalities).
- Low Mg in PICU: Increased need for mechanical ventilation, prolonged ICU stay and increased mortality

Hypomagnesemia can cause hypocalcemia

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- May present as a congenital defect with neonatal hypocalcaemia or may be an acquired defect in an older child

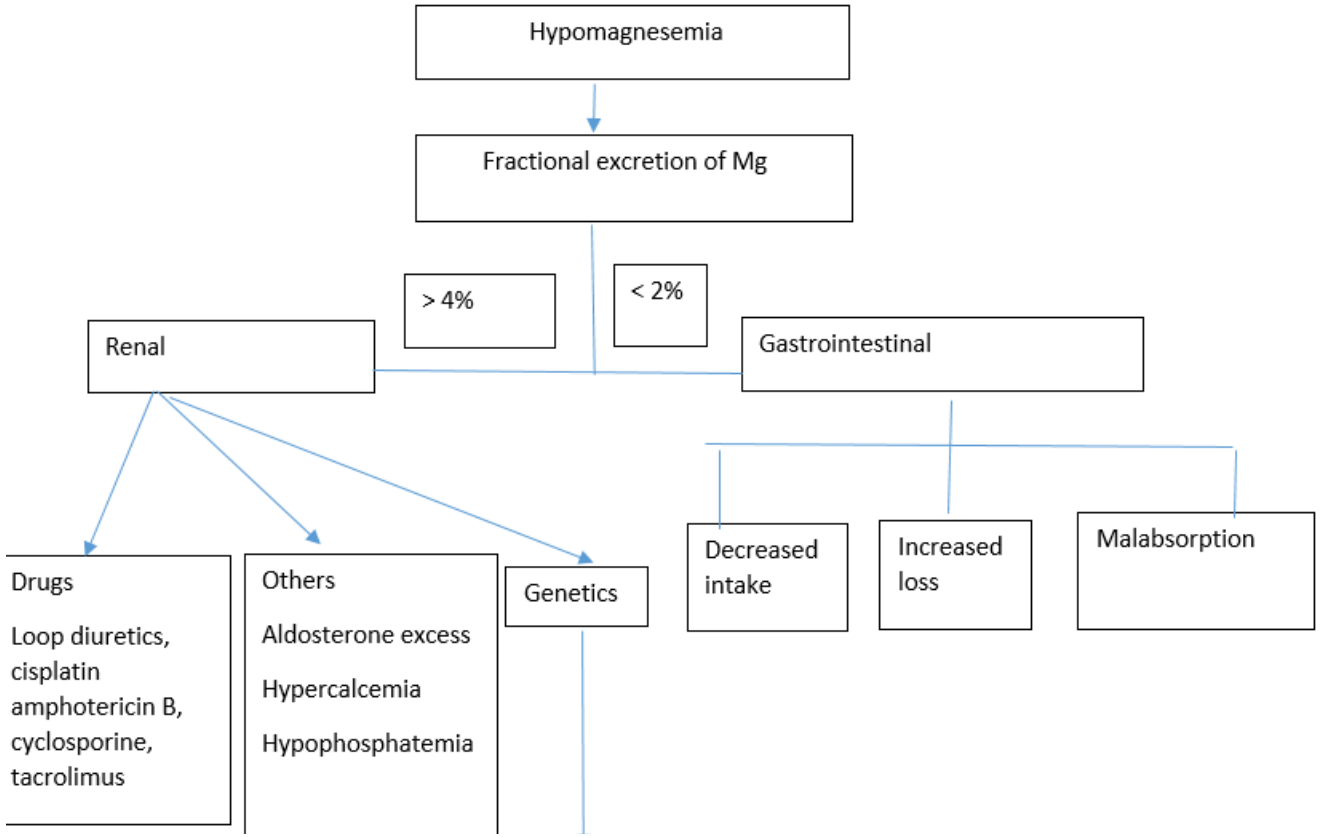
Invstigations

- Serum Mg, Ca, Phosphate,
- Sodium, potassium , bicarbonate
- Serum creatinine
- ABG
- Fractional excretion of Mg
- urine calcium, creatinine
- ECG

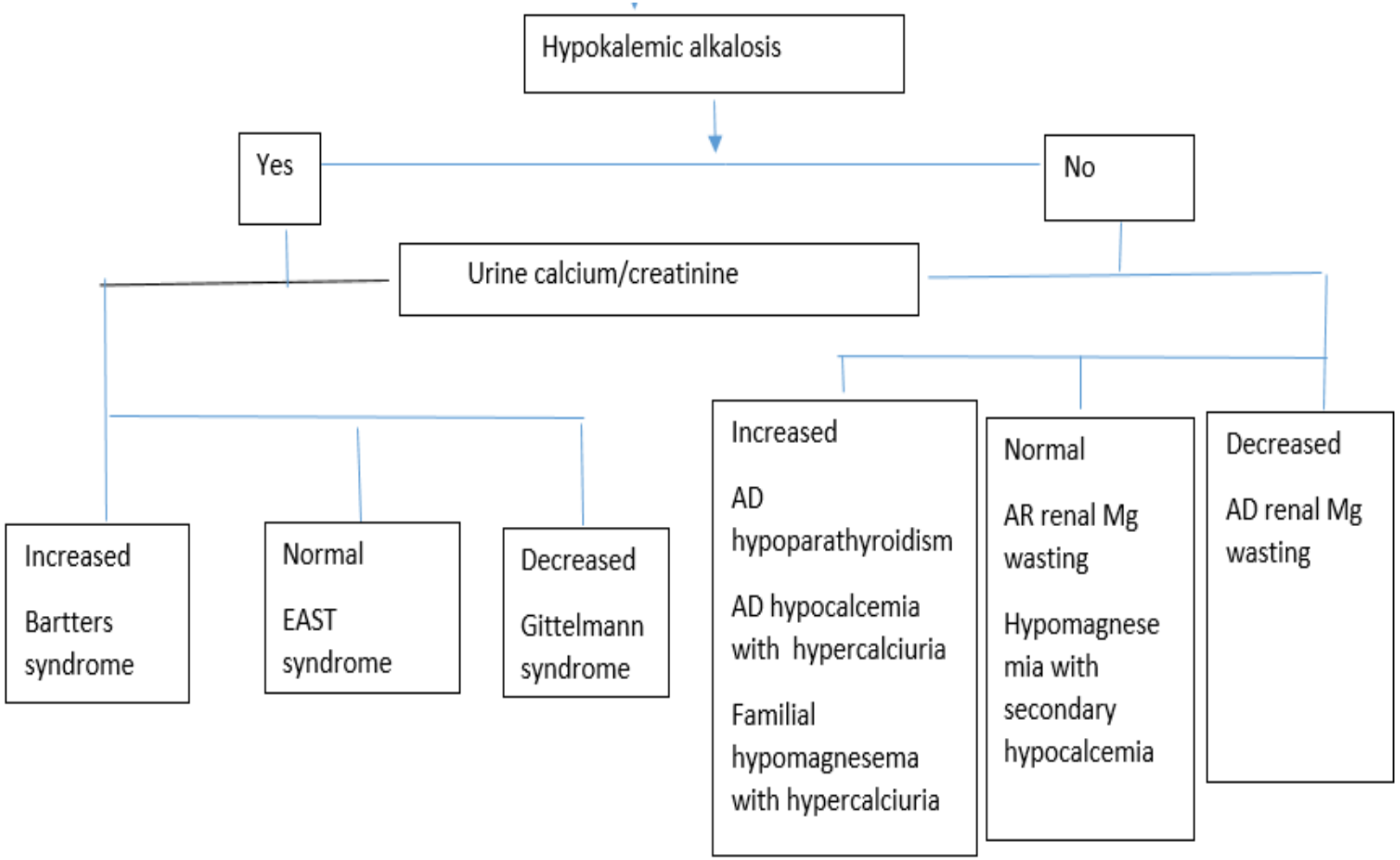
ECG changes in hypomagnesemia

- ST depression
- Tall peaked T waves
- U waves
- Prolonged PR
- Widened QRS complex
- Torsades de Pointes

Approach to hypomagnesemia



Genetic causes of hypomagnesemia



Treatment

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- The dose is reduced in renal insufficiency.
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- Respiratory depression, areflexia
- Reduce rate if patient develops diaphoresis, flushing or a warm sensation
- IV Cacl or Ca gluconate is the antidote for hypermagnesemia

Asymptomatic hypomagnesemia

- Oral magnesium replacement (Magnesium Oxide/magnesium sulphate)
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- Increase to 10 - 20 mg/kg (0.4 - 0.8 mmol/kg) up to 4 times daily orally if required
- Tolerance is better with smaller, more frequent dosing

- Thankyou

Hypomagnesaemia with secondary hypocalciuria (HOMG1)

- A selective defect in magnesium absorption in the small intestine with no evidence of any additional malabsorption.
- A mutation in TRPM6 on chromosome 9q22 which is expressed in intestinal epithelia and renal tubules
- Hypocalcaemic fits in the first few weeks of life
- Low plasma magnesium levels of less than 0.5 mmol/l .
- Initially parenteral magnesium followed by oral magnesium.

Hypomagnesaemia with Hypermagnesuria

- Hypomagnesaemia with associated hypocalciuria (HOMG2)
- Isolated renal magnesium loss
- Autosomal dominant disorder due to mutations in the FXYD2 gene on chromosome 11q23
- Hypocalciuria is also present
- Milder than HOMG1.

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- A rare autosomal recessive condition
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- Psychomotor retardation and seizures with brisk reflexes

Renal hypomagnesaemia(HOMG6)

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- Normal urinary magnesium excretion level
- A defect in tubular reabsorption.

Gitelman’s syndrome

- Mutations in the thiazide-sensitive sodium chloride transporter
- Hypokalaemic alkalosis with salt wasting, hypomagnesaemia and hypocalciuria.
- Present after the age of 5 years
- Episodes of muscle weakness, lethargy, tetany and muscle cramps.
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- Prolonged cardiac Q-T interval - arrhythmias and syncopal attacks.
- Potassium and magnesium oral supplementation.

Hypomagnesaemia with hypercalciuria and nephrocalcinosis (HOMG3)

- Mutations in the gene for claudin 16 (paracellin 1) which is localized to the tight junctions of the epithelium of the ascending loop of Henle.
- Excessive excretion of both magnesium and calcium.
- Self-limiting or progressive renal failure
- Renal replacement therapy in 50% of cases by the second decade.
- Hypocalcaemia is occasionally present.

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- Drugs which cause excess renal magnesium wasting -cisplatinum, amphotericin B, cyclosporine and tacrolimus.
- Severe burn injury

Hypomagnesemia

14.9.24

Nephkid electrolyte workshop 2024

Physiology

- Third most common intracellular cation
- Most intracellular Mg is present in muscle and liver.
- 50-60% is in bone
- Only 1% is extracellular(60%ionized,15%complexed,25% protein bound

Physiology

- 30-50% of dietary Mg is absorbed.

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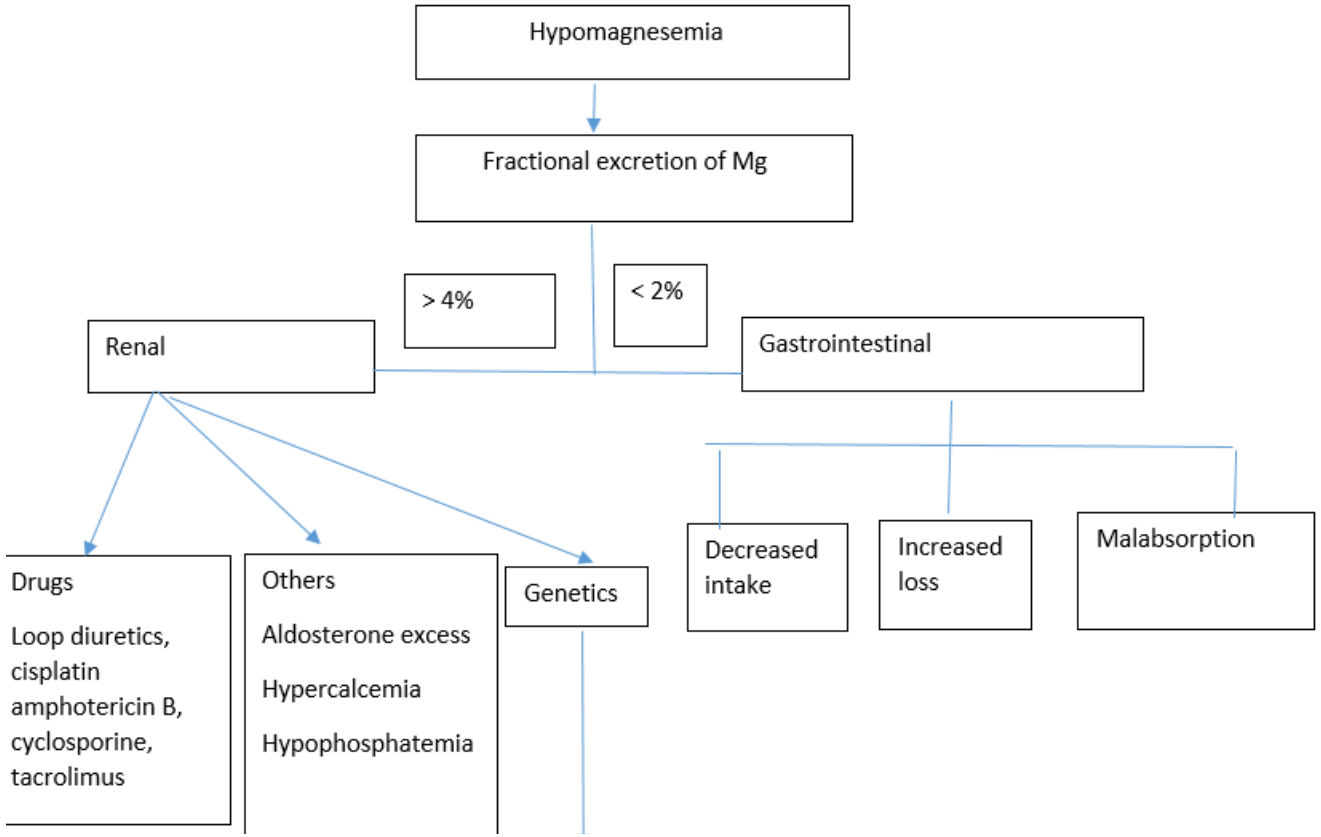

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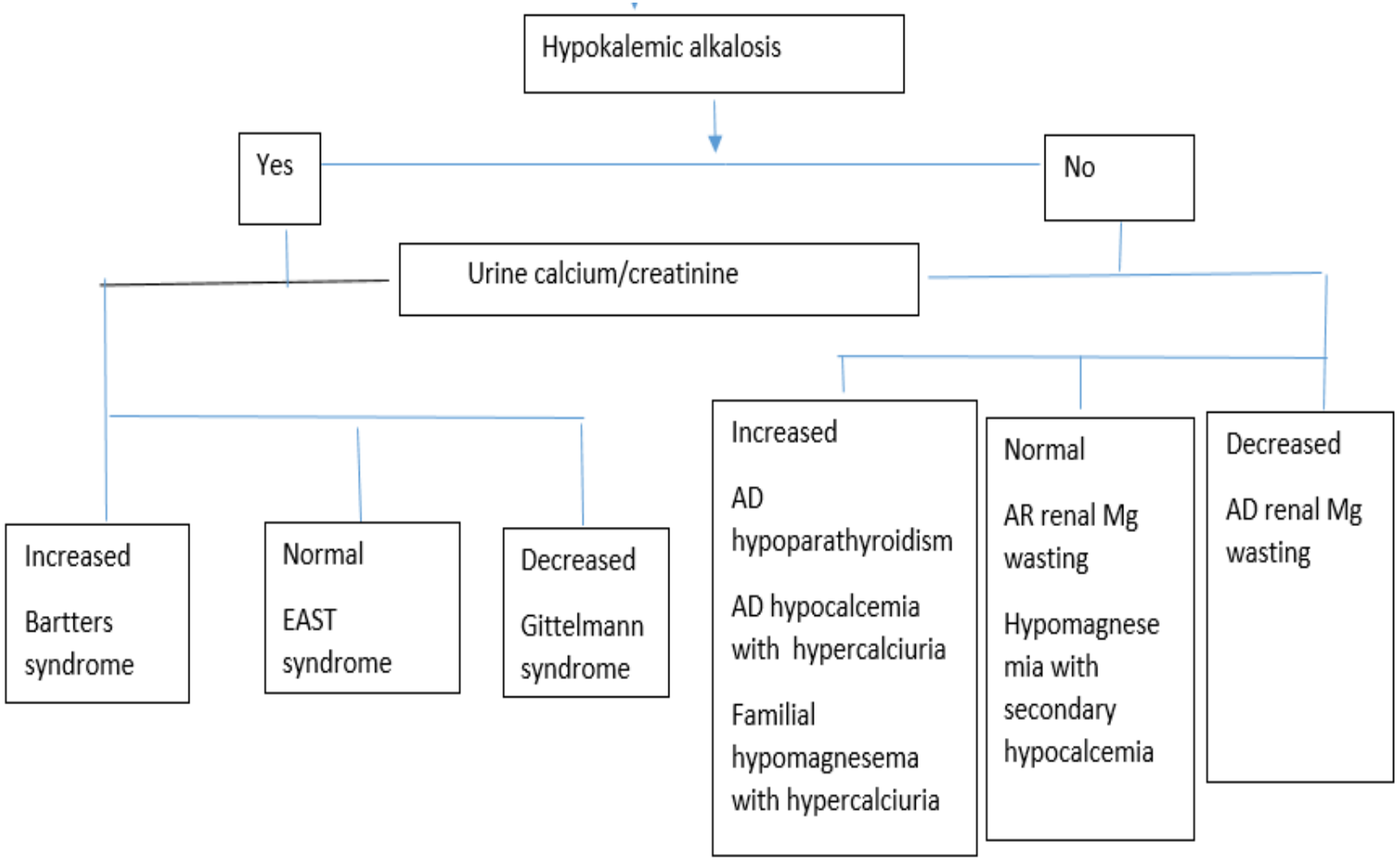

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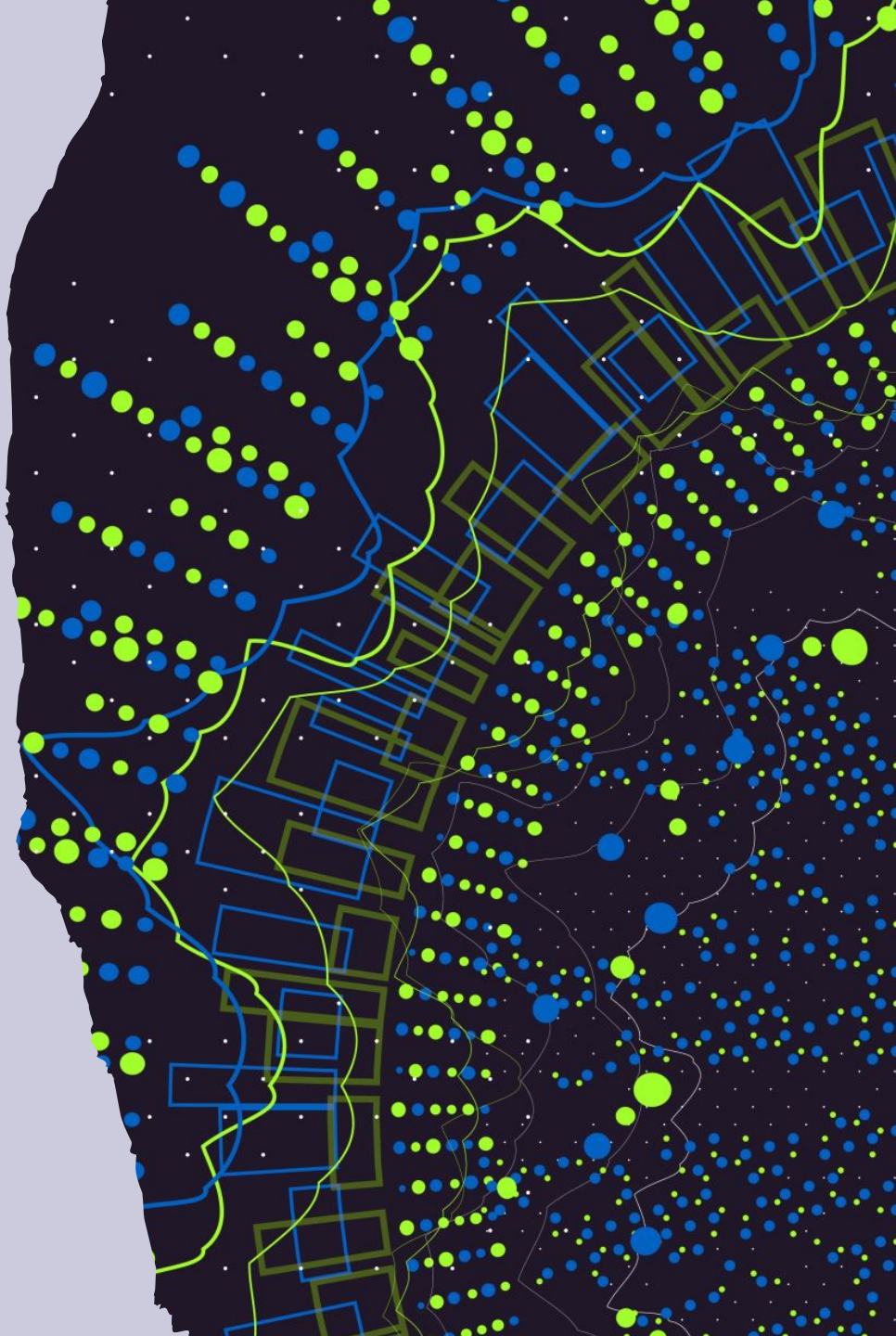
POSTERIOR URETHRAL VALVES – WHAT IS THE NEED FOR LONG TERM FOLLOWUP BY THE PEDIATRICIAN

Dr.
SRIPATHI V
Dr. VIDHYA
T

Pediatric Urology Unit

Apollo Children's Hospital, Chennai



Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

PUV - JAN 2015 – 31ST AUGUST 2024

- **Our experience - 111 valve fulgurations**
- **Newborn valves – 37**
- Primary fulguration (in infants and older children) – 48
- Redo fulgurations in older children +/- vesicostomy / ureterostomy closure – 25

- Diversions – 4 (loop ureterostomy)
- Severe urethral strictures – 2

Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

WHY IS LONG TERM FOLLOWUP NEEDED?

To ensure

- **Adequate / Optimal growth**
- **Good renal function**
- **Avoid ESRD and need for RRT**

- The factors involved (over 15 – 19 years and beyond) include
- **Pediatric physician**
- **Pediatric Nephrology specialists**
- **Pediatric Urology specialists**

CASE 1- MR R – NOW 19YEARS

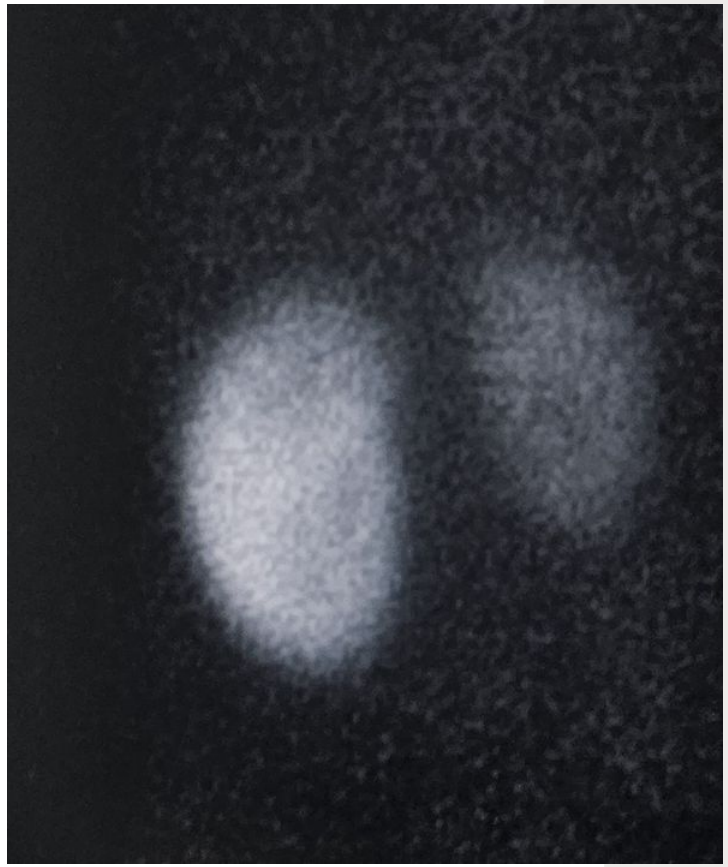
- Has been under combined care from 5 months of age

- At birth – **Left ureterostomy** done (sick baby with urosepsis, massive left VUR)
- 5 months of age – **Cystoscopy valve ablation** done
- 1 year of age – **Ureterostomy closure and complete valve ablation** confirmed

- 3 years of age – MCUG done – to confirm absence of VUR
- 5 years of age – Anticholinergics stopped
- 8 years of age – Started on alpha blockers as there was postvoid residue and LK was 38%
- 9 years of age – Alpha blockers working – dose adjusted
- 11 years of age – Alpha blockers stopped
- 14 years of age – Last visit **(can we stop coming to see you??)**

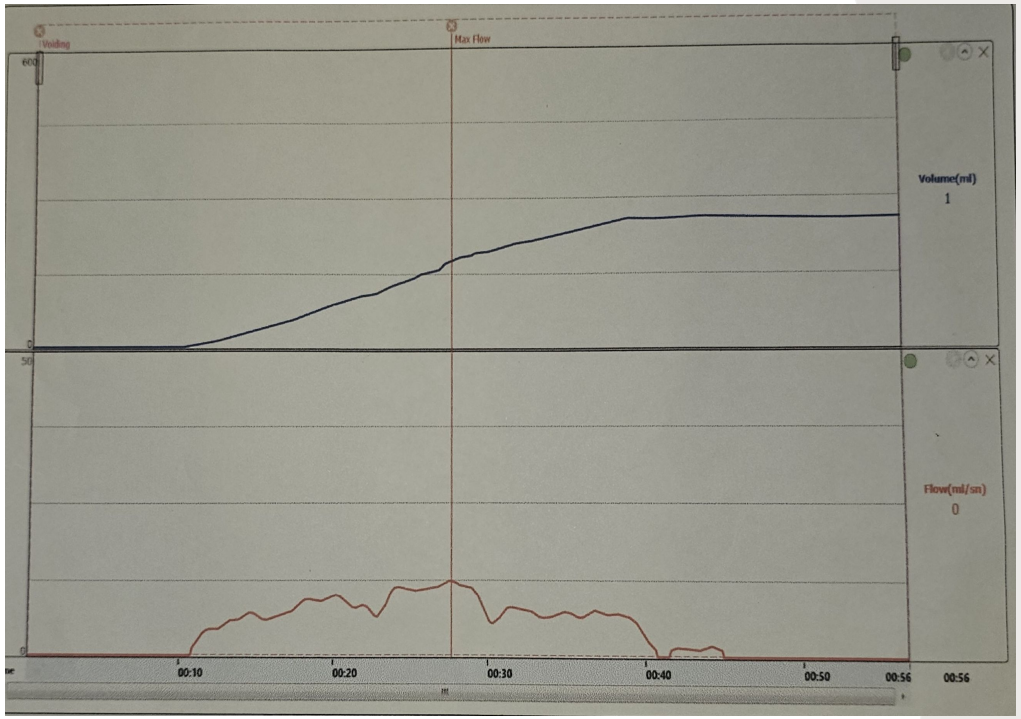
CASE 1 – MR R CONTINUED

- 19 years of age – I am having a sensation of incomplete emptying??
- Ultrasound KUB – Prevoid 500 mls, postvoid 50 mls
- DMSA – Marginally smaller LK
- In view of Spot Urine P/Cr – 0.25, increase renal echoes, marginally small kidney – nephrology review requested
- Uroflow asked for / Constipation treated



CASE 1 – MR R - CONTINUED

- Uroflow confirms poor flow
- Started again on alpha blocker (Tamsulosin)
- Will review and reassess with adult urologist (?prostate)



What did we achieve??

- ✔ **Salvaged his left kidney**
- ✔ **Carefully managed his bladder**
- ✔ **Made sure he grew well**
- ✔ **Avoided CRF**
- ✔ **All because we talked to our colleagues and managed his care in a combined manner P + PN + PU**

CASE 2 – MASTER NW – ANTENATAL

- 27 weeks gestational age – appears to be PUV – can you counsel??
- **First Pregnancy beyond legal termination date**
- Bilateral UHN, thick walled bladder – normal liquor

Fetal Urine

Beta 2 microglobulin

- **First sample 9.2 (27 weeks)**
- **Second sample 8.6 (28 weeks)**

- Our advice – No need for fetal intervention but there appears to be renal compromise, you need to see us regularly till child becomes an adult

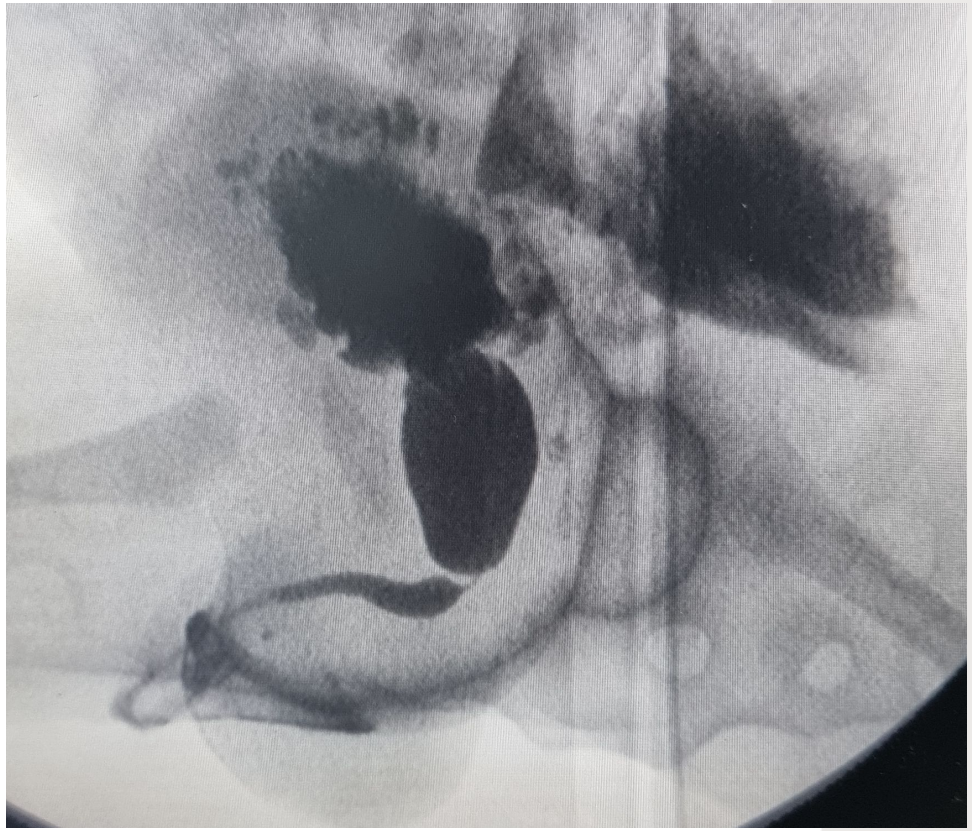
CASE 2 – MASTER NM

Underwent cystoscopy and PUV fulguration in newborn period

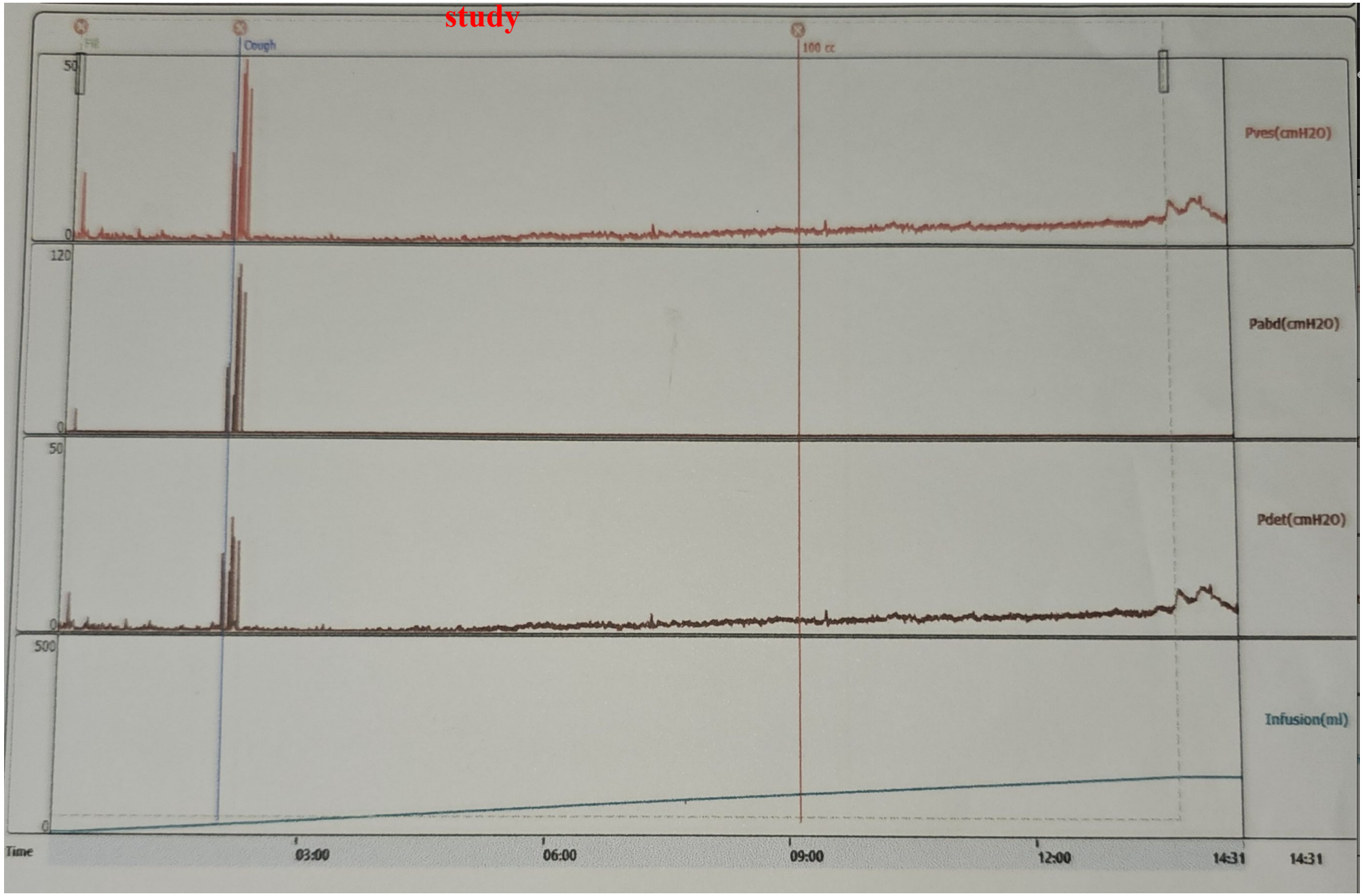
- At 7 mos of age admitted with chronic UTI and failure to thrive
- At 1 year of age – have check scopy (to confirm complete valve ablation) & circumcision
- At 1 year of age – DMSA renal scan RK 71%, LK 39%
- Started on Anticholinergic (Mirabegron) and Alpha Blocker (Terazosin)

- Reviewed at 2 years 9 months of age – 8.4 kgs
- **Grade 3 CKD / Metabolic acidosis**
- DMSA renal scan – LK had dropped in function to 29%
- Ultrasound – Bladder wall thickening with trabeculations persists. Bilateral HUN, Grade 2 parenchymal disease

- Our question – **Is the bladder the cause for the CKD and drop in renal function on the left side?? – Video UDS planned**
- Serum Creatinine – 2.2 at birth, 0.81 now



Video Urodynamic study



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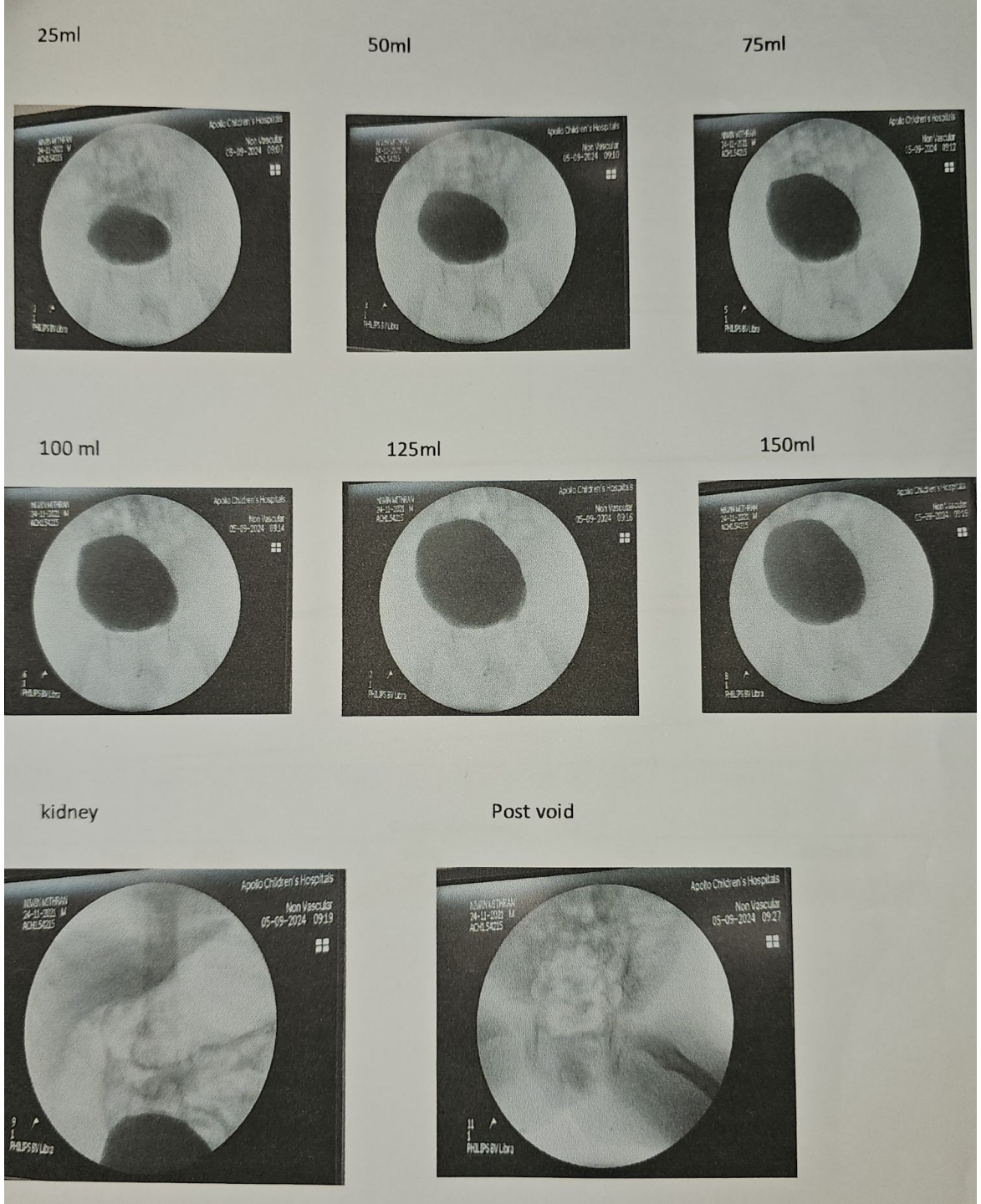
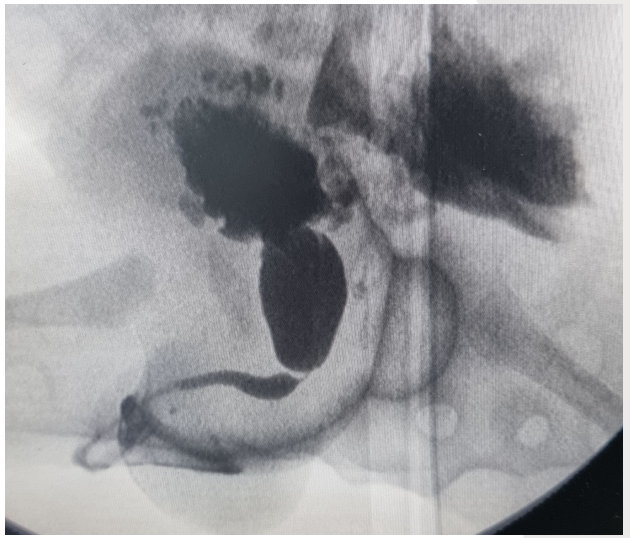
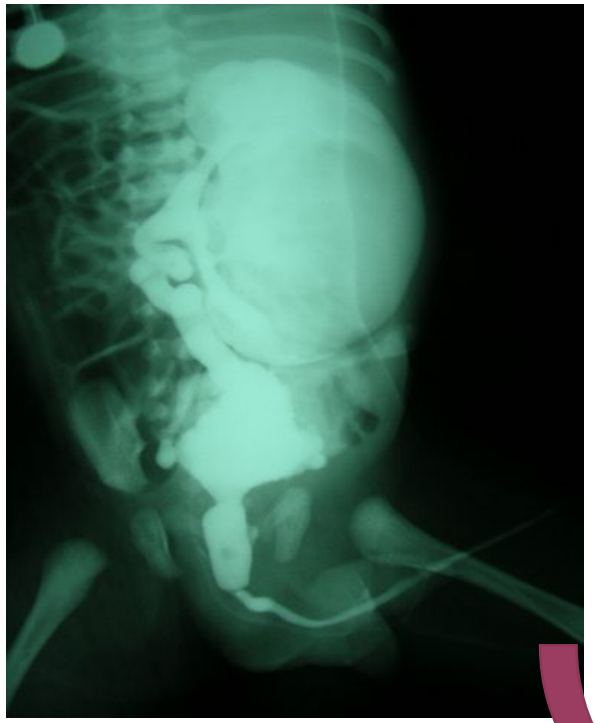




CASE 2 – WHAT DID WE ACHIEVE

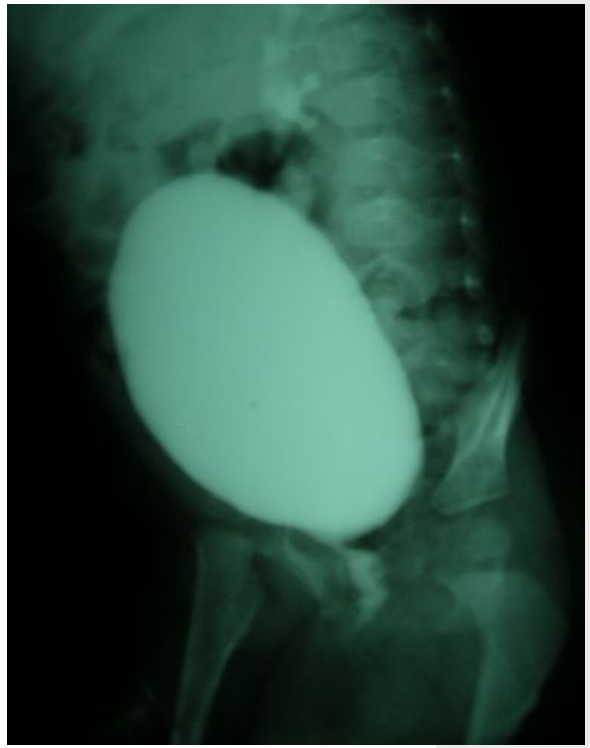
- ✔ **Anticholinergics and alpha blockers over 2 years have made the bladder into a compliant low pressure receptacle which empties completely**
  - Fall in LK function by 10% indicates a renal cause (nephrologists domain)
- ✔ **Bladder has perhaps become too compliant / there fore drugs need to be tapered and stopped**
- ✔ **The value of antenatal counseling, careful monitoring and combined care is shown by this case**

REFLUX IN PUV



- VCUG -NEONATE

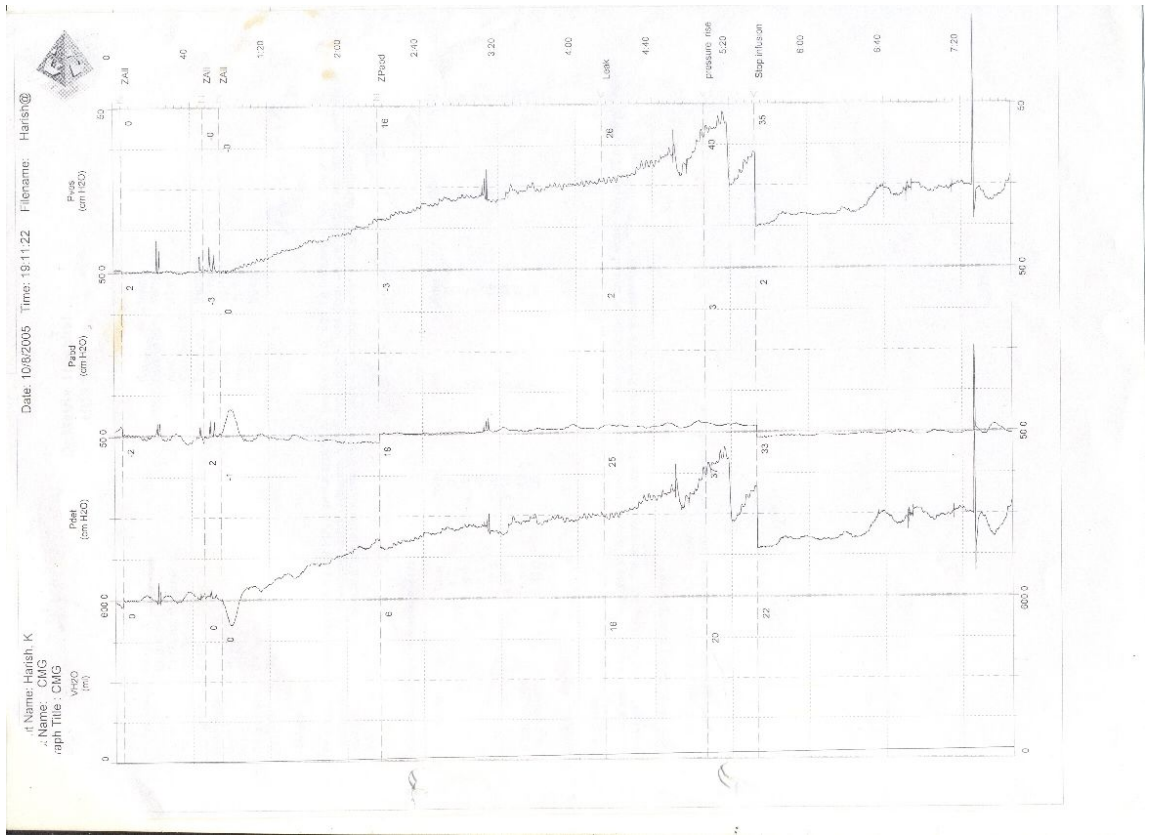
- Reflux resolves within the first year of life
- Resolution unrelated to the grade of reflux
- If persistent ,consider early urodynamics



- VCUG AT 7 MONTHS

Reflux ,no matter what the pattern, has not been a significant prognostic factor : J Urol: 2003: 170: 1677 -1680

Case 3 - Poorly compliant bladder –how do you manage??



Severe pressure rise even with 20 mls filling – Botox 200 units injected into detrusor

Master H – vesicostomy at birth

- **PUV fulguration and closure of vesicostomy at 2 mon**
- **Developed severe upper tract sepsis and underwent left ureterostomy (20% function) at 4 months**
- **At 2 yrs – can ureterostomy be closed safely?**

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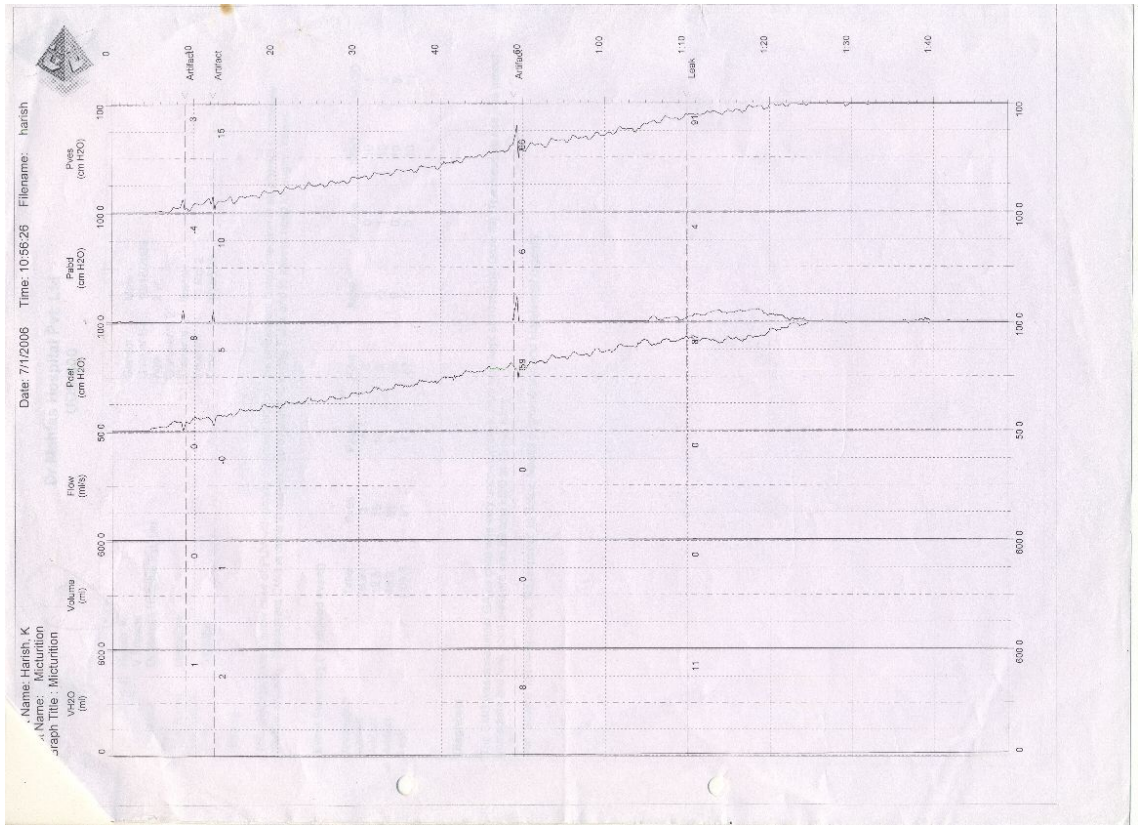
TOUCHING LITTLE LIVES

After Botox…

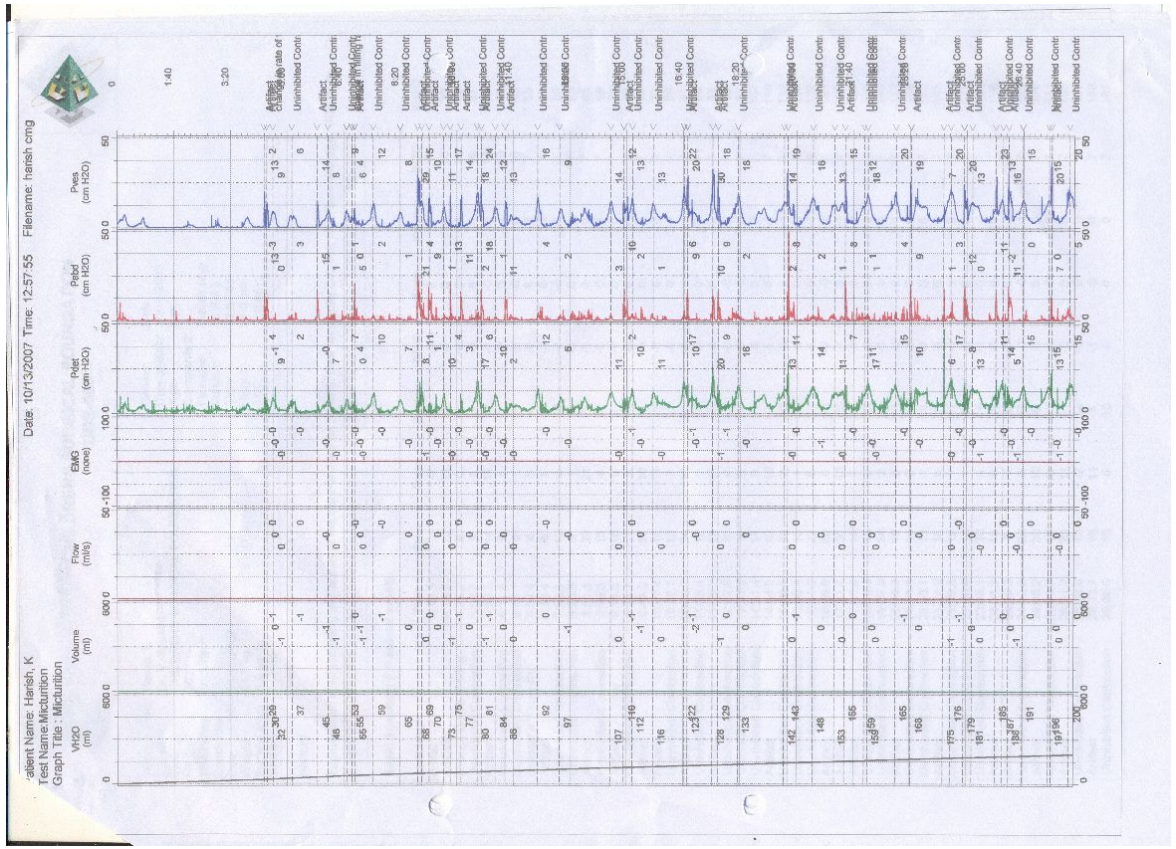


- **UDS five months after Botox – has pressure dropped ?**

Severe non compliance persists – augmentation is the only answer

Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

After Augmentation Cystoplasty what happened to pressures??



- **Augmentation colocystoplasty** done at 3 years of age
- Six months after augmentation pressures reached base line

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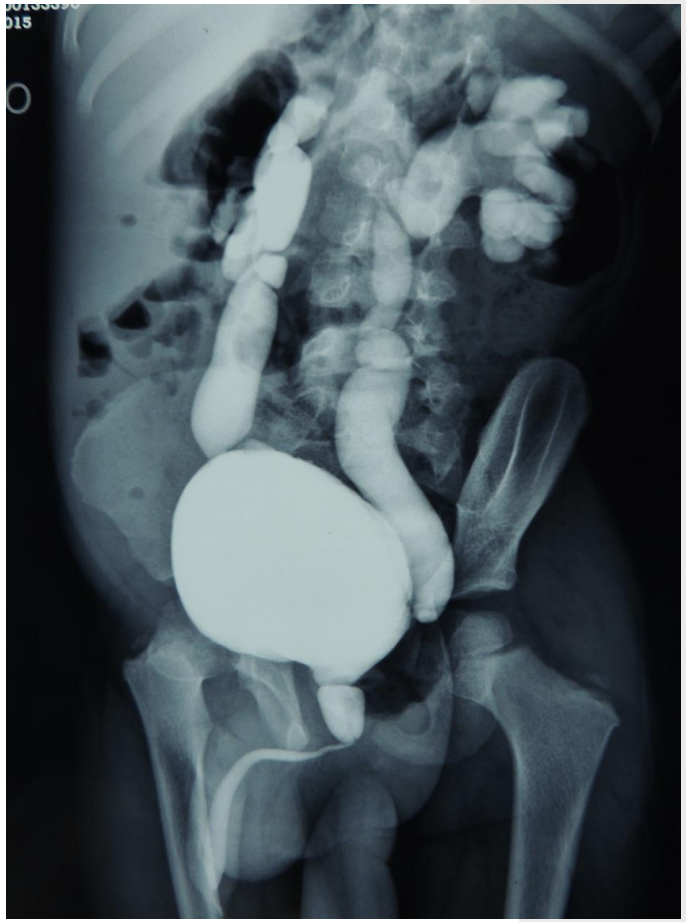
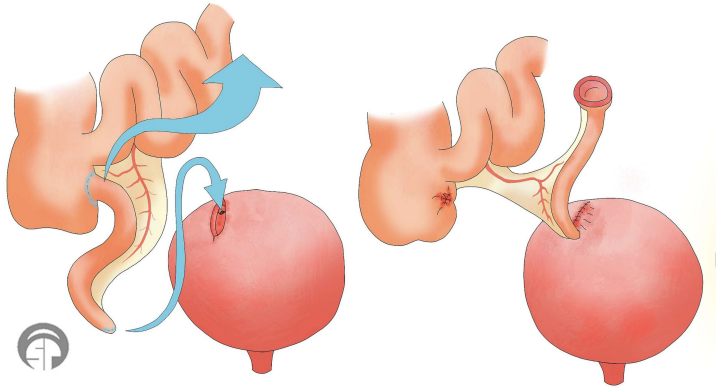
BILATERAL HIGH GRADE VUR IN PUV – VALUE OF NIGHT TIME DRAINAGE

- PUV ablation – 4 mos of age
- Redo ablation – 1.5 years
- Recc UTI, high grade bilateral VUR, large postvoid residues (in spite of therapy) –
- Appendix Mitrofannof done at 3 years of age – for painless bladder drainage at night
- UDS at 9 years of age
- UDS at 15 years of age





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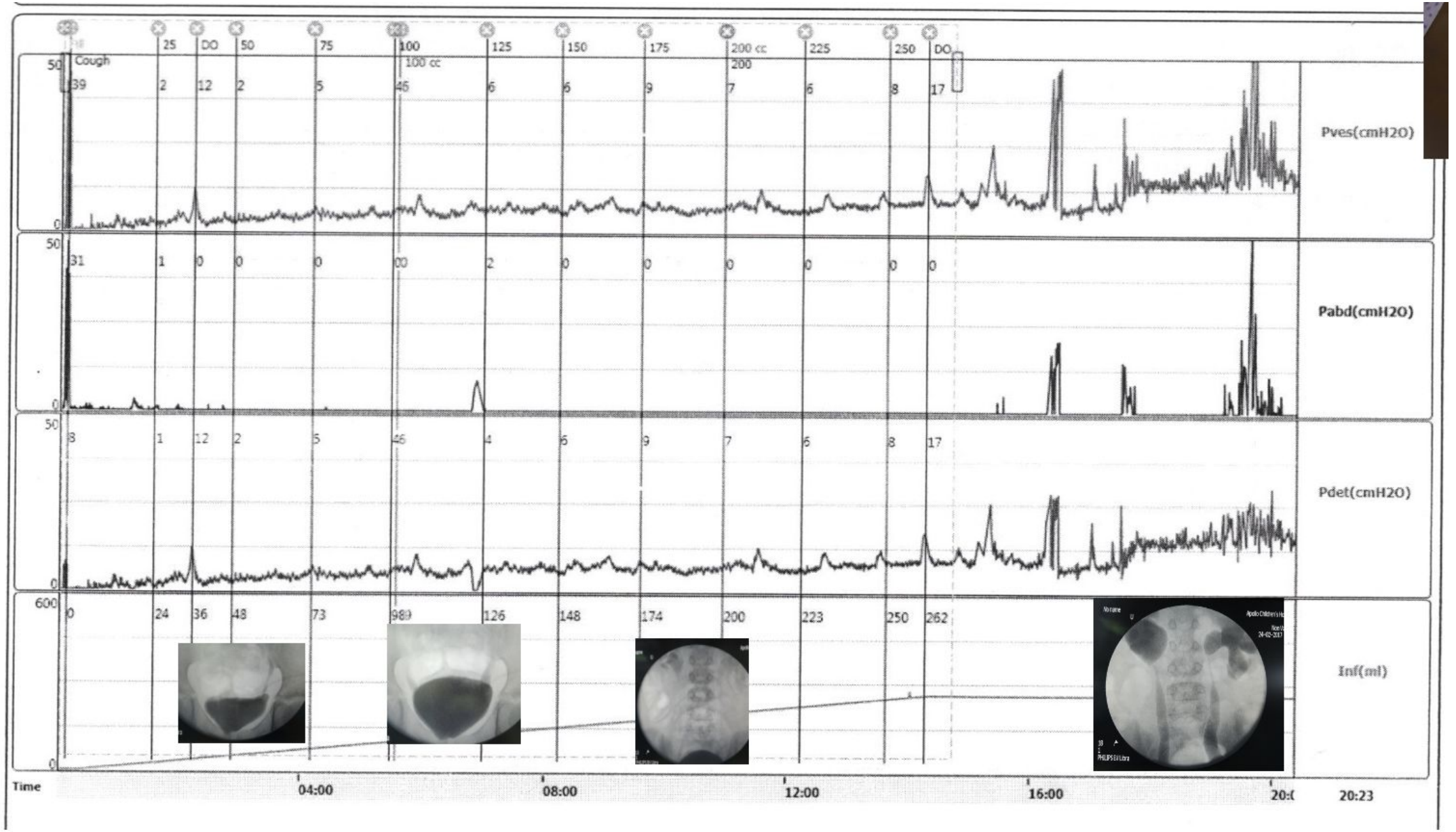
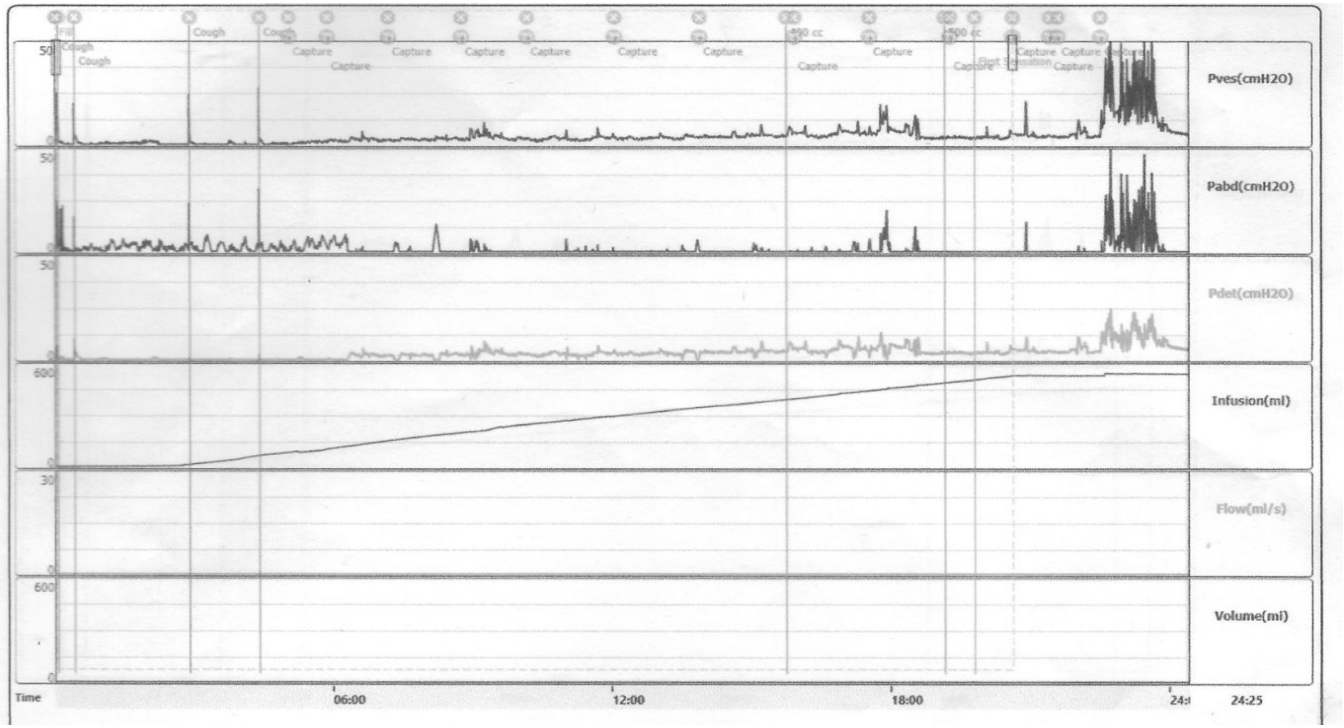
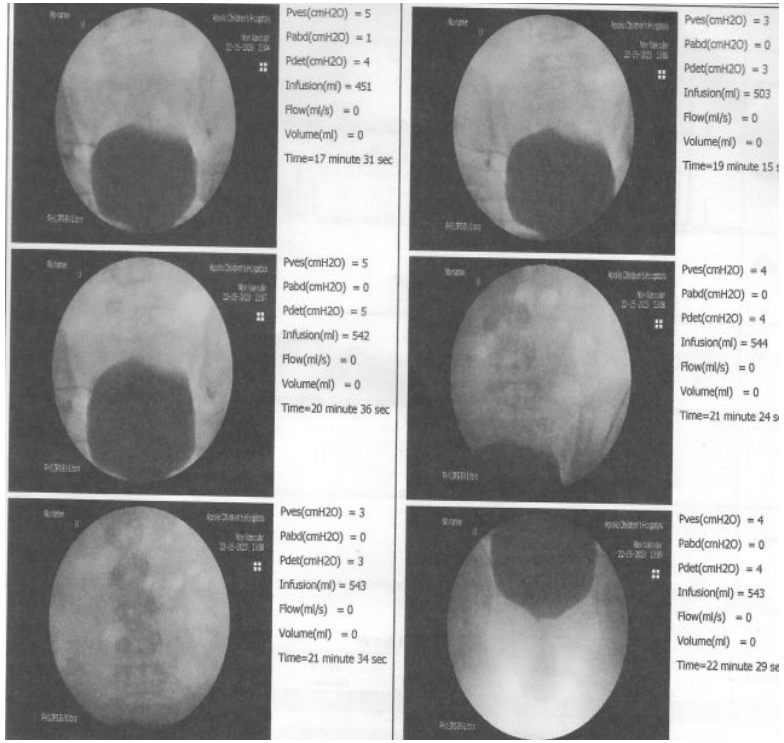


STATUS AT15 YEARS OF AGE

- After 12 years of Night Time Drainage
- UDS shows stable bladder with no filling phase VUR
- No UTI’s





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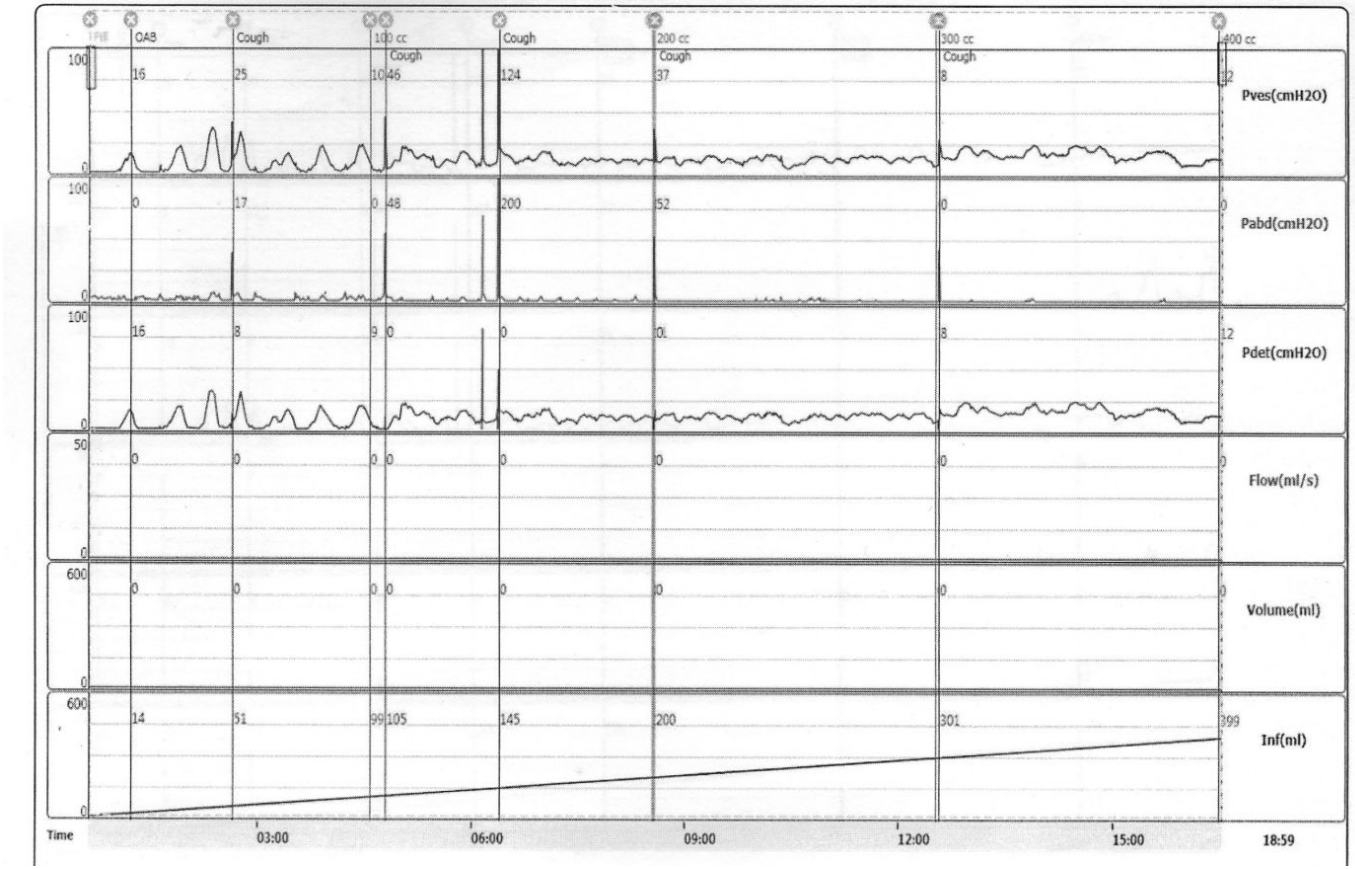
- Stable bladder fit for transplant
- Needs CIC for emptying



PUV FOLLOWUP ALGORITHM

- PUV fulguration primarily / confirm and redo if needed / circumcise
- Follow-up on 6 monthly basis – P + PN + PU
  Ultrasound, urine routine, Spot Urine P/Cr, Serum Chemistry, Height, Weight
- DMSA yearly

❖ Drugs – anticholinergics / alphablockers – judiciously (case to case basis)

- Uroflow (non invasive UDS) often
- Invasive urodynamics only for new symptoms, fall in renal function, drugs not working

✔ Consider Clean Intermittent Catherisation and Night Time Drainage to optimize bladder
✔ Bladder Augmentation only when bladder is completely non-compliant
✔ In adolescence / adult hood – hand over to adult urologist
✔ If RRT is needed – carefully re-evaluate bladder before transplant

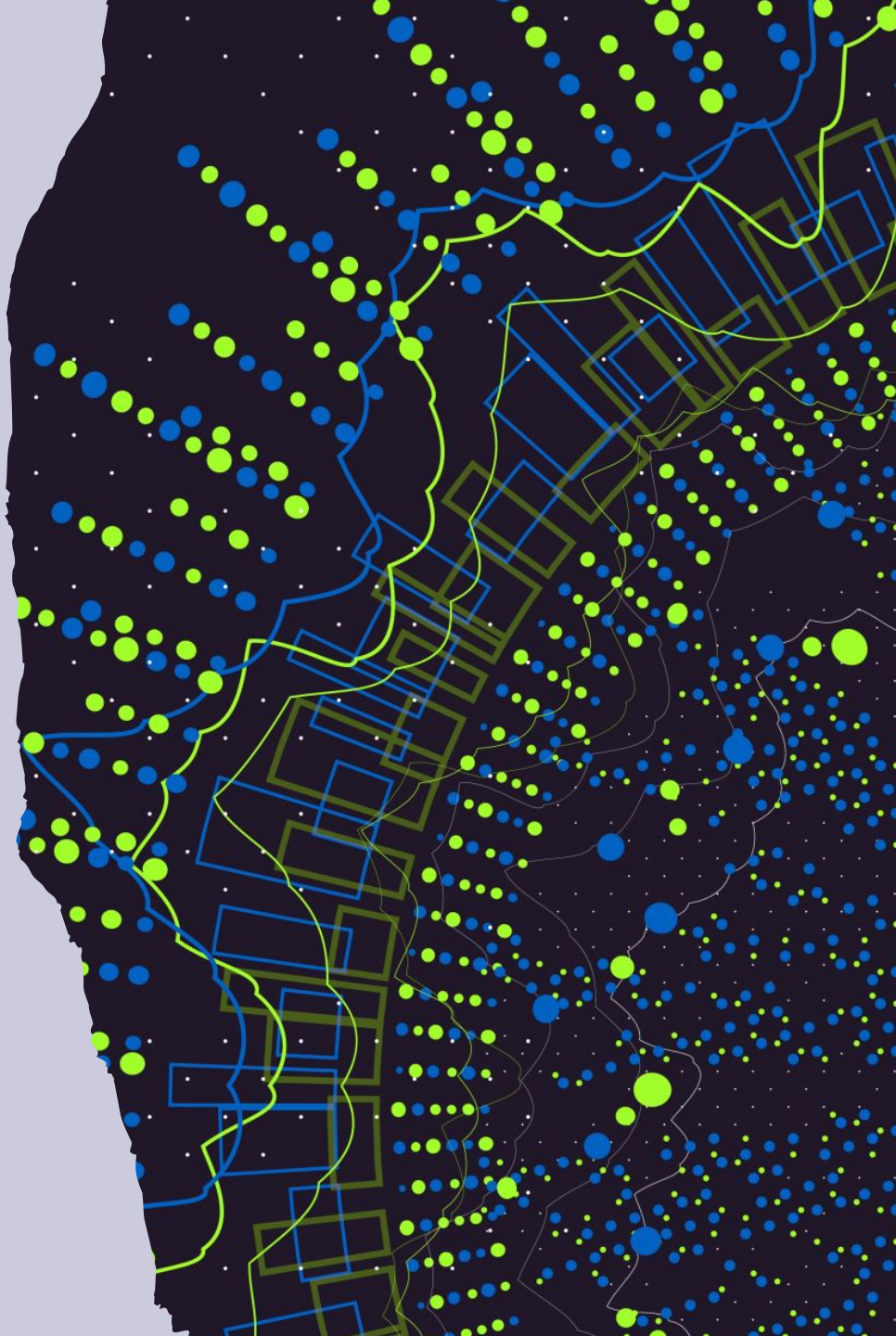
THANK YOU

POSTERIOR URETHRAL VALVES – WHAT IS THE NEED FOR LONG TERM FOLLOWUP BY THE PEDIATRICIAN

Dr.
SRIPATHI V
Dr. VIDHYA
T

Pediatric Urology Unit

Apollo Children's Hospital, Chennai



Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

PUV - JAN 2015 – 31ST AUGUST 2024

- **Our experience - 111 valve fulgurations**
- **Newborn valves – 37**
- Primary fulguration (in infants and older children) – 48
- Redo fulgurations in older children +/- vesicostomy / ureterostomy closure – 25

- Diversions – 4 (loop ureterostomy)
- Severe urethral strictures – 2

Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

WHY IS LONG TERM FOLLOWUP NEEDED?

To ensure

- **Adequate / Optimal growth**
- **Good renal function**
- **Avoid ESRD and need for RRT**

- The factors involved (over 15 – 19 years and beyond) include
- **Pediatric physician**
- **Pediatric Nephrology specialists**
- **Pediatric Urology specialists**

CASE 1- MR R – NOW 19YEARS

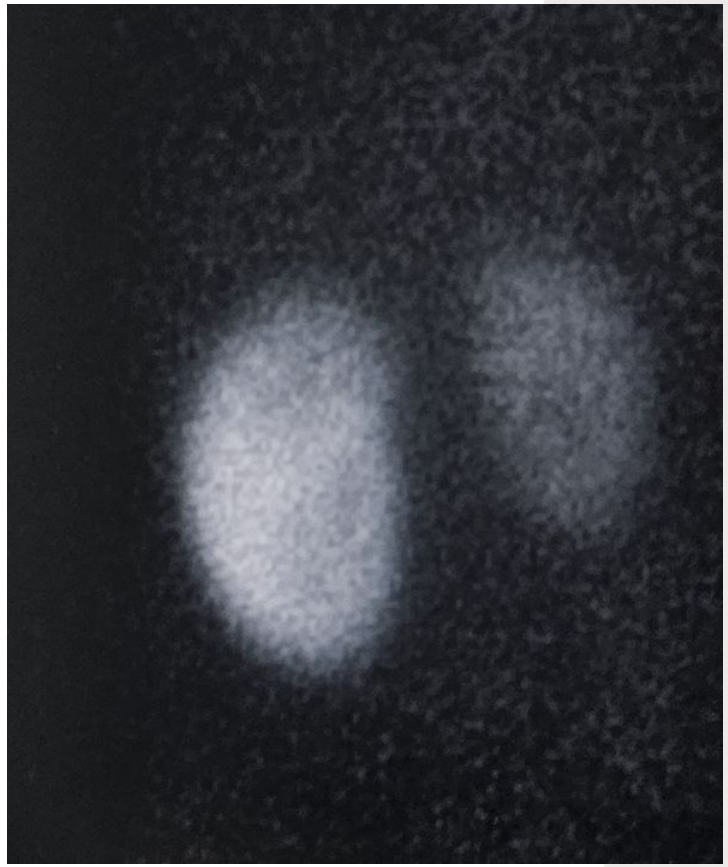
- Has been under combined care from 5 months of age

- At birth – **Left ureterostomy** done (sick baby with urosepsis, massive left VUR)
- 5 months of age – **Cystoscopy valve ablation** done
- 1 year of age – **Ureterostomy closure and complete valve ablation** confirmed

- 3 years of age – MCUG done – to confirm absence of VUR
- 5 years of age – Anticholinergics stopped
- 8 years of age – Started on alpha blockers as there was postvoid residue and LK was 38%
- 9 years of age – Alpha blockers working – dose adjusted
- 11 years of age – Alpha blockers stopped
- 14 years of age – Last visit **(can we stop coming to see you??)**

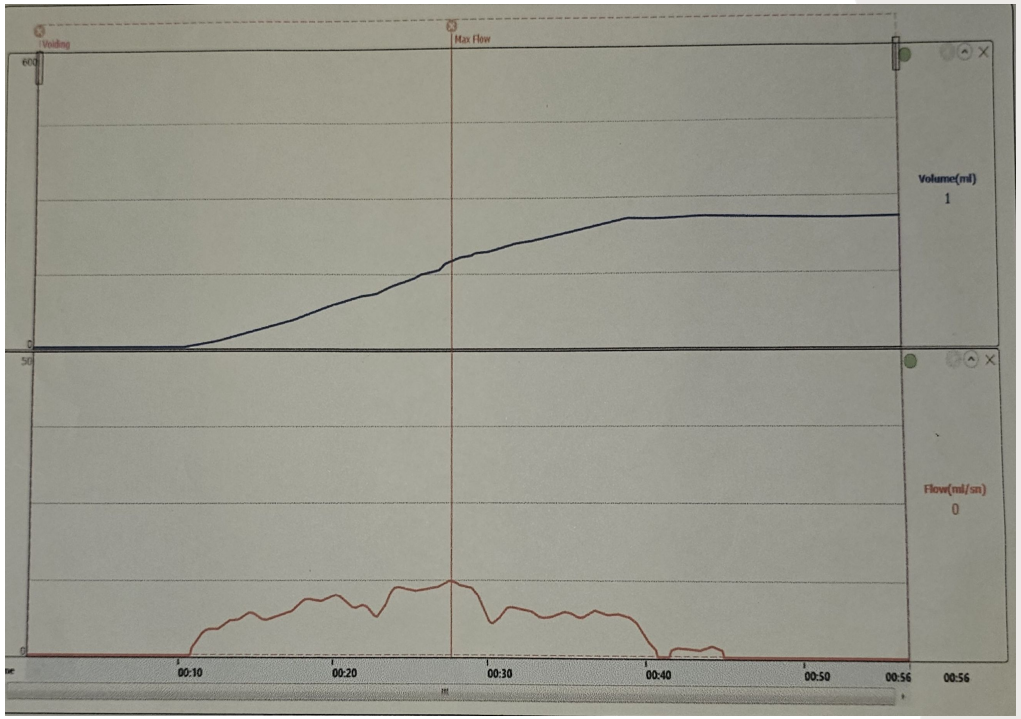
CASE 1 – MR R CONTINUED

- 19 years of age – I am having a sensation of incomplete emptying??
- Ultrasound KUB – Prevoid 500 mls, postvoid 50 mls
- DMSA – Marginally smaller LK
- In view of Spot Urine P/Cr – 0.25, increase renal echoes, marginally small kidney – nephrology review requested
- Uroflow asked for / Constipation treated



CASE 1 – MR R - CONTINUED

- Uroflow confirms poor flow
- Started again on alpha blocker (Tamsulosin)
- Will review and reassess with adult urologist (?prostate)



What did we achieve??

- ✔ **Salvaged his left kidney**
- ✔ **Carefully managed his bladder**
- ✔ **Made sure he grew well**
- ✔ **Avoided CRF**
- ✔ **All because we talked to our colleagues and managed his care in a combined manner P + PN + PU**

CASE 2 – MASTER NW – ANTENATAL

- 27 weeks gestational age – appears to be PUV – can you counsel??
- **First Pregnancy beyond legal termination date**
- Bilateral UHN, thick walled bladder – normal liquor

Fetal Urine

Beta 2 microglobulin

- **First sample 9.2 (27 weeks)**
- **Second sample 8.6 (28 weeks)**

- Our advice – No need for fetal intervention but there appears to be renal compromise, you need to see us regularly till child becomes an adult

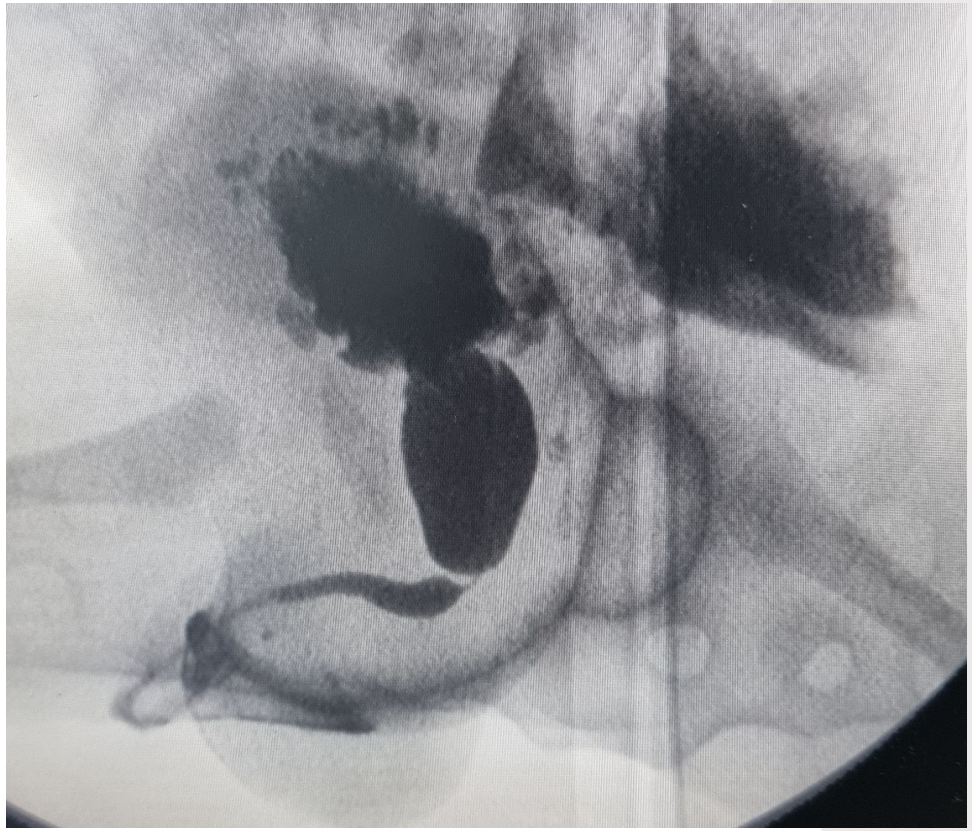
CASE 2 – MASTER NM

Underwent cystoscopy and PUV fulguration in newborn period

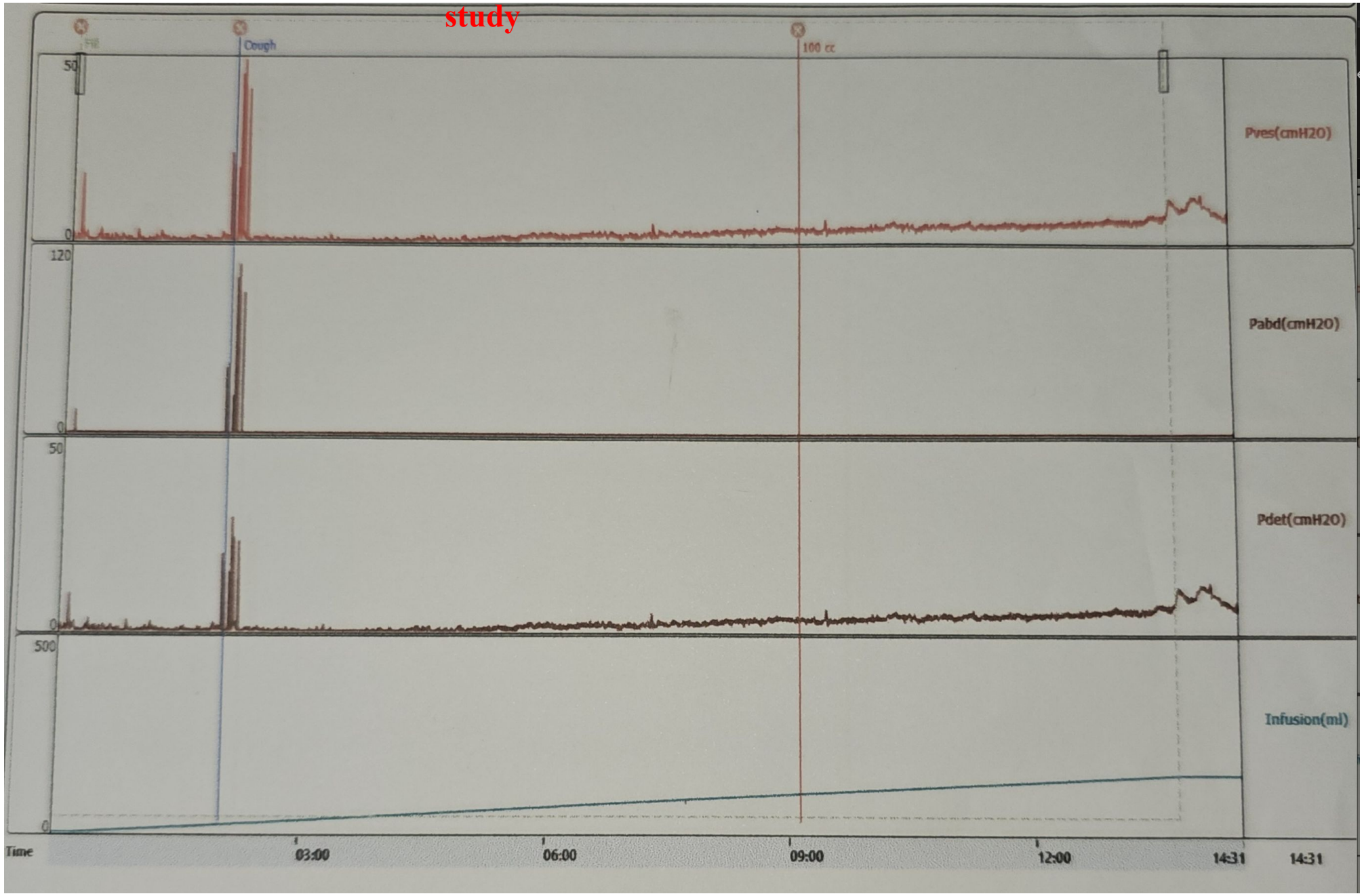
- At 7 mos of age admitted with chronic UTI and failure to thrive
- At 1 year of age – have check scopy (to confirm complete valve ablation) & circumcision
- At 1 year of age – DMSA renal scan RK 71%, LK 39%
- Started on Anticholinergic (Mirabegron) and Alpha Blocker (Terazosin)

- Reviewed at 2 years 9 months of age – 8.4 kgs
- **Grade 3 CKD / Metabolic acidosis**
- DMSA renal scan – LK had dropped in function to 29%
- Ultrasound – Bladder wall thickening with trabeculations persists. Bilateral HUN, Grade 2 parenchymal disease

- Our question – **Is the bladder the cause for the CKD and drop in renal function on the left side?? – Video UDS planned**
- Serum Creatinine – 2.2 at birth, 0.81 now



Video Urodynamic study



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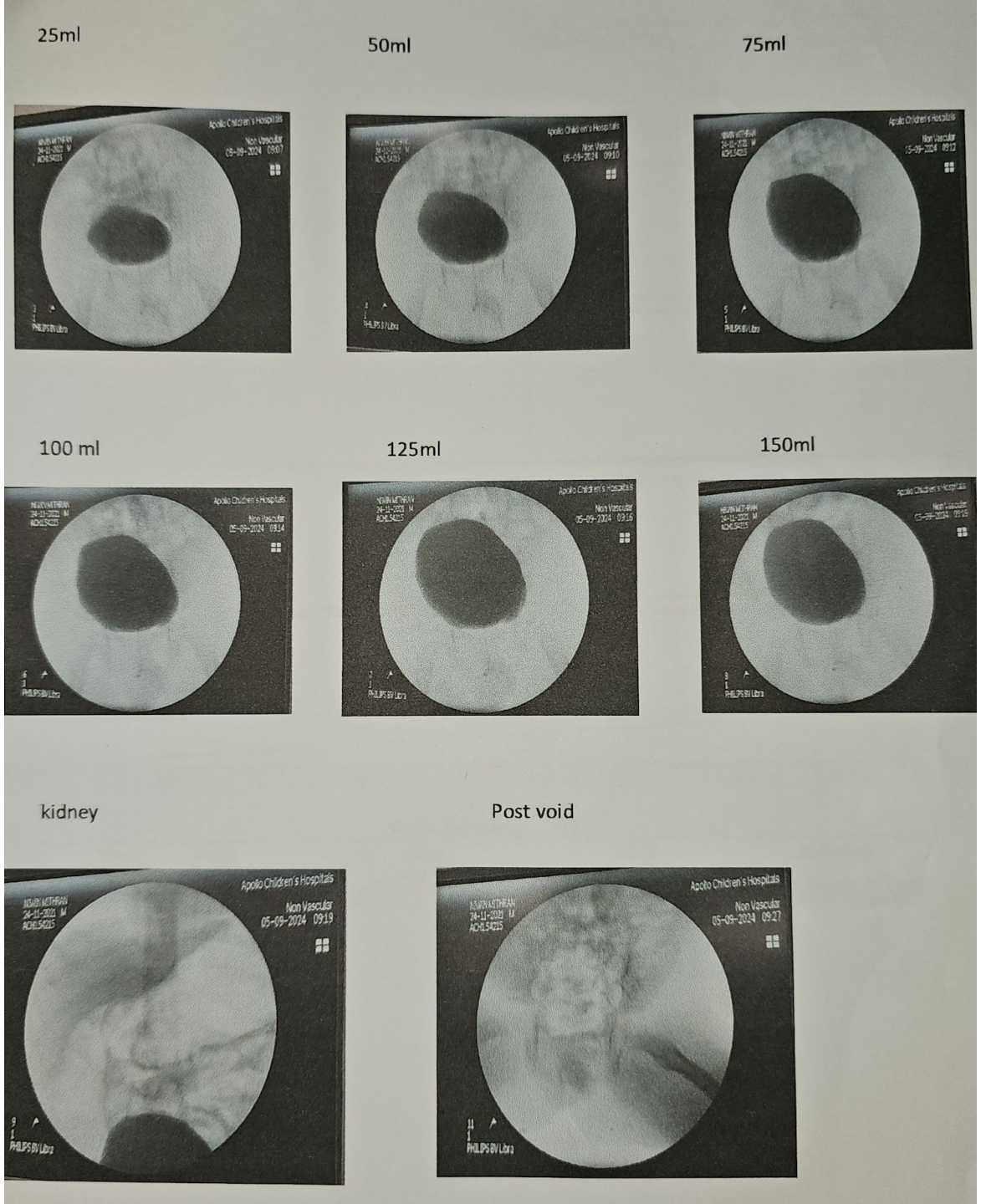
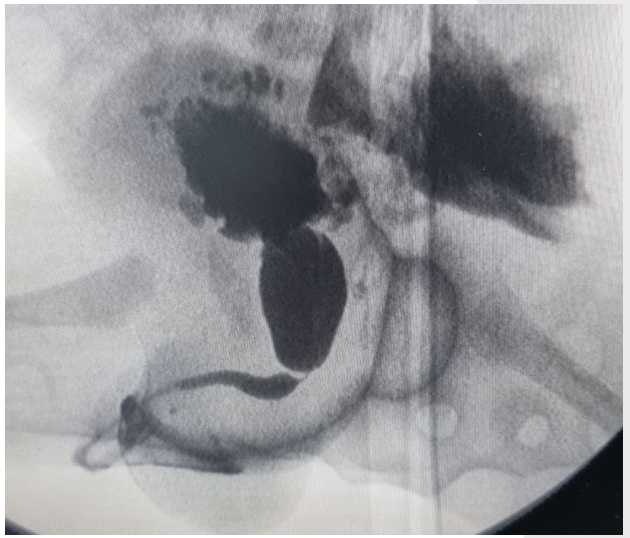
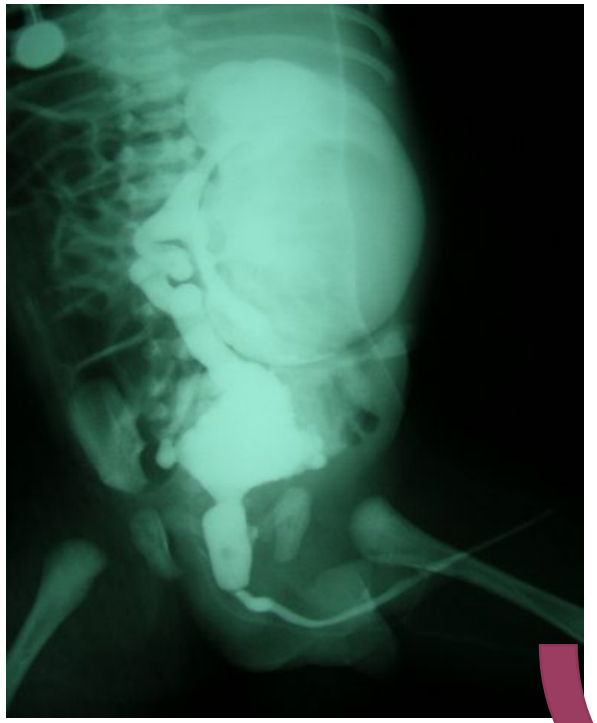




CASE 2 – WHAT DID WE ACHIEVE

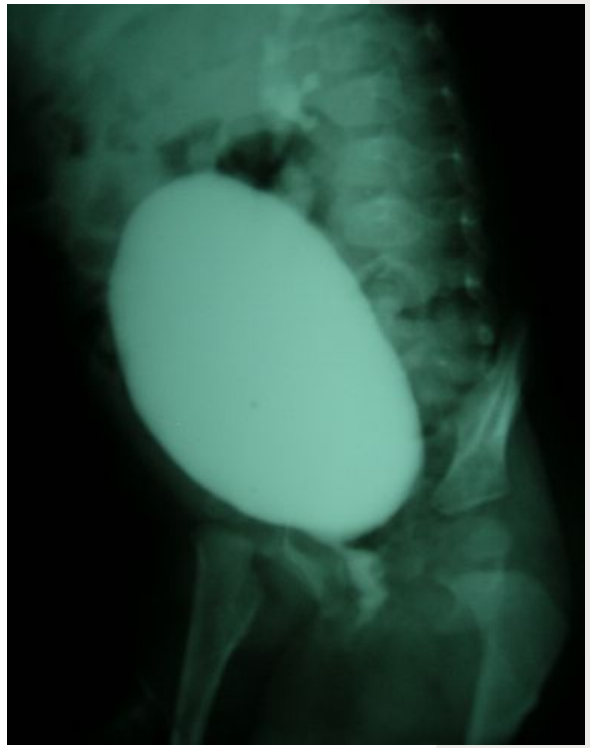
- ✔ **Anticholinergics and alpha blockers over 2 years have made the bladder into a compliant low pressure receptacle which empties completely**
  - Fall in LK function by 10% indicates a renal cause (nephrologists domain)
- ✔ **Bladder has perhaps become too compliant / there fore drugs need to be tapered and stopped**
- ✔ **The value of antenatal counseling, careful monitoring and combined care is shown by this case**

REFLUX IN PUV



- VCUG -NEONATE

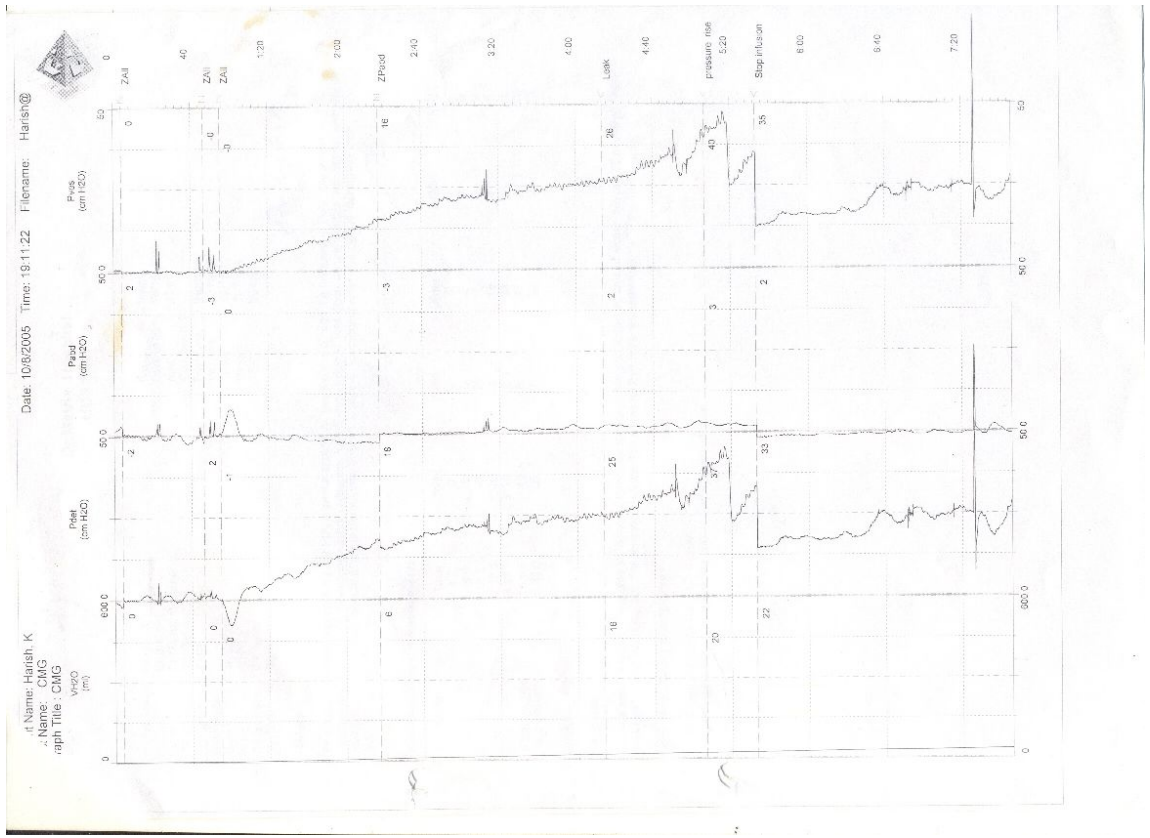
- Reflux resolves within the first year of life
- Resolution unrelated to the grade of reflux
- If persistent ,consider early urodynamics



- VCUG AT 7 MONTHS

Reflux ,no matter what the pattern, has not been a significant prognostic factor : J Urol: 2003: 170: 1677 -1680

Case 3 - Poorly compliant bladder –how do you manage??



Severe pressure rise even with 20 mls filling – Botox 200 units injected into detrusor

Master H – vesicostomy at birth

- **PUV fulguration and closure of vesicostomy at 2 mon**
- **Developed severe upper tract sepsis and underwent left ureterostomy (20% function) at 4 months**
- **At 2 yrs – can ureterostomy be closed safely?**

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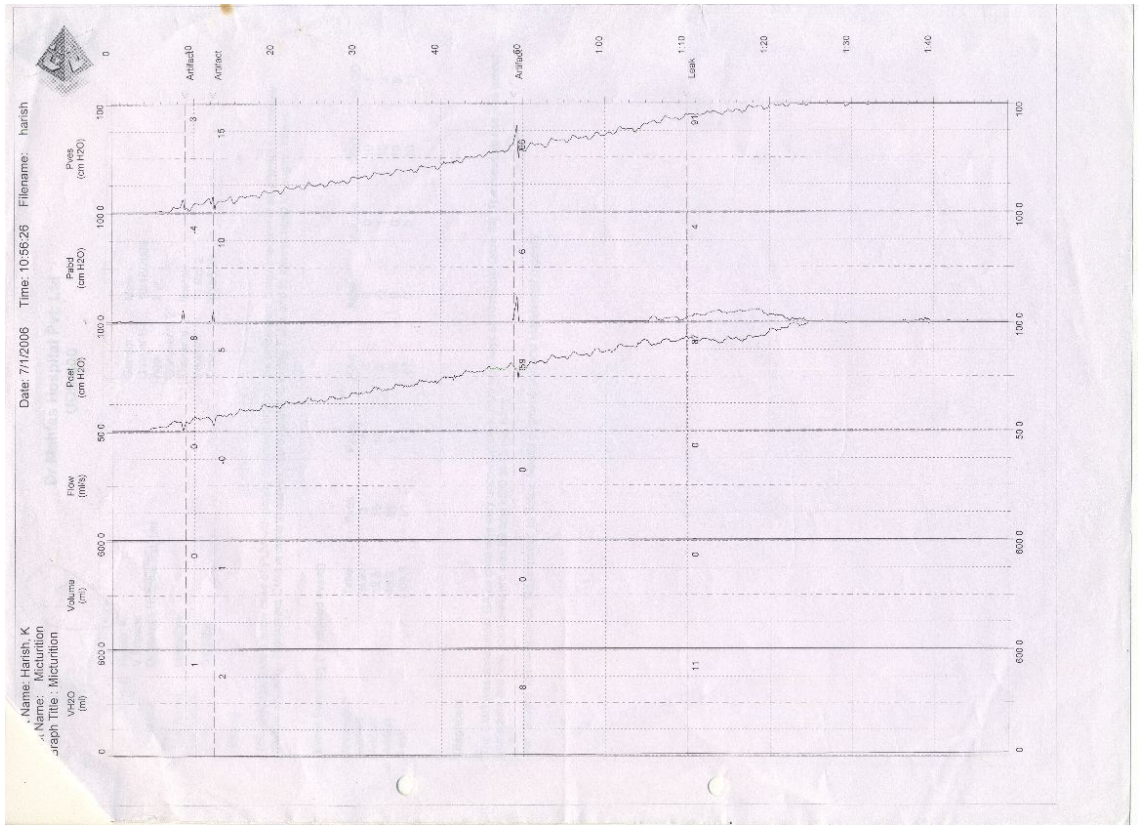
TOUCHING LITTLE LIVES

After Botox…

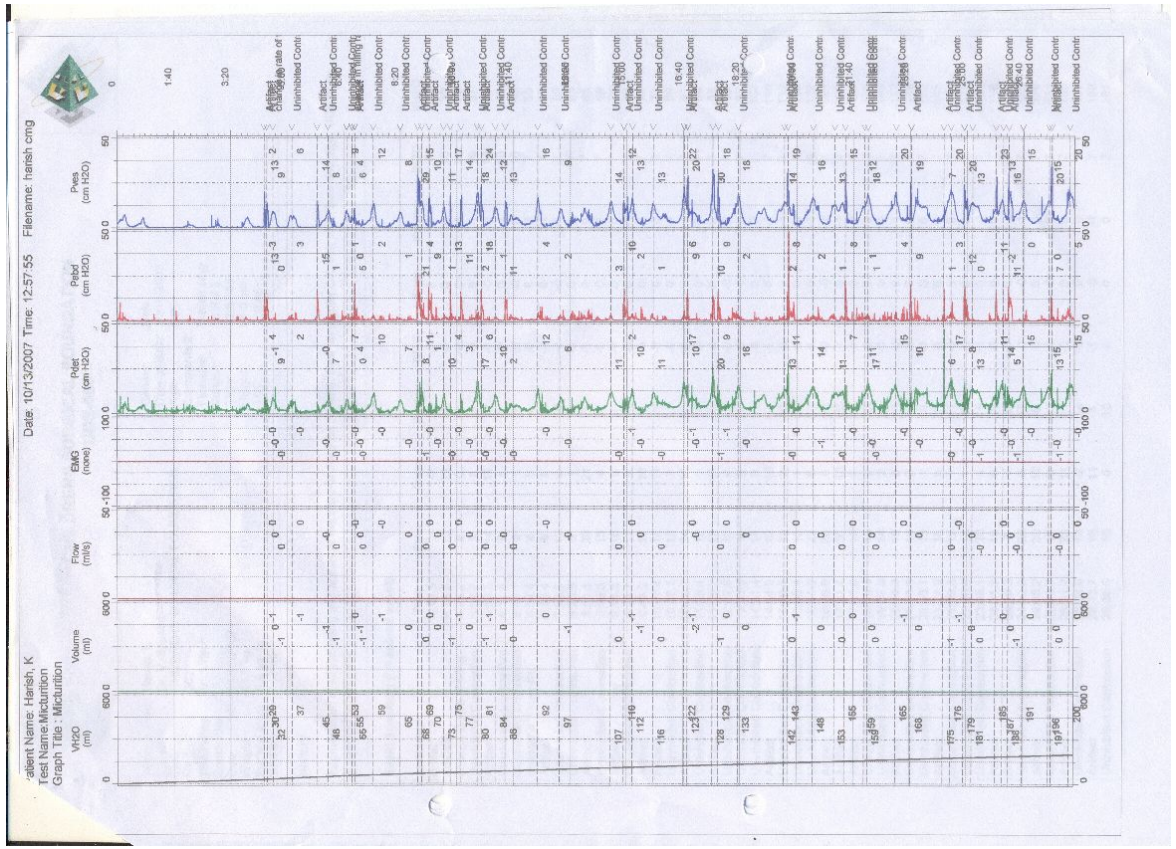


- **UDS five months after Botox – has pressure dropped ?**

Severe non compliance persists – augmentation is the only answer

Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

After Augmentation Cystoplasty what happened to pressures??

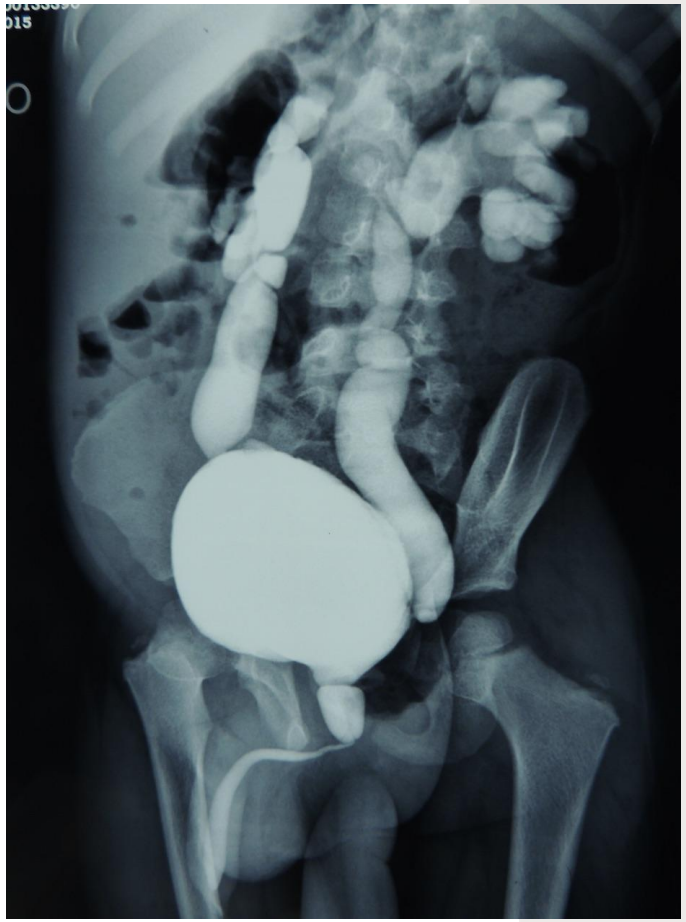


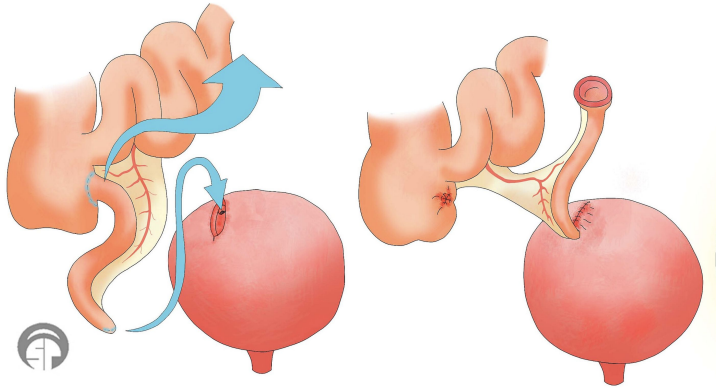
- **Augmentation colocystoplasty** done at 3 years of age
- Six months after augmentation pressures reached base line

Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

BILATERAL HIGH GRADE VUR IN PUV – VALUE OF NIGHT TIME DRAINAGE

- PUV ablation – 4 mos of age
- Redo ablation – 1.5 years
- Recc UTI, high grade bilateral VUR, large postvoid residues (in spite of therapy) –
- Appendix Mitrofannof done at 3 years of age – for painless bladder drainage at night
- UDS at 9 years of age
- UDS at 15 years of age





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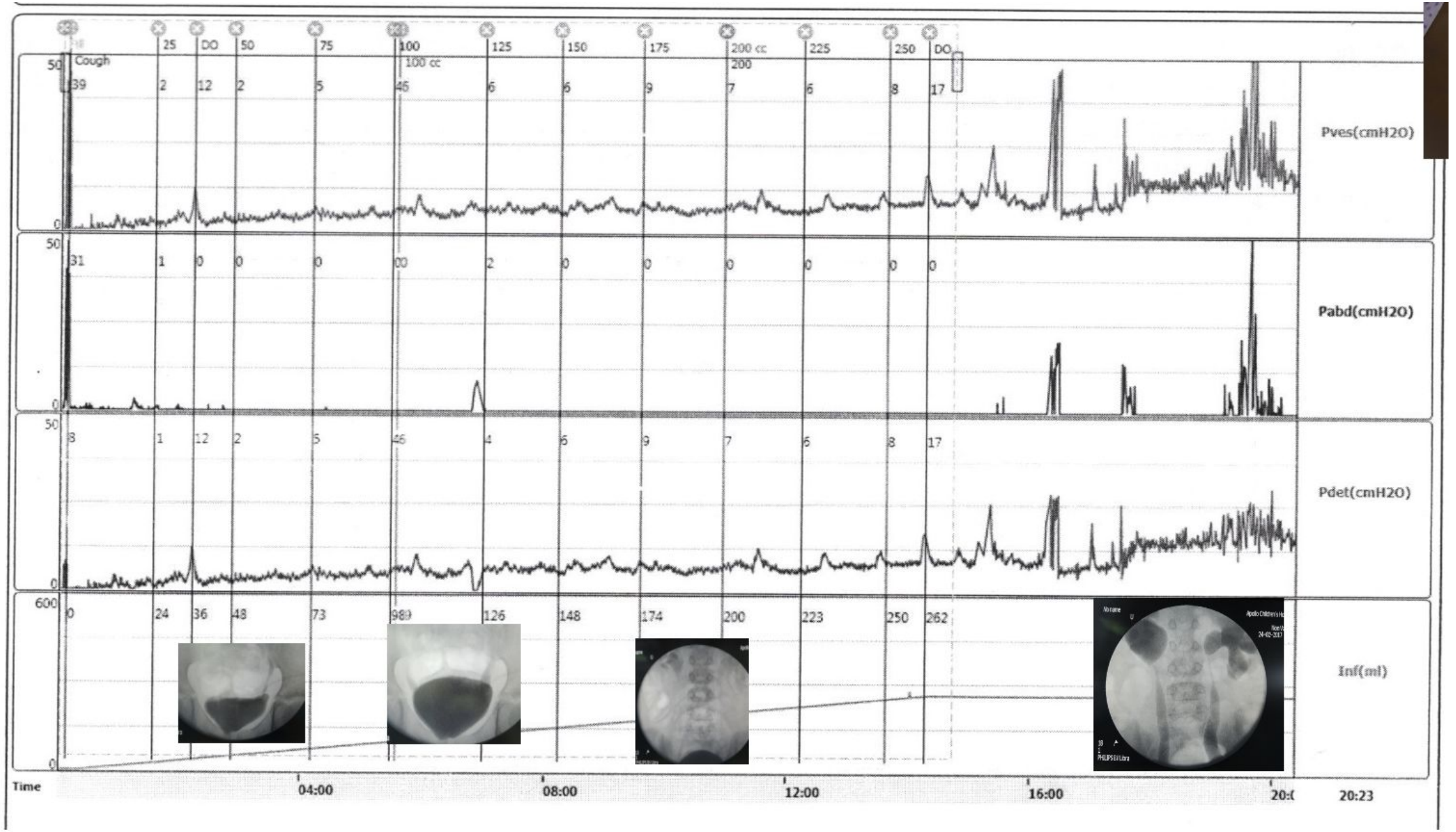

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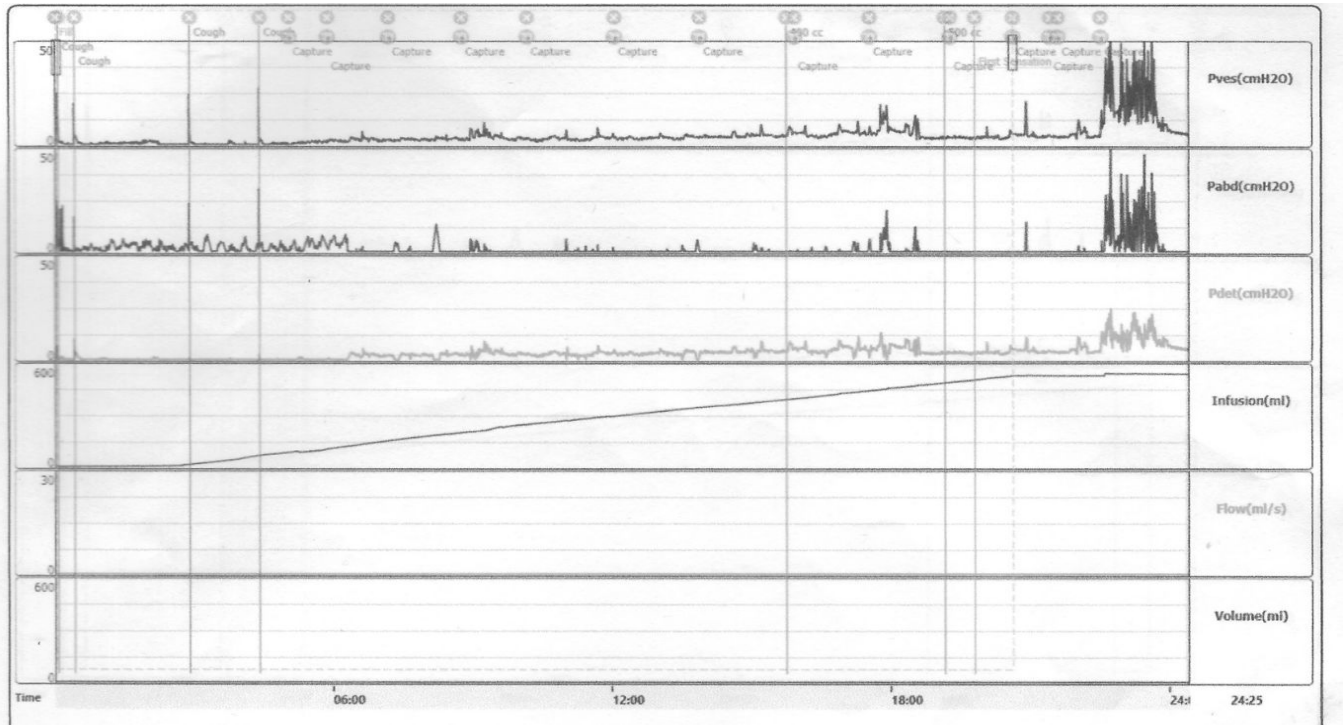

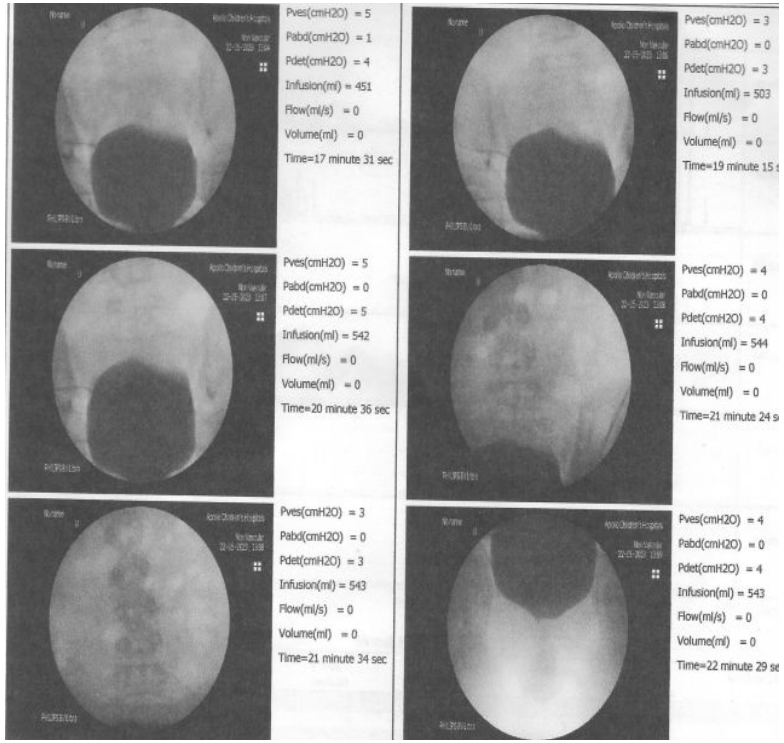

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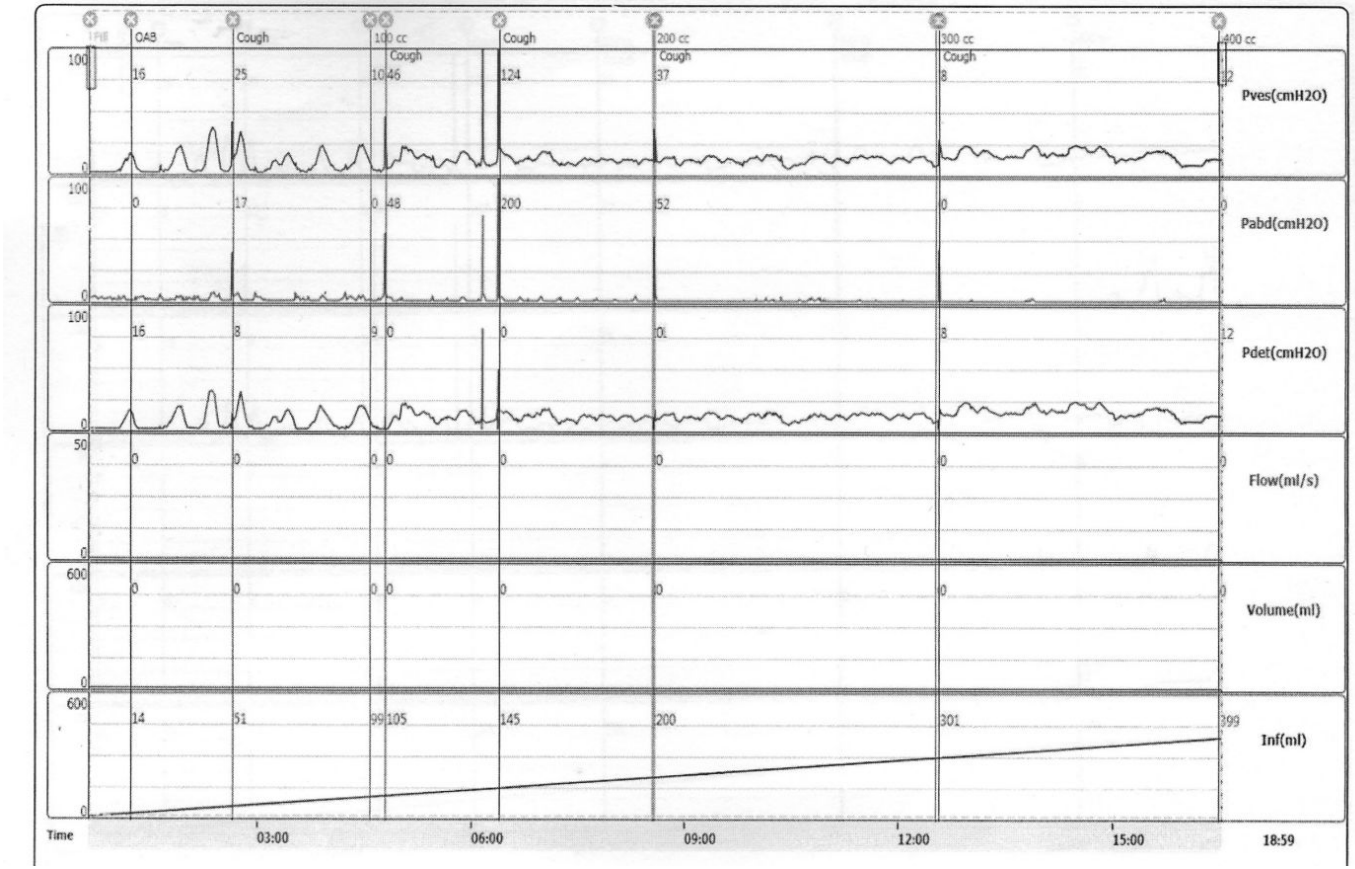

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✔ In adolescence / adult hood – hand over to adult urologist
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THANK YOU

Greetings from CHSC

Pediatric Kidney Replacement therapy : what a pediatrician should know

Lt Col Dr Suprita Kalra
Prof Pediatrics & Pediatric Nephrologist
Command Hospital, Pune

Not a miniature adult

- Pediatric dialysis 0.1%
- Only half at Pediatric Center

Differences

- ✓ Etiology
- ✓ Indications
- ✓ Modalities
- ✓ Access
- ✓ Anticoagulation
- ✓ Socio-cultural factors
- ✓ Financial considerations:Numbers

Chand et al. AJKD.Volume 69, Issue 2, 278 - 286

Continuum AKI-AKD-CKD

- Incidence of AKI 26.7% in PICUs
- 5.8% require RRT
- 30–50% mortality in children requiring RRT
- Early/Timely initiation prevents complications and improves outcomes

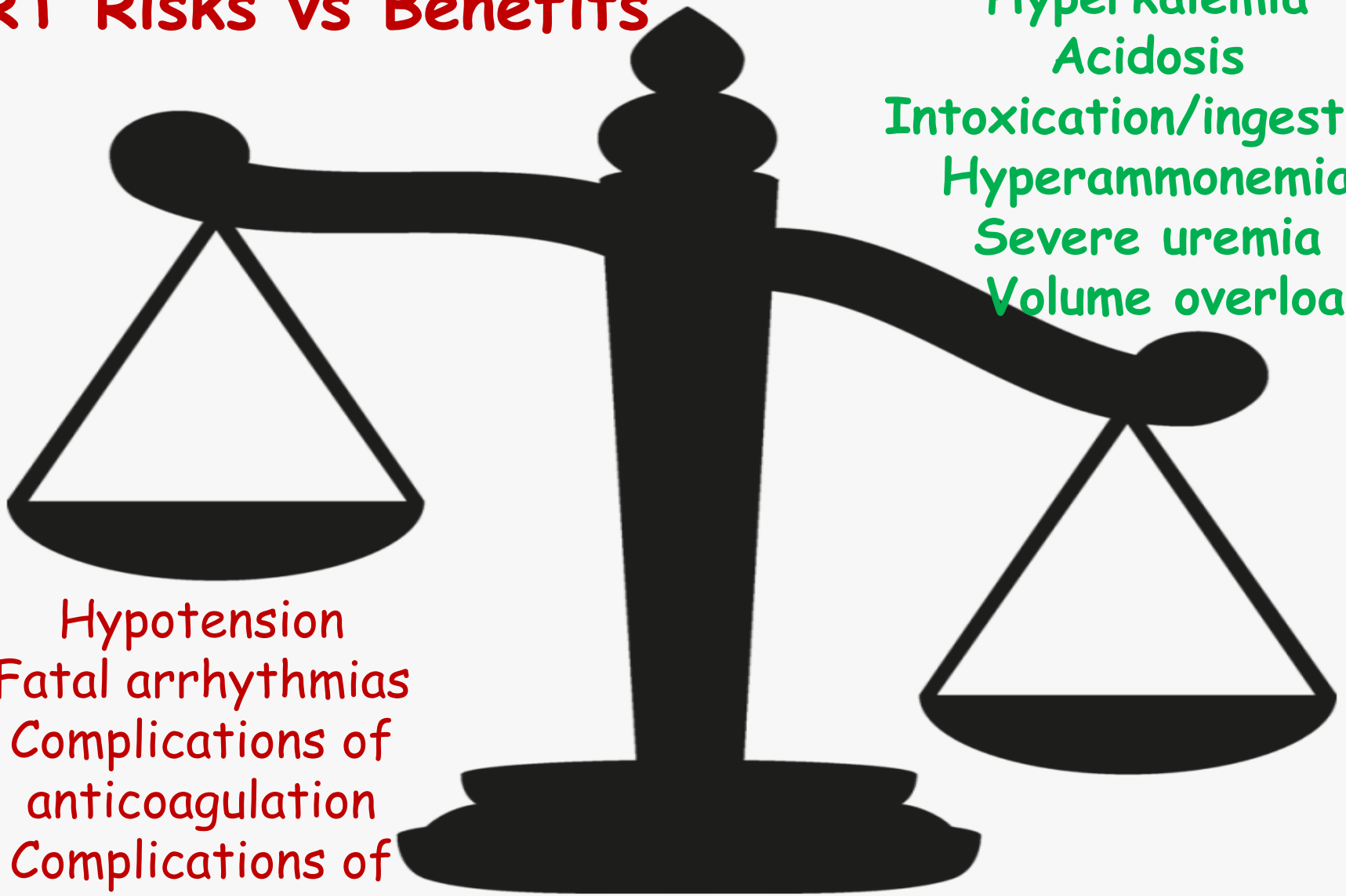
Cortina G et al. Pediatr Crit Care Med. 2019;20:314–22.

- 20–50% progress to CKD after AKI
- 10–12% require chronic dialysis in 5 yrs

Sigurjonsdottir VK et al. Pediatr Nephrol 2018; 33:2047–2055.

Uber AM et al.Pediatr Nephrol 2020; 35:213–220.

KRT Risks vs Benefits



Hyperkalemia
Acidosis
Intoxication/ingestion
Hyperammonemia
Severe uremia
Volume overload

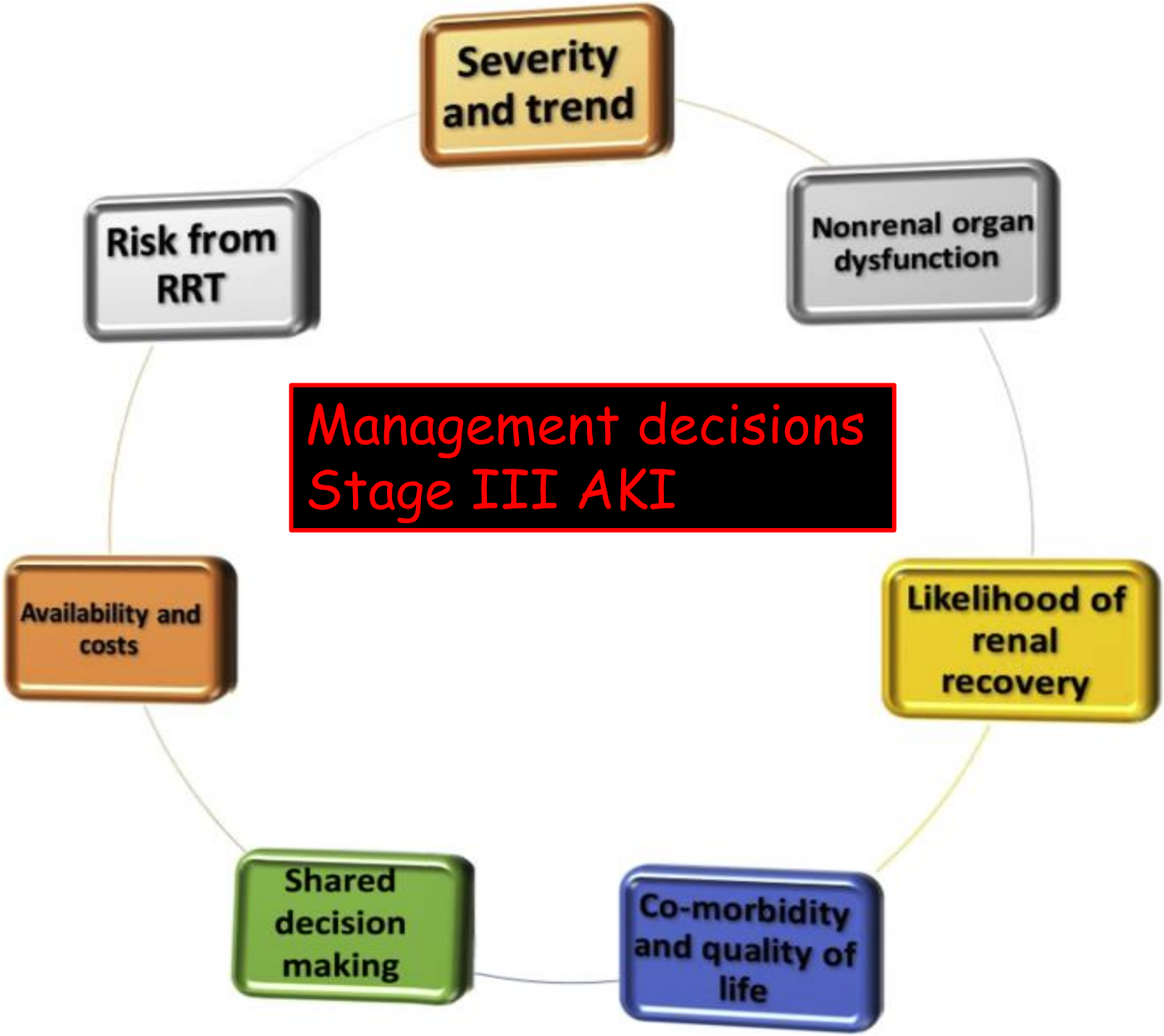
Hypotension
Fatal arrhythmias
Complications of anticoagulation
Complications of vascular access

No single value of Serum Urea,Creatinine or Cystatin C definite indication

Fluid input – fluid output (L) × 10
ICU admission weight (Kg)

- FO > 20% independently associated with mortality
  Sutherland SM et al. Am J Kidney Dis 2010; 55:316–325.
- IV Furosemide intermittent or continuous no effect on AKI/need for KRT/death

  SPARK study. J Crit Care. 2017 Dec;42:138-146.
- Bumetanide increases UO in preterms with oliguric AKI but increases serum creatinine
  Oliveros M et al. Pediatr Crit Care Med 2011;12:210–214.
- Dopamine/Fenoldopam/mannitol/ANP/nesiritide/ rasburicase no role in prevention/treatment of AKI
- Lauschke A et al. Kidney Int 2006;69:1669–1674.
  Costello JM et al. Pediatr Crit Care Med 2006;7:28–33.


Severity and trend
Nonrenal organ dysfunction
Likelihood of renal recovery
Co-morbidity and quality of life
Shared decision making
Availability and costs
Risk from RRT
Management decisions
Stage III AKI

Choice of dialysis modalities

Peritoneal Dialysis (PD)

Intermittent Hemodialysis (IHD)

Continuous Renal Replacement Therapies (CRRT)

PIRRT / SLEDD

CRRT
- CVVH
- CVVHD
- CVVHDF

Patient size

Hemodynamic stability

Institutional expertise

de Galasso L et al. Pediatr Nephrol. 2020;35(5):753-765.

Case Vignette 1

- 12 day old female neonate
- Born to 24 year old primi through SVD
- BW 2800gm
- Discharged at day 3
- Day 8 lethargy, poor feeding,oliguria
- O/E severe dehydration, 15% weight loss
- Serum Na:174meq/l
- Urea/creatinine:300/6.8mg/dl
- No urine output after 2 boluses

Questions

- Does the neonate need KRT
- What modality
- What would be your prescription

Modalities of KRT

Parameter	Peritoneal dialysis (PD)	Intermittent hemodialysis (IHD)	Sustained low-efficiency dialysis (SLED)	Continuous kidney replacement therapy (CKRT)
Duration	Continuous	2–4 h/d	6–12 h/d	Continuous
Technicality	Simple	Complex	Complex	More complex
Hemodynamic alterations	Minimal	Large	Mild	Minimal
Control of fluid removal	Least	Modest	Better	Very accurate
Anticoagulation	Not required	Generally required	Necessary	Necessary
Mechanism of solute clearance	Diffusion	Diffusion	Diffusion ± convection (SLED-F)	Convection (SCUF, CVVH) ± diffusion (CVVHD, CVVHDF)
Risk of cerebral edema	-	+++	++	-
Rapidity of toxin removal	+	+++	++	+
Middle molecule clearance	Poor	+	+	+++
Patient mobility	+	+++	++	-
Cost of therapy	-	+	+	+++

Acute PD is BLS for kidneys:must know

Bag and mask for kidneys
Bed side life saving skill
No special equipment or training required

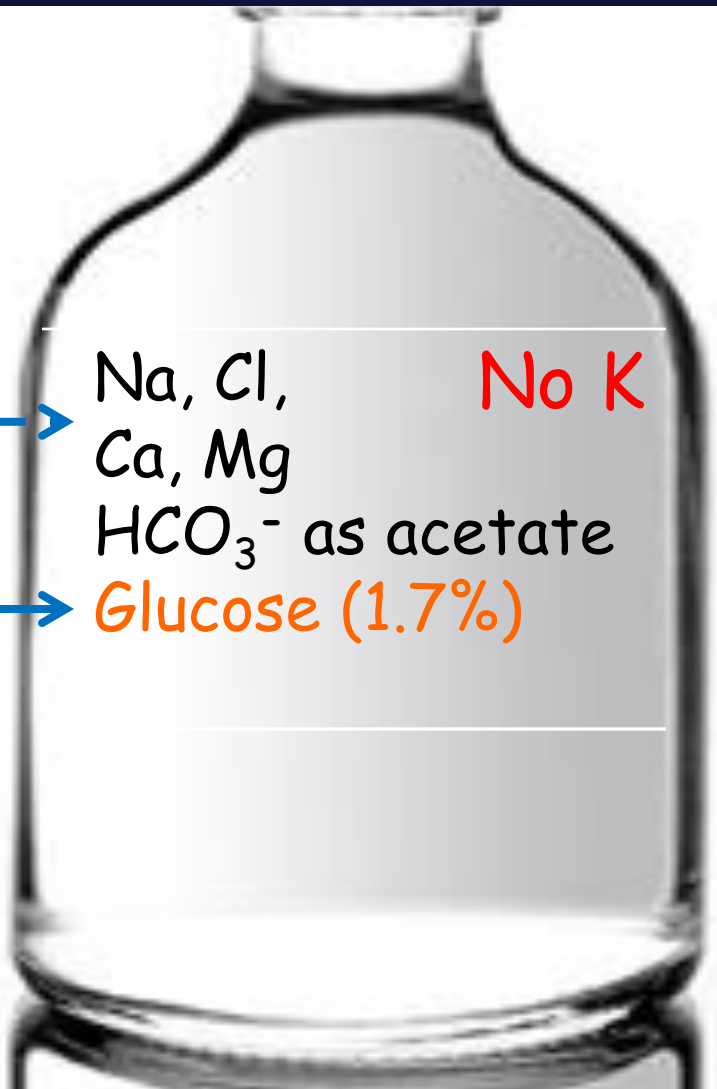
Principle of PD

Peritoneal capillary in patient with AKI

Urea,
Creatinine
,
K
Water

Peritoneal Membrane

Dialysis Fluid in peritoneal cavity



Diffusion & Convection

Acute Peritoneal Dialysis

Access

- **Soft** (Tenckhof) catheter, inserted surgically or bedside
- **Rigid** (stiff) catheters
- **Improvisations** (NGT/ICD)

Dwell vol

- 30–40 mL/kg (800–1100 mL/m^2)
- Lesser vol dwells when using PD soon after surgical catheter placement

Dwell time

Short cycles
20-30 mins for first 4-6h for rapid correction of acidosis/ ↑K
continous flow

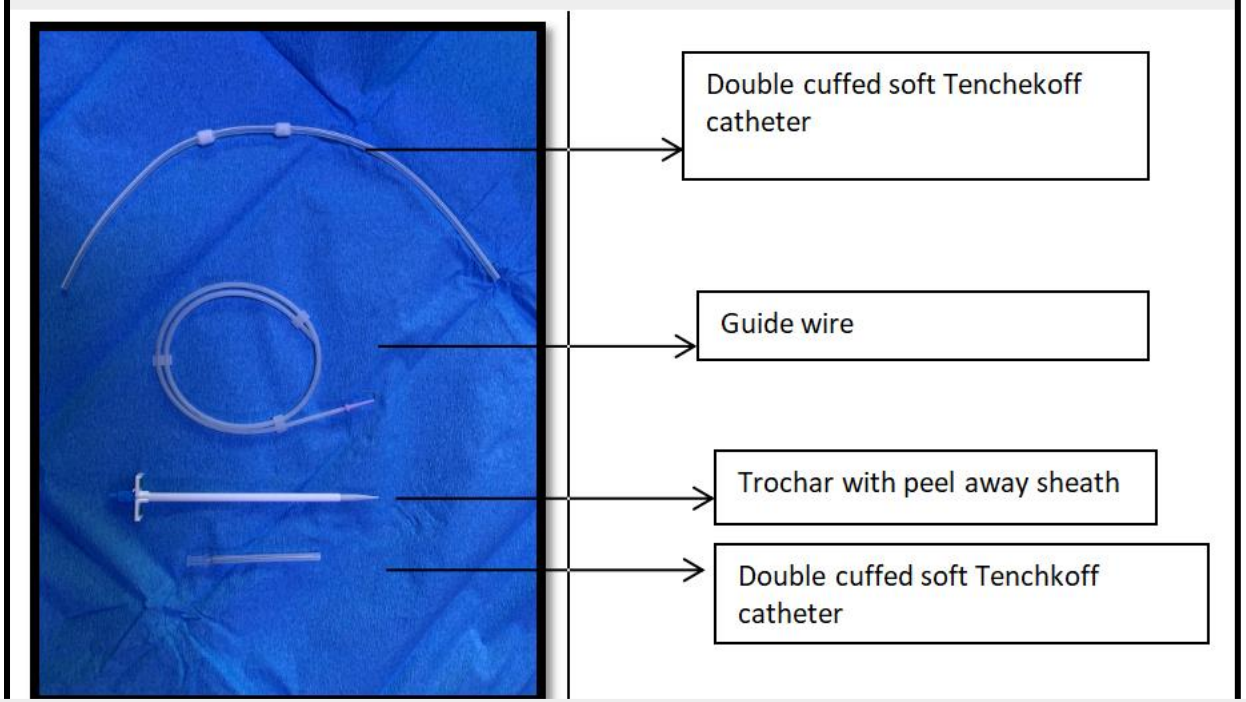
Prescription tailored as per clinical condition

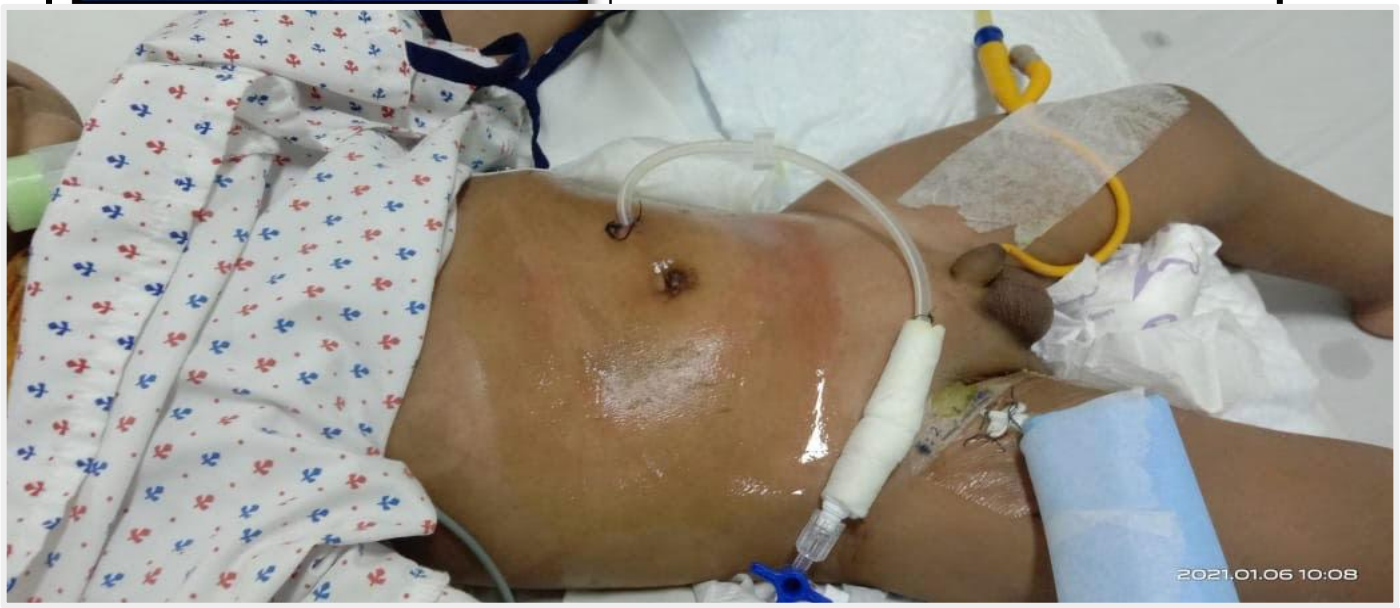
- Higher dextrose (2.5%–4%) for fluid overload
- Bicarbonate based preferred to lactate solutions
- Sodium/K/Heparin can be added as per requirement

PD Monitoring Chart

Cycles	Time	Inflow (ml)	Outflow (ml)	UF	Cumulative UF (ml)
1.	9 am	300	320	-20	-20
2.	10 am	300	300	0	-20
3.	11 am	300	320	-20	-40
4.	12 pm	300	330	-30	-70
5.	1 pm	300	320	-20	- 90

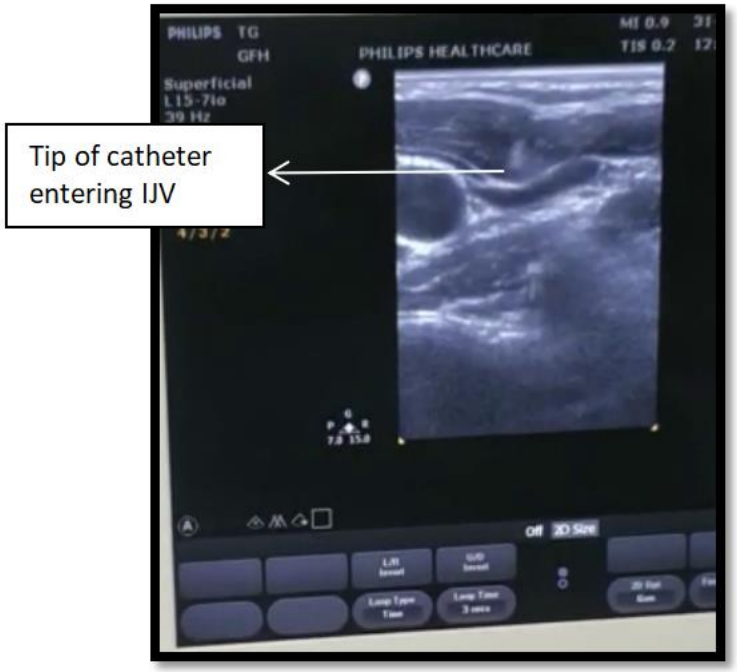
Close monitoring for complications required

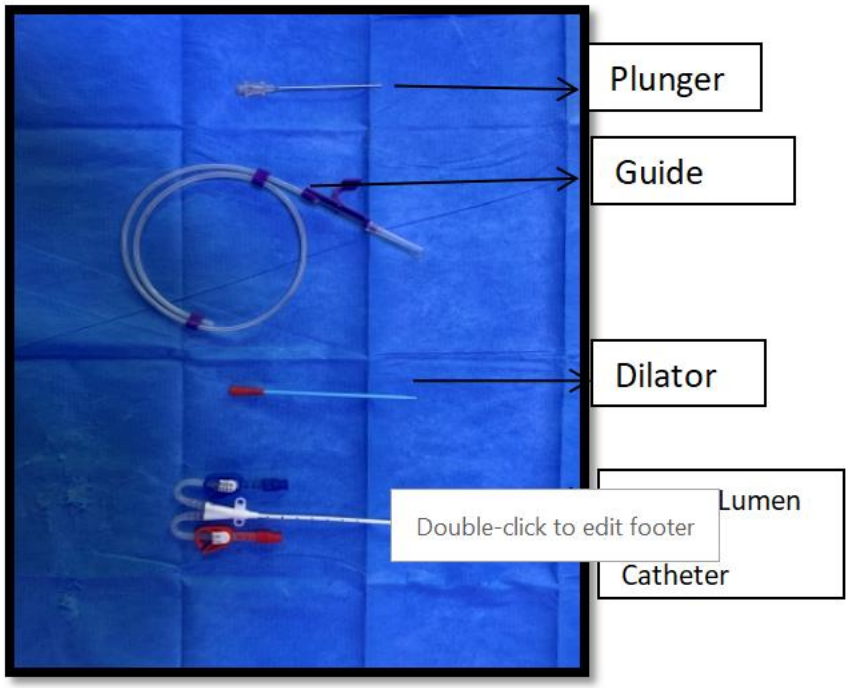




Soft Techekoff Peritoneal dialysis Catheter

Temporary Hemodialysis Catheter





Patient size	Catheter size	Insertion site
<3 Kg	4-6 F Single /Double-lumen 7F	Femoral vein
3-6 kg	Double lumen 7 F	IJV or Femoral
6-15 kg	Double-lumen 8 Fr	IJV or Femoral
15-30 kg	Double-lumen 9/10 Fr	IJV or Femoral
>30 kg	Double-lumen 10 F or 11.5 F	IJV or Femoral

Intermittent Hemodialysis

- Useful in hemodynamically stable children
- Rapid & Efficient solute clearance
- Preferred in FO, poisoning, TLS, hyperammonemia,

Prescription

- **Dialyzer size**: 0.7–1 × body surface area
- **Tubings** : neonatal, pediatric, or adult
- **Blood flow rate**: 5-7 mL/kg/min
- **Dialysate flow**:1.5–2× BFR
- **Ultrafltration**: ≤ 10ml/h/kg or ≤5% weight
- **Duration**: 3–4 h daily or alternate day

de Galasso L et al. Pediatr Nephrol. 2020;35(5):753-765.

Case Vignette 2

- 6 year old presented with severe pain abdomen and recurrent vomitting × 48h
- Examination:tachycardia,tachypnea,weak pulses ,normal BP
- Moderate to severe dehydration,tenderness epigastrium
- Evaluation s/o Acute Pancreatitis
- Conservative mangement
- Developed AKI with features of fluid oveload & worsening SIRS,urea/creatinine 200/4.8 mg/dl

Questions

- Does the child need KRT
- What modality
- What would be your prescription

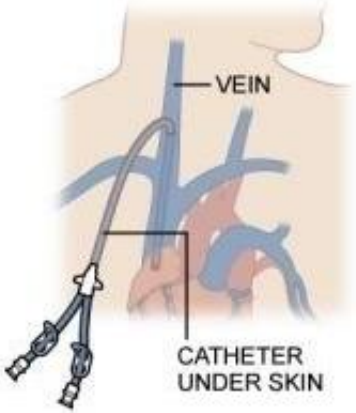
- Taken up for HD session
- Noticed to have encephalopathy,2 episodes of vomitting
- What can be the cause

Rule out Dialysis Disequilibrium Syndrome

CONNECTION TYPES

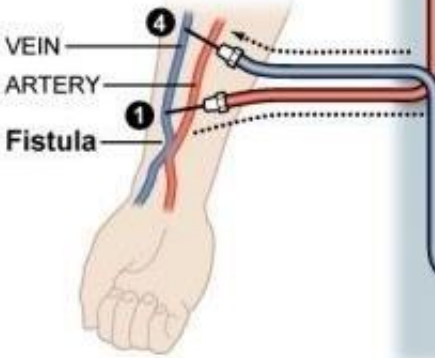
A Catheter

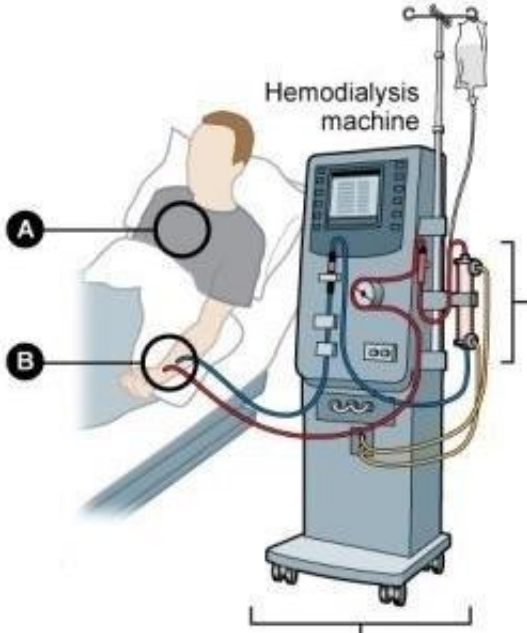
A tube inserted into a vein in the neck, chest or leg

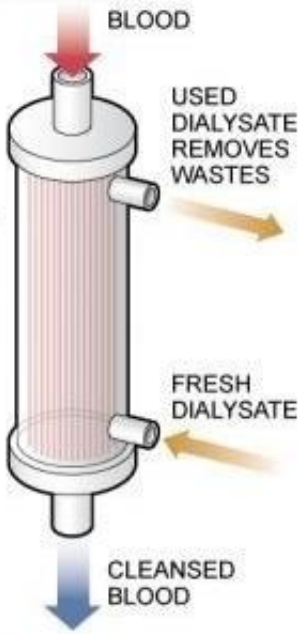


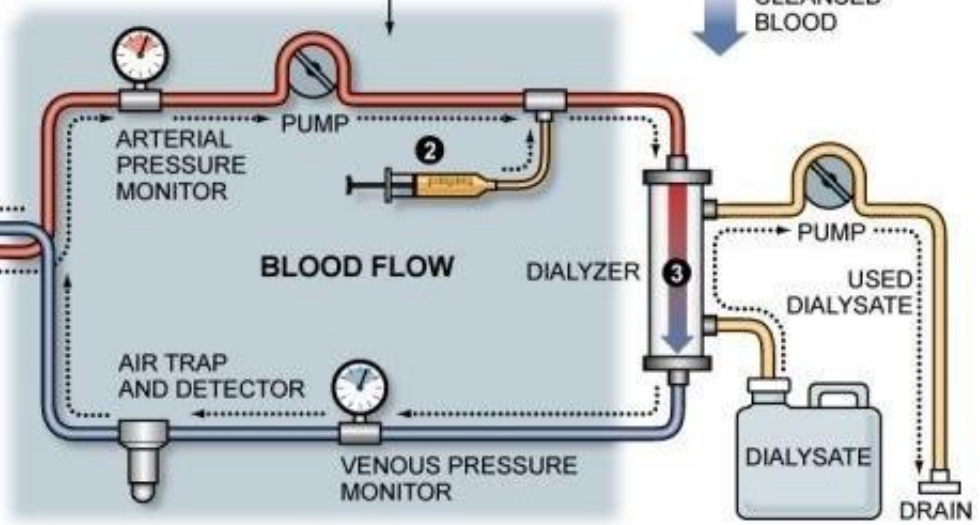
B Fistula

A surgically created connection of an artery to a vein









1 Blood is pumped out of a patient's catheter or fistula into the blood line.

2 Heparin, a blood thinner, is added to prevent clotting.

3 Blood flows into the dialyzer, where impurities, salt, and excess fluid are drawn into the dialysis solution.

4 Cleansed blood is returned.

Graphic by Al Granberg

IHD vs PD

- Uremia control and catheter-related complications comparable
- 30 day survival 60.7 % & 36.5 % with PD & daily HD (p = 0.019) respectively
- Adjusted mortality higher with HD (HR 1.75, p = 0.022)
- 94 % fatalities in HD group during or in 1 hour of HD
- Age <1 year, time lag from disease onset to RRT initiation, mechanical ventilation and vasopressor dependence independently predicted death

Basu B et al. Pediatr Nephrol. 2016 Oct;31(10):1681-9

PIRRT/SLED/SLED-F

- Alternative to CRRT in critically ill with AKI
- Extracorporeal blood purification of ≥6 h with BFR 3–5 ml/kg/min & DFR twice BFR
- Gradual fluid removal: ↓ hemodynamic instabilty

PCRRT recommendation for PIRRT. Hemodial Int. 2020 Apr;24(2):237-251.

- Several studies demonstrated efficacy and safety
- cost effective & no additional training required

Yadav M. Indian J Pediatr. 2023 Apr;90(4):355-361

Shiri S. Pediatr Crit Care Med. 2023 Mar 1;24(3):e121-e127.

Continous Kidney Replacement Therapy(CKRT)

- Useful in critically ill hemodynamically unstable patients
- Earlier initiation of CRRT improves survival

Modem V et al. Crit Care Med. 2014 Apr;42(4):943-53

- Rapid solute clearance : like IEM/Hyperammonemia

Modalities:

- Continuous venovenous hemofiltration (CVVH) : Convection
- Continuous venovenous hemo-dialysis (CVVHD) : Diffusion
- Continuous venovenous hemodiafiltration (CVVHDF): Both
- SCUF

- CYTOSORB: Cytokine storm/MISC/OXIRIS for Sepsis
- Can be combined with ECMO

See E, et al.emin Dial. 2021 Nov;34(6):576-585.
John JC et al.Kidney Res Clin Pract. 2019 Dec 31;38(4):455-461.

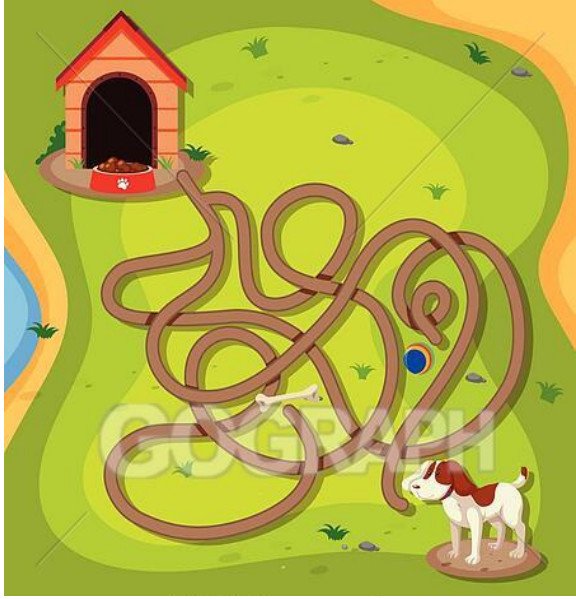
CKRT Prescription: ESPNIC Guidelines 2023

- Modality
- Access:patient size/Site
- Appropriate Filter:patient size/clinical condition
- Priming: Albumin/PRBC/Saline
- Anticoagulation : Heparin/Citrate
- Dose: 2L/1.73m^2
- UF:0-2ml/kg/h Effluent: 30-35ml/kg/hr

Filter membrane	Surface area (m^2)	Blood volume in set	Priming volume	Application
HF 20 (PAES)	0.42 m^2	60 ml	500 ml	>8 kg
M60 (AN 69)	0.6 m^2	97 ml	1000 ml	>11 kg
M100 (AN 69)	0.9 m^2	152 ml	1000 ml	>30 kg
ST60 Set (AN 69)*	0.6 m^2	93 ml	1000 ml	>11 kg
ST100 set (AN 69)*	1,0 m^2	152 ml	1000 ml	>30 kg
HF 1000 (PAES)	1.1 m^2	165 ml	2000 ml	>30 kg

CKRT in child with ALL with sepsis & AKI

Take home messages



- Children with AKI require **timely KRT** before setting in of serious complications
- Different modalities of KRT have distinct advantages but ***best modality*** what **can be done as per availabilty/feasibilty and expertise**
- **Close monitoring** required for children on KRT for procedure related as well complications of underlying condition

MODERATOR COMMENTS

DKA, SAM, DEHYDRATION

DR.S.THANGAVELU

Ulage mayam

- For all: Initial 10 ml/kg over one hr needed? (Earlier only mainten)
- Shock: 20 ml/kg over 30 mins and repeat till shock correction. (Earlier <50 ml/kg in 4-6 hrs)
- Resuscitation fluid: NS or ½ NS RL or plasmalyte, anything is ok (earlier only isotonic NS no colloids)
- Replace the estimated fluid deficit (minus initial fluid bolus
- amount) over 24–48 h.(Over 48 hrs only)
- Deficit % age 7-8%
- Countercheck (1.5 -2.0 times mainten)

Some constant principles among confusion

- No shock: Initial 10 ml/kg over one hr followed by mainten
- Shock: 20 ml/kg over 30 mins and repeat till shock correction. If > 40 mL, use vasoactive agents
- Resuscitation fluid: NS or or plasmalyte
- Replace the estimated fluid deficit (minus initial fluid bolus
- amount) over 48 hrs only)
- Deficit % age 7-8%
- Countercheck (1.5 -2.0 times maintenance)
- E.g: 20 kg child, DKA without shock (7%) , Total fluid 1400+1500+1500/48= 91 ml/hr. (1.5-2.0 mainten is 90-120 ml)
- For all calculation actual BW is used

Changing IVF

Time	Na	Glu	K	IV Fluid
First hour	NS	---	---	NS
Second hour	NS	---	40 mmol/L	NS with K
After 6-12 hrs	½ NS (S.Na> 140)	---	Same	½ NS with K
		D5		
Glucose <300	DNS/D1/2 NS		Titrate based on S.K	½ DNS with K
Rapid fall in Gluc	D5-7.5-10-12.5 NS or ½ NS		KCL / K PO4	10 or 12.5% ½ DNS with K

Insulin infusion only in second hour

IN A SAM CHILD

DIFFICULTIES IN ASSESSMENT: (skin turgor) is prolonged due to loss of subcutaneous fat, oral mucosa may be dry due to atrophy of salivary glands and eyes may be dry due to atrophy of lacrimal glands or vitamin A deficiency. Assessment of dehydration difficult in the presence of edema.

DIFFICULTIES ENCOUNTERED BY SAM KIDS: a) They may not mount a fever and appropriate tachycardia or tachypnea, due to deranged physiological status.

b) They have high total body Na and low total body K, but the measured serum K may be normal and serum sodium low. (due to the suboptimal functioning of sodium potassium ATPase.)

c) Difficulty in handling Na and water, hence (IVF) Is restricted to situations such as shock and dehydration is corrected with (ORS).

d) Treatment edema as these children have high total body water. in the interstitial space.

- Supplement potassium 3-4mmol/kg/day.
- Magnesium is recommended to be given at a dose of 0.3 mL/kg of 50% $MgSO_4$ (1.2 mmol/kg) IM on day 1 followed by 0.1-0.15 mL/kg/day (0.4-0.6 mmol/kg/day) for 2 weeks.

10 kg Moderate dehydration (70 X 10 =700 ml)

- 0-1 hr: Restoration of Intravasc.vol:
  200 ml over one hr (NS/RL)
- 1-24 hrs Deficit correction + Maintenance
  500 + 1000 ml =1500 ml over 24 hrs
  (G5 NS with K 20 mmol/L)

- 0-8 hrs: 750 ml; 9-24 hrs: 750 ml

Apollo Children's HOSPITALS
TOUCHING LITTLE LIVES

Urinary Tract Infection – Recent Guideline

Dr Sudha Ekambaram, DNB(Ped),Fellow Ped Nephro,FISN (Singapore)
Sr Consultant Pediatric Nephrology

Introduction

- UTI is identified by growth of a significant number of a single species in urine along with symptom
- BBD & VUR are important risk factors
- ESKD is caused predominantly by kidney dysplasia rather than by scarring secondary to UTI
- The paradigm shift in our understanding has resulted in significant change in UTI management
- Significant new evidence has emerged in the last decade, hence ISPN has revised UTI guidelines

Pediatric Nephrology
https://doi.org/10.1007/s00467-023-06173-9

GUIDELINES

Evidence-based clinical practice guideline for management of urinary tract infection and primary vesicoureteric reflux

Pankaj Hari[1] · Jitendra Meena[1] · Manish Kumar[2] · Aditi Sinha[1] · Ranjeet W. Thergaonkar[3] · Arpana Iyengar[4] · Priyanka Khandelwal[1] · Sudha Ekambaram[5] · Priya Pais[4] · Jyoti Sharma[6] · Madhuri Kanitkar[7] · Arvind Bagga[1] · on behalf of Indian Society of Pediatric Nephrology

Received: 25 June 2023 / Revised: 27 August 2023 / Accepted: 17 September 2023

Abstract

We present updated, evidence-based clinical practice guidelines from the Indian Society of Pediatric Nephrology (ISPN) for the management of urinary tract infection (UTI) and primary vesicoureteric reflux (VUR) in children. These guidelines conform to international standards; Institute of Medicine and AGREE checklists were used to ensure transparency, rigor, and thoroughness in the guideline development. In view of the robust methodology, these guidelines are applicable globally for the management of UTI and VUR. Seventeen recommendations and 18 clinical practice points have been formulated. Some of the key recommendations and practice points are as follows. Urine culture with $> 10^4$ colony forming units/mL is considered significant for the diagnosis of UTI in an infant if the clinical suspicion is strong. Urine leukocyte esterase and nitrite can be used as an alternative screening test to urine microscopy in a child with suspected UTI. Acute pyelonephritis can be treated with oral antibiotics in a non-toxic infant for 7–10 days. An acute-phase DMSA scan is not recommended in the evaluation of UTI. Micturating cystourethrography (MCU) is indicated in children with recurrent UTI, abnormal kidney ultrasound, and in patients below 2 years of age with non-*E. coli* UTI. Dimercaptosuccinic acid scan (DMSA scan) is indicated only in children with recurrent UTI and high-grade (3–5) VUR. Antibiotic prophylaxis is not indicated in children with a normal urinary tract after UTI. Prophylaxis is recommended to prevent UTI in children with bladder bowel dysfunction (BBD) and those with high-grade VUR. In children with VUR, prophylaxis should be stopped if the child is toilet trained, free of BBD, and has not had a UTI in the last 1 year. Surgical intervention in high-grade VUR can be considered for parental preference over antibiotic prophylaxis or in children developing recurrent breakthrough febrile UTIs on antibiotic prophylaxis.

Keywords Children · Pediatrics · Recommendation · Urinary tract infection · Vesicoureteral reflux

Case 1

- A 2 year old boy was treated for symptomatic culture positive UTI and completed 7 days of antibiotics. He symptomatically improved. No fever or urinary symptoms. His Pediatrician repeated his urine routine and culture by bag sample
- Urine routine:
  - Albumin NIL
  - Pus cell 1-2
  - Nitrite negative
- Urine culture E.Coli 10^5 CFU/ml

Do you think this child suffers from UTI?

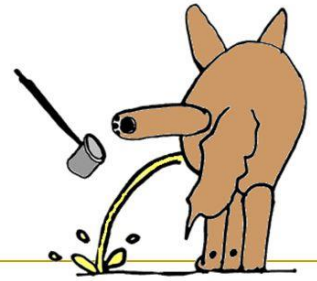
What is the ideal method of collecting urine in children?

- Toilet trained:
  - clean catch
- Not toilet-trained:
  - clean catch if feasible
  - catheter (sick children)
  - suprapubic aspirate (sick children)

Bag sample is not the ideal method for urine culture (30-80% contamination)
Negative bag sample rules out UTI

Voided Urine Sample Collection

- Use a clean container
- Wash prepuce or vulva (when possible)
- Try to collect mid-stream urine



Saadeh SA. Pediatr Nephrol 2011. 26 : 1967–1976

This child does not suffer from UTI
Bag collection
Urine culture need not be repeated after therapy if patient shows clinical response

Case 2

- A 2 year old boy presents with fever for 5 days associated with vomiting & cry during micturition
- Examination: Renal angle tenderness +
- Investigations:
  - TC 27,300 mm^3
  - DC P_{85} L_{13} E_2
  - CRP 120 mg/L
  - Urinalysis: Pus cells plenty, Nitrate & LE positive

Is this UTI?
Will you start on antibiotics?

Screening Test for UTI

	LE	Nitrite	LE or Nitrite	Leucocyturia	Bacteriuria
Sensitivity	79%	45%	84%	76%	86%
Specificity	90%	98%	88%	80%	94%

- A screening test with poor sensitivity may result in some children not receiving antibiotic therapy for UTI

Current Recommendation for Screening test

- Urine microscopy requires test to be performed in freshly voided urine
- Whereas, dipstick is easy to perform in OP setting – Preferred screening modality

Urine dipstick (LE & Nitrite combination) is the first line screening test for UTI (2⊕⊕○○)

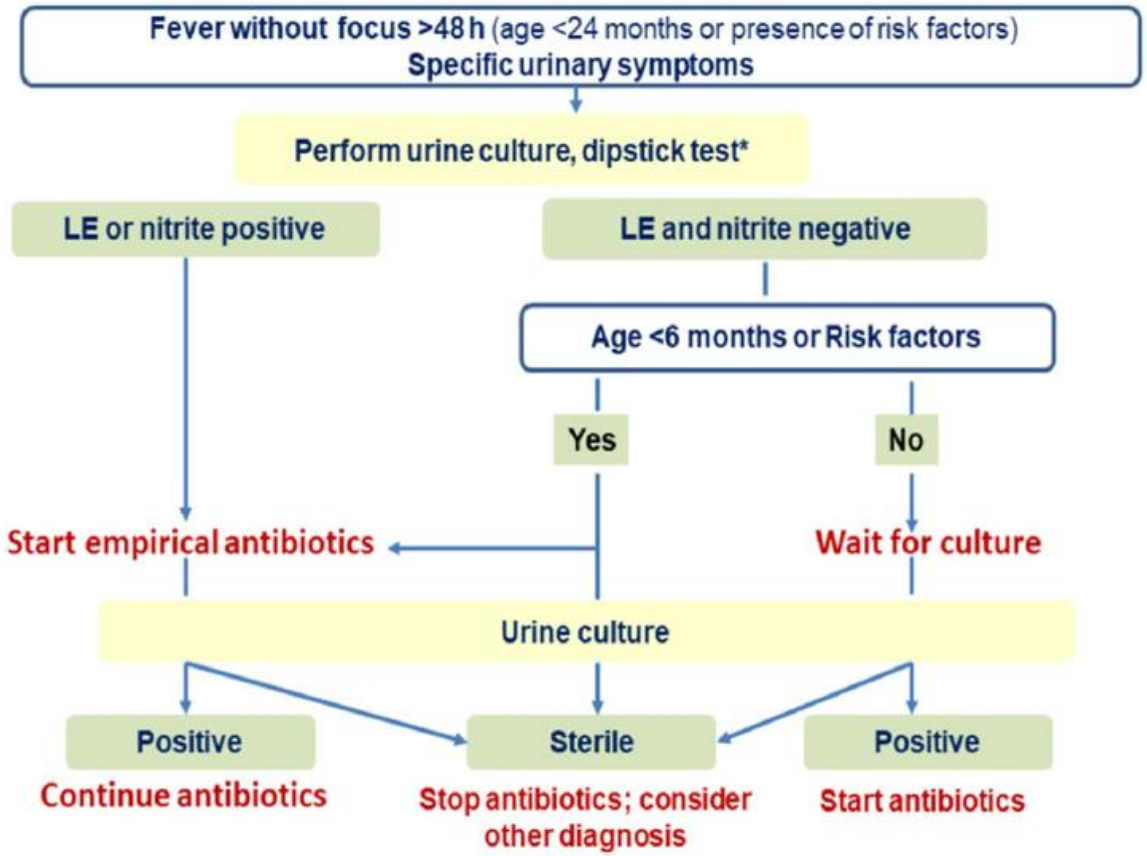
When feasible, urine microscopy (bacteriuria and leukocyturia) in a freshly voided sample can be used as an alternative to dipstick

Next Step…..Will you start antibiotics?

- Early diagnosis & prompt treatment (within 48 hrs) reduce the risk of renal scarring
- Hence antibiotics should be started within 48-72hrs of fever onset
- In suspected UTI introduce antibiotics (3rd generation cephalosporins or amoxicillin-clavulanic acid) after sending urine cultures

Hiraoka M et al. Pediatr Nephrol 18:115–118
Saadeh SA. Pediatr Nephrol 2011. 26:1967–1976

Approach to UTI diagnosis



Case Management

- In view of fever and vomiting, child admitted & started on IV Ceftriaxone
- Urine culture E.coli 10^4 CFU/ml (sensitive to ceftriaxone, cefixime)

Is the colony count significant?
How many days of antibiotics?
Intravenous or Oral?

Significant Colony Count

- Urine culture is considered significant if it demonstrates growth of a single bacterium with the following colony counts:
  - Any growth by SPA
  - $>10^4$ CFU/mL by urethral catheterization
  - $>10^{4\text{-}5}$ CFU/mL by midstream

Recent recommendation for route of antibiotics

- Oral route is preferred (2⊕◯◯◯)
- Intravenous route indications
  - Infants <2mo of age
  - Severely ill child
  - Unable to ingest oral antibiotics
- If IV antibiotic therapy initiated, it may be switched to oral therapy after 3-4 days (1⊕⊕◯◯)

Case Management

- Child received 3 days of IV ceftriaxone
- Vomiting settled and oral intake improved
- Switched to oral cefixime
- Received antibiotics for 10 days

Antibiotics – Total 10 or 14 days for APN?

How many days of antibiotics indicated?

7 – 10 days: Upper UTI (10-14 d)
3 – 7 days: Lower UTI (7-10 d)

Studies have shown that there is no significant difference in treatment failure rates between short course (6-9 days) vs long course (>10 days)

Case 3

- A 3.6 yrs old female child with grade IV VUR on left side, on regular follow up (sulfamethoxazole – trimethoprim prophylaxis) was brought with breakthrough febrile UTI (culture positive)
- She had regular bowels but had skipped prophylaxis for 2 months
- She was admitted and started on IV antibiotics
- What are the indications of antibiotic prophylaxis? When can we stop prophylaxis in VUR?

Indications for uroprophylaxis

- High grade VUR **(3-5 VUR)**
- Children with **BBD** & recurrent UTI irrespective of VUR
- **Infants** with recurrent febrile UTI and low grade VUR
- Not indicated after 1st episode of UTI and normal urinary tract

Risk of UTI is 2.7 times higher in high grade VUR
Studies show - uroprophylaxis is beneficial in preventing rUTI in high grade VUR
Efficacy of uroprophylaxis was not observed in preventing kidney scar
Risk of rUTI was 3 fold higher in children receiving uroprophylaxis

When to stop Prophylaxis in VUR?

Age > 2 years if

✓ Toilet trained
✓ BBD free
✓ UTI free for past 1 year

Clinical practise guideline for management of UTI and primary VUR (ISPN guideline 2022)

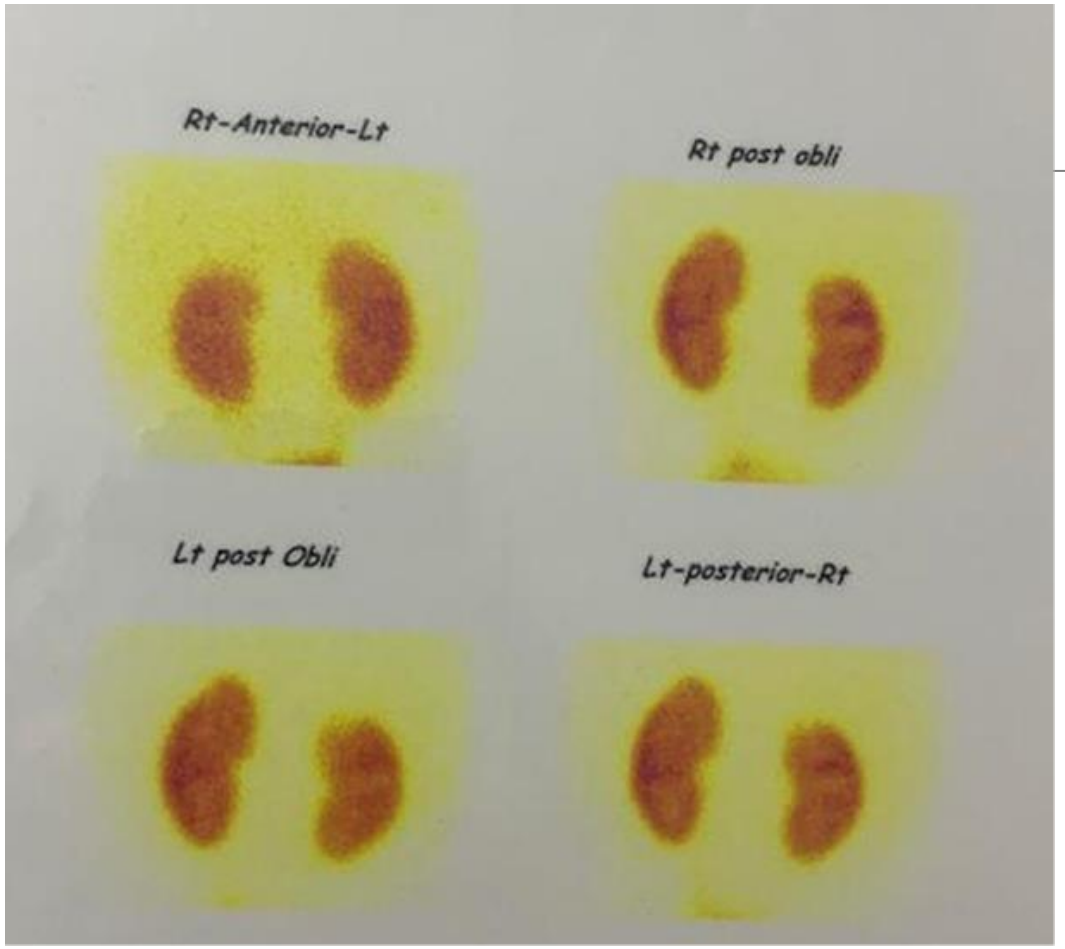
On further probing her bowels were irregular.
Advised dietary modification and laxatives
Advised to restart uroprophylaxis

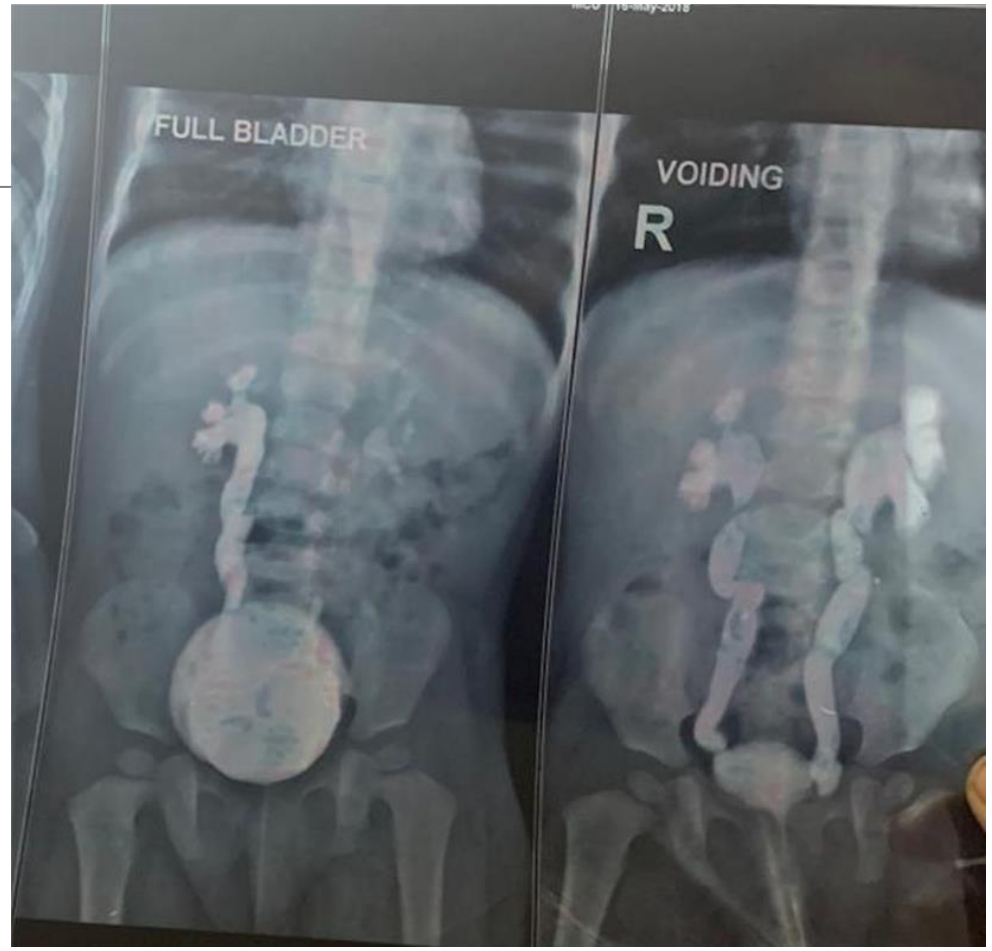
Child on regular follow-up with no breakthrough infections for past 10 mo

Case 4:

- A 2yr old female child presented with high grade fever and was diagnosed to have UTI
- She had Right antenatal hydronephrosis which was not followed
- USG KUB: Suggestive of Right APN
- UTI treated and started on uroprophylaxis with co-trimoxazole
- Had recurrent breakthrough UTI on uroprophylaxis
- No H/O constipation

INVESTIGATIONS



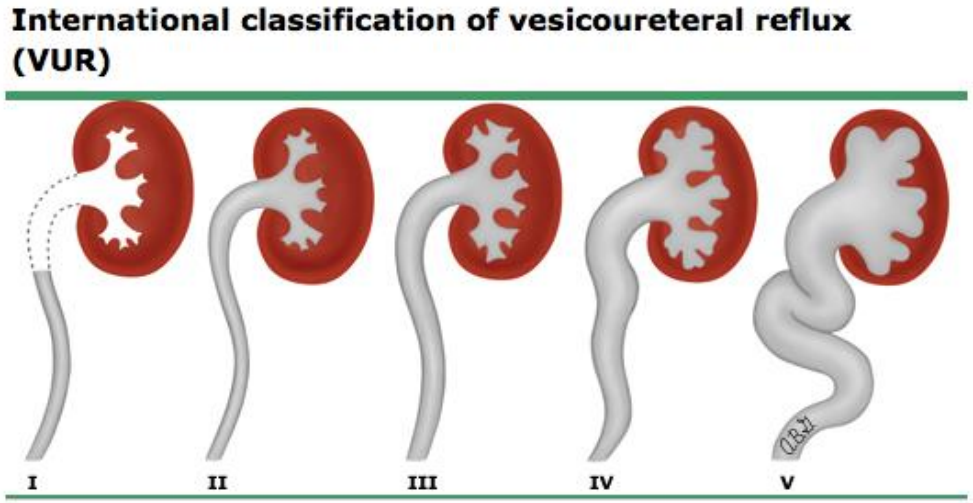


DMSA: LK-55%, RK-45%, photopenic areas in upper pole of RK , MCU: B/L grade IV VUR

Is Surgery indicated in this child?

Indications for surgery

- High-grade VUR with recurrent febrile UTI despite antibiotic prophylaxis
- Surgical intervention may be an alternative for parental hesitancy to use antibiotics in case of high grade VUR



Summary of the AUA guideline on management of primary vesicoureteral reflux in children. J Urol 184:1134–1144

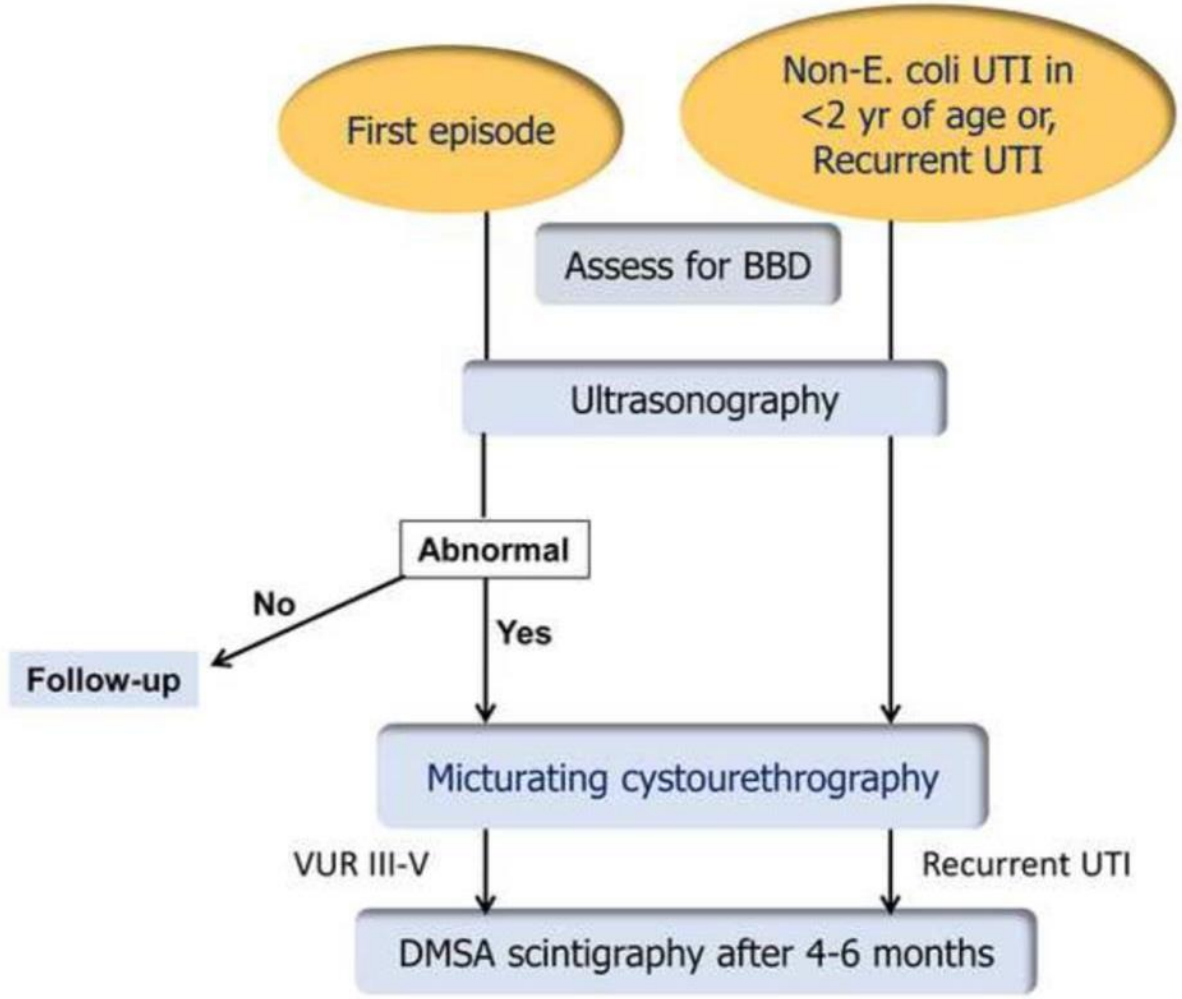
TREATMENT

B/L Cohen's Reimplantation done

Indication

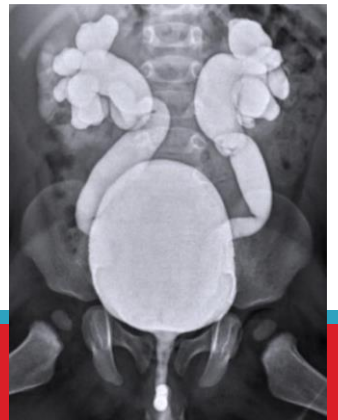
High grade VUR with Recurrent UTI on Uroprophylaxis

UTI Imaging – What does the new guideline say?



Why the change?

- Rationale behind aggressive imaging in UTI has been questioned for several reasons
  - Modalities in VUR diagnosis involves painful catheterisation/ radiation exposure
  - VUR is present in 1/3rd of children with UTI
  - No intervention has proven beneficial in preventing ESKD associated with VUR
  - But, uroprophylaxis /surgical correction helps in preventing recurrences
- Hence considering the balance, recent guideline emphasises less aggressive imaging following UTI



Case 5

- A 3 year old girl presents with fever for 3 days
- Examination: Renal angle tenderness +
- Investigations:
  - TC 27,300 mm^3
  - DC P_{85} L_{13} E_2
  - CRP 120 mg/L
  - Urinalysis: Pus cells plenty, Nitrate & LE positive
  - Urine C/S – E Coli 10^5 CFU/mL

What is the next investigation of choice? Timing?

Imaging

- USG-KUB should be performed after first episode of UTI in all children
- USG can be performed any time after the episode of UTI
- If no clinical improvement within first 48 hr of antibiotic therapy, do USG to diagnose pyonephrosis, renal abscess or obstruction

USG of Case 5 (3yrs)

- RK – 8.6cm, increased echogenicity, mild dilatation of PCS and ureter with pelvic wall thickening
- LK – 7.5cm, normal CMD, PCS & ureter not dilated
- UB normal

Do you think the next level of imaging is necessary? Indication & Timing?

Next Investigation

MCU is the next imaging modality to be considered

Indications:

- UTI caused by non-Ecoli in children <2 years
- Abnormal USG (small kidney, abnormal echoes, PCS/ureteral dilatation, pelvic wall thickening, F/O PUV)
- History of recurrent UTI

Timings:

Anytime after completion of therapy with antibiotics

MCU

What are the Pros and Cons of MCU?

PROS:

Provides anatomical details of the genitourinary tract

Allows grading of VUR

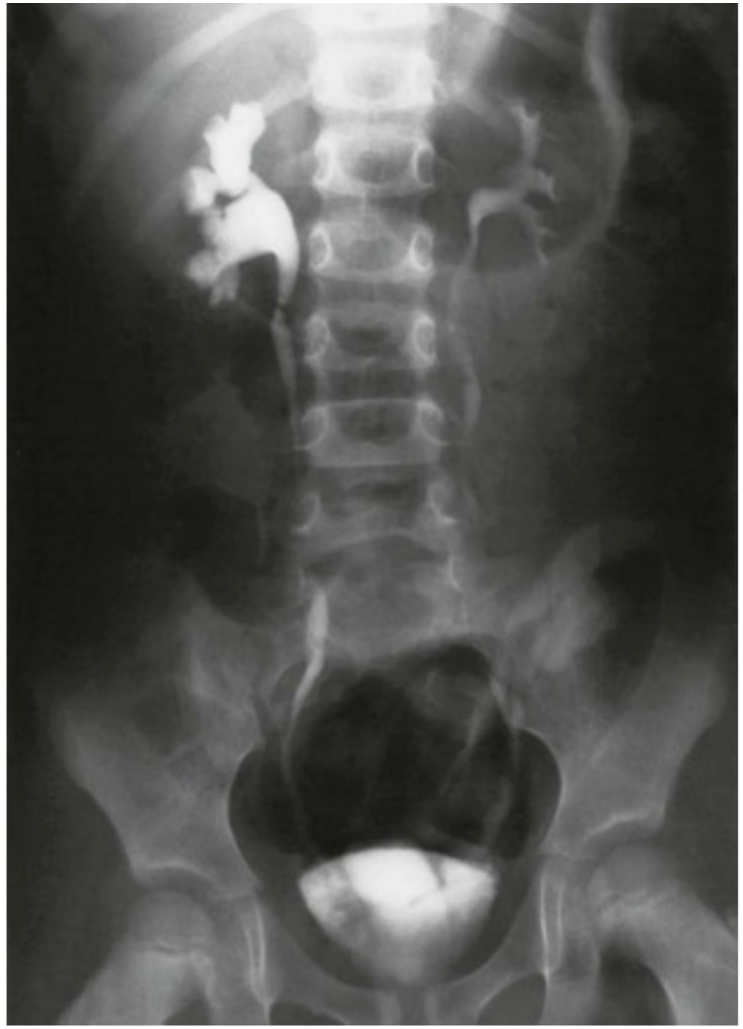
Allows to decide whether therapy is necessary (Medical/surgical)

CONS:

Discomfort of urethral catheterization

Exposure to ionizing radiation

Rare UTI



MCU of Case 1 – Left gr 1 & Right gr 3

What is the next investigation of choice?
Indications & Timing?
What are the Pros and Cons?

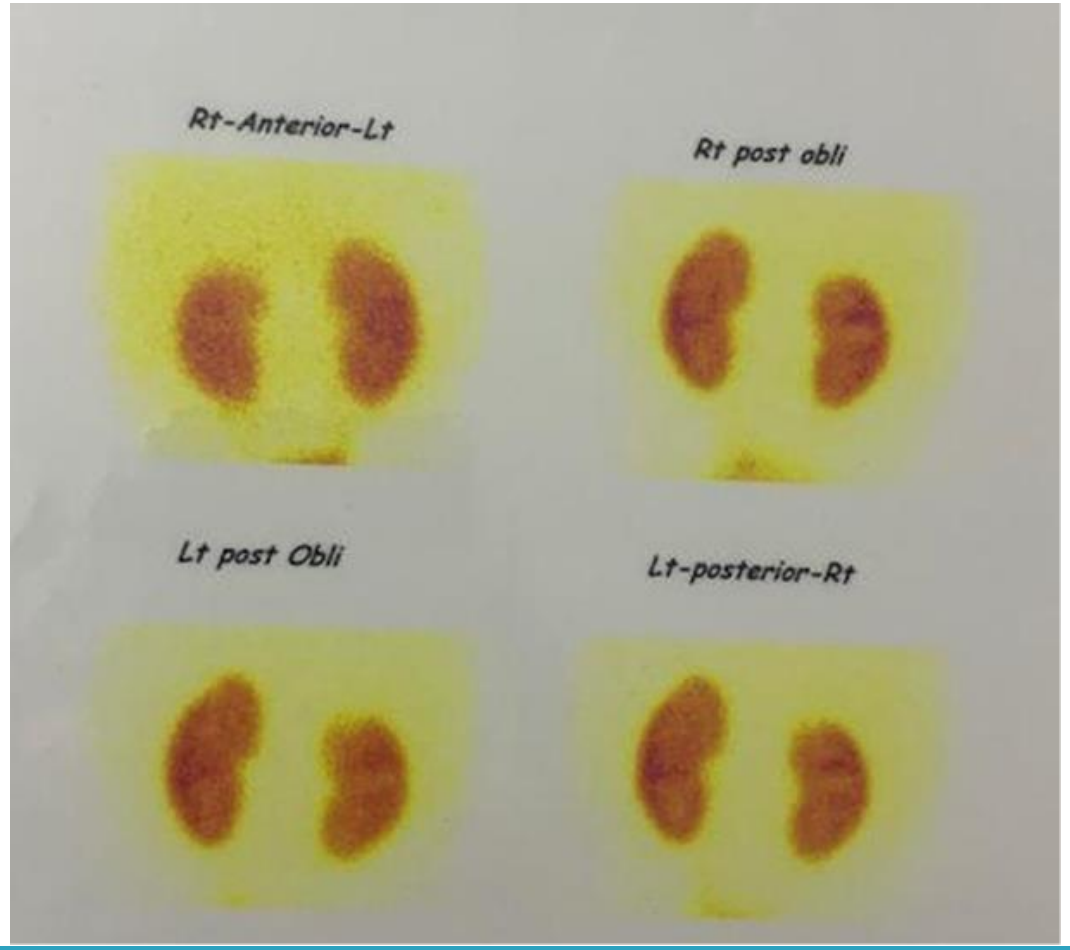
DMSA scan

- Late phase DMSA to assess kidney scarring in children at higher risk
- Indications: High grade VUR, recurrent UTI
- Timing: 4-6 months after the episode of UTI
- Radiation exposure is 0.02mSv as compared to CT scan with 7.7mSV

Acute Vs Late phase DMSA scan

- Acute phase DMSA scan is not useful in differentiating between acute uptake defect and permanent kidney scars

DMSA



RK - 42% , scars in upper pole

LK - 58% , normal

Follow up.....

- This child was initiated on uroprophylaxis for 1 year and stopped
- Counselled for regular bowel and bladder habits
- There was no breakthrough UTI

What are the Indications & Timing of repeat USG during follow up?

Follow up USG - Renal growth

Children with

- High-grade VUR
- Reflux nephropathy

Periodic follow-up to detect long-term complications

Younger children with high grade VUR - **annually**

Less frequently in asymptomatic/ older children

Parents want to know if a repeat DMSA is required to look for the resolution of scars

What are the indications of repeat DMSA? Is it indicated in this child?

Indications for Repeat DMSA

Recurrent febrile UTI in children with VUR (4-6 mo)

To assess:

* Worsening of kidney damage
* Appearance of new scar

In this child repeat DMSA is not indicated as there is no breakthrough UTI

Parents are convinced

They would like to know if we should repeat MCU to look for resolution of reflux

Indications & Timing of repeat MCU?

Indications of & Timing of repeat MCU?

- Repeat MCU for documenting resolution of reflux is not required
- It may be done 4–8 yrs following the initial diagnosis in high grade VUR if physician thinks its necessary
- For patients with reflux nephropathy & progressive kidney failure, a repeat cystography may be required before kidney transplantation

Follow up….

- Child is 9 years old and has done well with no breakthrough UTI
- Parents want to know if VUR has resolved but worried as they feel MCU would be painful

Can you advice an alternative investigation for MCU?

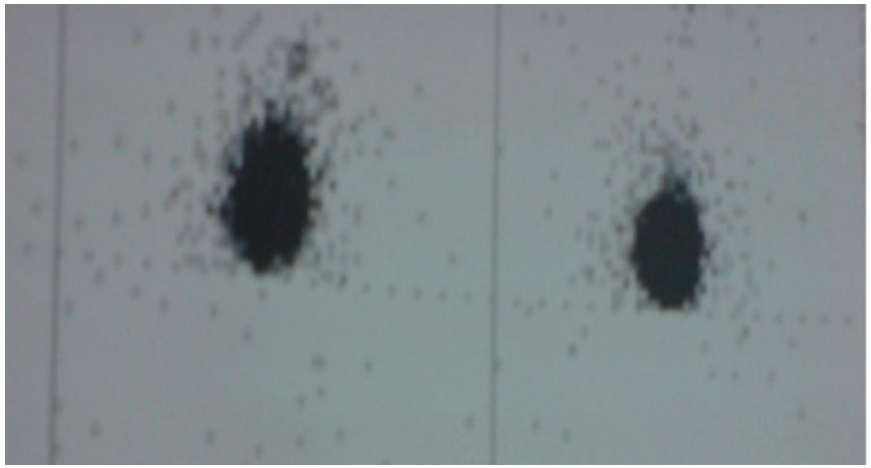
Pros and Cons

DRCG (Direct Radionuclide Cystography)

- Both MCU and DRCG can be used for documenting resolution of reflux
- PROS: More sensitive, less radiation exposure, avoids catheterisation
- CONS: Grading and anatomical details are inadequate

Radionuclide exposure:

- DRCG: 0.048 mSV
- MCU: 0.24 mSv



Repeat DRCG showed resolution of reflux

Take Home Message

- Clean catch technique should be followed when feasible
- Urine dipstick (LE & Nitrite) is the first line screening test for UTI
- Initiate empiric antibiotic after urine culture within 48 hrs of fever
- Oral route is preferred for UTI management when possible
- A duration of 7 – 10 days of antibiotics is ideal for febrile UTI
- Children with VUR & BBD have the highest risk for recurrent UTI which needs appropriate management
- Ultrasound should be done after 1st episode of UTI

Take Home Message

- All 3 imaging modalities to be done in recurrent UTI
- Antibiotic prophylaxis is indicated in high grade VUR and children with BBD
- Surgery is considered for children who develop rUTI despite antibiotic prophylaxis & appropriate BBD management
- Reflux Nephropathy requires appropriate follow up
- Guidelines are to guide management but treatment has to be individualised
- It is primary care Pediatrician's share to appropriately diagnose & treat UTI

Question 1

- A 2mo old boy has fever without focus. Urinalysis and urine cultures are sent. Urine nitrates and LE are negative. What will be the best option in treating this child

a. Wait for urine culture reports and then decide on abx based on sensitivity
b. Start antibiotics and wait for urine culture reports
c. Do an Ultrasound KUB and decide on management
d. Leave it to parents choice on starting antibiotics till you get urine C/S report

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Question 2

- An 8mo old girl has febrile UTI and treated with 7 days of antibiotics. On examination she had vulval synechiae for which she was treated. Her USG done showed normal kidneys and bladder with no dilatation of ureter. What is the next step in evaluation?

a. Immediate DMSA to check for inflammation and decide on MCU
b. Late DMSA to check for scar and decide on MCU
c. Do MCU as child is < 1year
d. Keep the child under follow up without any further investigation

Question 2

- An 8mo old girl has febrile UTI and treated with 7 days of antibiotics. On examination she had vulval synechiae for which she was treated. Her USG done showed normal kidneys and bladder with no dilatation of ureter. What is the next step in evaluation?

a. Immediate DMSA to check for inflammation and decide on MCU
b. Late DMSA to check for scar and decide on MCU
c. Do MCU as child is < 1year
d. Keep the child under follow up without any further investigation

Question 3

- According to recent ISPN guidelines when is uroprophylaxis not indicated

a. High grade VUR (3-5 VUR)
b. Children with BBD & recurrent UTI
c. Infants with recurrent febrile UTI and low grade VUR
d. In all children <1 year after 1st episode of UTI

Question 3

- According to recent ISPN guidelines when is uroprophylaxis not indicated

a. High grade VUR (3-5 VUR)
b. Children with BBD & recurrent UTI
c. Infants with recurrent febrile UTI and low grade VUR
d. In all children <1 year after 1st episode of UTI

Question 4

- Which statement is false regarding UTI management according to current ISPN guideline

a. Antibiotics should be given for 7-10 days for upper UTI

b. Oral antibiotics is the preferred route for UTI management

c. Complete 5-7 day course of IV antibiotics if initiated & then switch to oral

d. IV route indicated if child is <2mo of age

Question 4

- Which statement is false regarding UTI management according to current ISPN guideline

a. Antibiotics should be given for 7-10 days for upper UTI

b. Oral antibiotics is the preferred route for UTI management

c. Complete 5-7 day course of IV antibiotics if initiated & then switch to oral

d. IV route indicated if child is <2mo of age

Thankyou

ELECTROLYTE

-WORKBOOK-

Organized by

Department of Pediatrics and Pediatric Nephrology,
Apollo Children's Hospitals, Chennai

Organizing

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NephKids 2024

www.nephkids.in

PROGRAMME

DAY 1

Saturday, September 14th, 2024

FLUID AND ELECTROLYTE WORKSHOP

Conveners: Dr. Thangavelu S, Dr. Sharada RC

TOPIC	MODERATOR	SPEAKERS	09:30- 10:30	10:30- 11:30	11:30-12:30
Hyponatremia	Dr Rajkumar PS	Dr Srinivasan G Dr Muthiah P Dr Swathi Kiran Shiri	Group A	Group B	Group C
Fluid in special situations	Dr Thangavelu S	Dr Sudarsan K Dr Murali T Dr Chidhambharam L	Group B	Group C	Group A
Metabolic Acidosis	Dr Poovazhagi V	Dr Sivaraman D Dr Dhakshayani R V Dr Naresh Kumar S	Group C	Group A	Group B
LUNCH	**12:30 hrs – 13:30 hrs**				
Hypernatremia	Dr Anitha VP	Dr Shyamala J Dr Priyavarthini V Dr Sharada R C	Group A	Group B	Group C
Hypocalcemia/ Hypomagnesemia	Dr Shanthi S	Dr Mani Kumar S Dr Anita Tarigopula Dr Mithuna Shree J	Group B	Group C	Group A
Hypo/ Hyperkalemia	Dr Gowrishankar NC	Dr Prem Kumar L K Dr Ekambaranath TS Dr Venkateswari R	Group C	Group A	Group B

Dr. B.R. Nammalwar

Organising Chairperson, NEPHKIDS

INTRODUCTION

Homeotasis is the fundamental basis for survival for all living creatures. Body water, electrolytes, acid bases and divalent ions have explicit role in maintaining the homeostasis. A solid foundation in understanding the composition of body fluid, fluid requirements, and regulations; assessing and managing dehydration, understanding the physiologic functions of electrolytes, and managing electrolyte derangements is critical. Study of water, electrolytes, acid bases and divalent ions is an important and difficult area of in medicine. Students, Residents (why not teachers) study it intensely, yet too often come away without clarity and confidence they want and need. Why is this? Body water, electrolytes, acid-bases and divalent ions cannot be seen, neither felt, nor palpated or auscultated. It is a mist. The nearer you go, the faster it disappears. In physiology it is taught as a pure science. In clinical medicine it is presented as a group of symptoms with solutions as per guidelines. No life in it. There is diversity in the methodology of teaching of this subject. What is needed is to teach this subject as an applied science. Pediatricians, Pediatric Nephrologists and Pediatric Intensivists with unbridled and non-exhausting enthusiasm for teaching with a team of similar minded colleagues from other teaching Institutions have been organizing "Workshop on fluids, electrolytes, acid-base and divalent ions" for last seven years. Partly it has been fulfilling the lacunae. With this booklet it is much more. To the readers, treasure it as a 'Rose' from your beloved. Express your feeling. If you are thankful, contribute your thoughts and knowledge. Knowledge is an ocean and no one person can fathom it. Someday, I know it will be a Monograph on Body water, electrolytes, acid bases and divalent ions. A dream will come true.

Faculty- Workshop

Dr Rajkumar PS, MD, DNB, MRCPCH Fellowship in Pediatric Intensive Care (UK)
Professor of Pediatrics, Sri Ramachandra Institute of Higher Education & Research, Chennai

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Registrar, Apollo Children's Hospital, Chennai

Dr Gowrishankar NC, MD DCH DNB FIAP
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Assistant Professor, PICU, Stanley Medical College, Chennai

Dr Venkateswari R, MBBS, DCH, DNB
Senior Consultant Pediatrician, Kanchi Kamakoti Childs Trust Hospital, Chennai

HYPONATREMIA

Contributors: Dr. Rajkumar PS, Dr Srinivasan G, Dr Muthiah P, Dr Swathi Kiran Shiri

Physiology of Sodium balance:

- Sodium is the dominant cation of ECF. Maintains ECF osmolarity and thereby cell volume of billion cells in the body, including that of brain.
- Sodium intake: Infants receive sodium from breast milk (7 mEq/L) and formula (7-13 mEq/L). An average Indian consumes 10.98 grams of salt per day - 119 % > recommended limit of 5 grams/day by WHO (1 g NaCl = 394 mg, 17 mEq or 17 mmol of Na and Cl).

- Excretion: Occurs through urine, stools and skin. ▪ Control: Body sodium content is most intimately coupled with extracellular water content. Water and Na are like olden days couple. Water balance, not sodium balance, usually determines its concentration. When the sodium concentration increases, the resultant higher plasma osmolality causes increased thirst and increased secretion of ADH, which leads to renal conservation of water. During hyponatremia, the decrease in plasma osmolality stops ADH secretion, and consequent renal water excretion leads to an increase in the sodium concentration. Renal sodium regulation plays a major role in sodium homeostasis.

- **What is the priority in a conflicting situation?** Correction of volume depletion takes priority over osmolarity. Volume depletion stimulates ADH secretion even when there is hyponatremia. E.g. Hyponatremic dehydration in acute diarrhea. Once dehydration is corrected with NS, ADH is switched off, water retention ceases and serum sodium levels raises.

Algorithmic approach to hyponatremia

1. Does the child have neurological symptoms?

2. True or pseudo hyponatremia?

3. Is it acute or chronic?

4. Volume status?

5. Urine sodium levels

Explanatory notes for algorithm

Step 1 – Does the child have neurological symptoms?

The clinical presentation of hyponatremia is usually variable, nonspecific and when severe presents with symptoms of cerebral edema and those of underlying disease as noted below:

<130mEq - Apathy, anorexia, nausea, vomiting

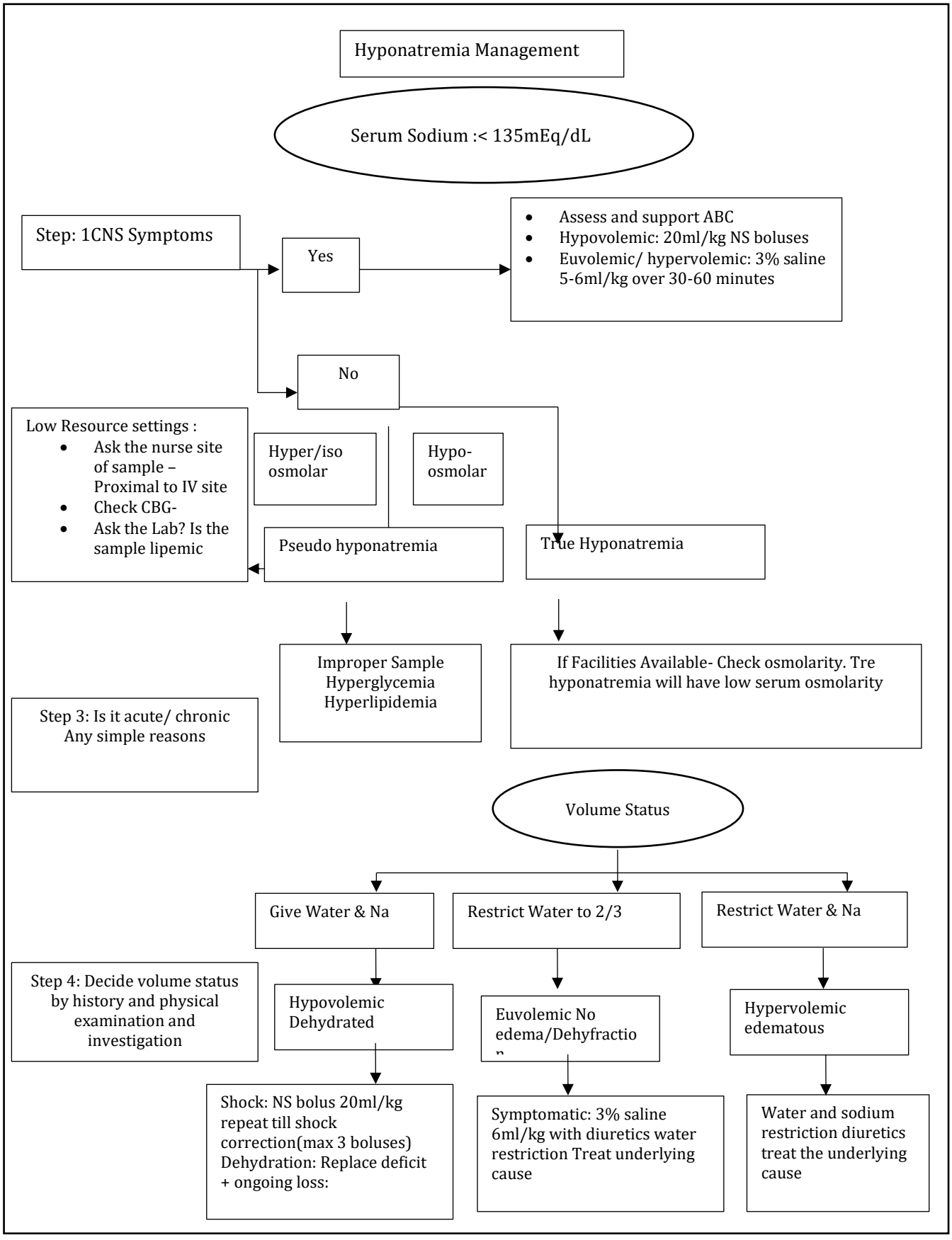
S. Sodium <120 mEq/dl - Muscular twitching, headache, seizures, coma.

Symptoms depend upon the degree and chronicity of hyponatremia. Patients with mild-to-moderate hyponatremia (greater than 120 mEq/L) or gradual decrease in sodium (greater than 48 hours) have minimal symptoms. Patients with severe hyponatremia (less than 120 mEq/L) or rapid decrease in sodium levels have multiple varied symptoms. Symptoms can range from anorexia, nausea and vomiting, fatigue, headache, and muscle cramps to altered mental status, agitation, seizures, and even coma.

Patients with neurological symptoms and signs need to be treated promptly to prevent permanent neurological damage.[18]

Symptomatic hyponatremia

When the child has neurological symptoms, regardless of underlying cause or volume status, or duration of the illness the deficit must be corrected to a safer level within 1-2 hours.


Hyponatremia Management
Serum Sodium :< 135mEq/dL
Step: 1CNS Symptoms
Yes
Assess and support ABC
Hypovolemic: 20ml/kg NS boluses
Euvolemic/ hypervolemic: 3% saline 5-6ml/kg over 30-60 minutes
No
Low Resource settings :
Ask the nurse site of sample – Proximal to IV site
Check CBG-
Ask the Lab? Is the sample lipemic
Hyper/iso osmolar
Hypo-osmolar
Pseudo hyponatremia
True Hyponatremia
Improper Sample
Hyperglycemia
Hyperlipidemia
If Facilities Available- Check osmolarity. Tre hyponatremia will have low serum osmolarity
Step 3: Is it acute/ chronic
Any simple reasons
Volume Status
Give Water & Na
Restrict Water to 2/3
Restrict Water & Na
Step 4: Decide volume status by history and physical examination and investigation
Hypovolemic
Dehydrated
Euvolemic No edema/Dehyfractio
Hypervolemic edematous
Shock: NS bolus 20ml/kg repeat till shock correction(max 3 boluses)
Dehydration: Replace deficit + ongoing loss:
Symptomatic: 3% saline 6ml/kg with diuretics water restriction Treat underlying cause
Water and sodium restriction diuretics treat the underlying cause

Safer levels mean 5 mEq above the current measured level. Eg. If measured Serum Sodium is 115mEq/dL, increasing it to 120mEq/dL is advised and definitely not raised to normal range immediately.

Clinical situation 1: In the presence of hypovolemic hyponatremia (acute diarrheal dehydration) and seizures -NS boluses in 20ml/kg aliquots is given, aiming at simultaneous volume and sodium correction. In the presence of dehydration/shock, both volume and sodium replacement is required. Once hypovolemia is corrected, ADH secretion is switched off and hyponatremia gets corrected.

Clinical situation 2: In normovolemic and hypervolemic hyponatremia with seizures, correction is done by using 3% saline 5mL/kg over 30 – 60 minutes. An increase of 5mEq/L over 2 hours is enough to tide over the crisis

Eg: 1 year old child, weighing 10 kg, serum Sodium is 110mEq/dL. Child is having seizures. In addition to management of seizures, we should raise the serum Sodium by 5 mEq/L. 60 ml of 3% saline is to be infused over 30-60 min. Close clinical monitoring and frequent (every 2-4 hrs) electrolyte estimation is mandatory. After the initial therapy, replacement is continued as that for an asymptomatic child.

Step 2 -If asymptomatic see whether it is pseudo hyponatremia? Confirm whether hyponatremia is true or false. Usually hyponatremia is associated with hypoosmolality. If facilities are available, check the serum osmolarity. If it is low it is true, if it remains normal or high it is pseudohyponatremia. If serum osmolarity is unavailable, simple history and examination can identify pseudohyponatremia.

Methods to identify pseudohyponatremia

- Improper sample – ask the nurse or resident whether sample was taken proximal to the IV cannula site. Blood obtained from a vein proximal to an infusion of hypotonic saline (1/2 GNS) will have a low sodium.
- Ask the lab persons whether the sample is lipemic. Presence of hyperlipidaemia can be identified as a cause of pseudohyponatremia. Pseudohyponatremia is a laboratory artifact seen in hyperlipidaemia and hyperproteinaemia where the serum osmolarity is normal. Hyperlipidaemia is suspected when serum is lipemic. Hyperproteinaemia is very rare in children.
- Check blood glucose by glucometer, which will identify hyperglycemia as a cause. Each 100mg raise of blood sugar will decrease serum sodium by 1.6 mEq/L Hyponatremia associated with hyperglycemia generally resolves as hyperglycemia is corrected. In hyperglycemia the serum osmolarity is high.

- Ask for the history of mannitol therapy, which also may be a cause for pseudohyponatremia. Step 3: Further evaluation when the child is asymptomatic and it is true hyponatremia If it is true hyponatremia, volume status needs to be evaluated based on history and physical examination

History: The following should be looked for: Diarrhea, vomiting, polyuria, oliguria, edema, breathlessness, altered level of consciousness or convulsions, any surgical procedure done, drugs and IV fluids administered.

Physical Examination: One has to look for signs of dehydration, features of shock, S3 gallop, respiratory distress, ascites, edema, pigmentation, stigmata of liver or renal disease and bony deformity suggestive of rickets. Genital examination is mandatory to look for signs of congenital adrenal hyperplasia.

Investigations needed: Serum electrolytes, glucose, urea, creatinine, chloride, x-ray chest, serum osmolarity, Urine osmolarity and urine sodium are the most useful investigations

Urine Na 20 mEq / L indicates extra renal loss

Urine Na 20 mEq / L indicates renal loss

HYPOVOLEMIC HYPONATREMIA

In hypovolemic hyponatremia, one should elicit history to identify cause of fluid loss. If child has vomiting/diarrhea/significant nasogastric tube aspirate - GI loss If child has polyuria or voiding urine despite dehydration-, consider renal loss. If the history does not point toward GI or renal loss – consider cutaneous loss, ask for excessive sweating.

a) GI LOSS:

If there is dehydration, correction needs replacement of water and sodium. So in a child with symptomatic hyponatremia and dehydration, correct with Normal saline bolus 20 mL/kg every 20-60 mins depending on the hydration status (20ml/kg aliquots will provide 5 mEq/kg).

- How? Eg – 10 kg child will receive 200 ml (20 mL/kg). Each 100 ml contains 15 meq and 200 mL will provide 30 mEq.
- How much sodium is needed to raise the serum level by 1 mEq? 10 x 0.6 x 1 = 6 mEq. Hence when we provide 200ml of NS, it will raise the serum sodium level by 5 mEq/L. For example, serum level increases from 115mEq/L to 120 mEq/L.
- In short, correct the dehydration with NS, hyponatremia will get corrected automatically

b) CUTANEOUS LOSS:

Because of excessive loss of sodium and chloride through the skin, from sweating, hyponatremia can occur and it can be worsened in those who consume plain water without electrolytes. This is more commonly seen in hot climates. In cutaneous loss as in cystic fibrosis and in marathon running, degree of dehydration will be mild and child will be mostly asymptomatic. In cystic fibrosis, metabolic alkalosis and hypokalemia are associated findings. Hence this can be corrected by replacing sodium by oral route either as salt containing oral fluid, dietary preparations such as butter milk, coconut water, vegetable soup, rasam (spicy soup containing salt, used with rice) or electrolyte solution such as ORS. Otherwise, it can be corrected by replacing maintenance fluid as isotonic fluid like normal saline in addition to oral supplements, periodically monitoring serum sodium levels. Drinking plain water should be replaced by electrolyte solution to prevent hyponatremia. Rapid

correction may not be necessary in this situation

c) URINARY LOSS:

Rapidity of correction depends on the severity of dehydration. If the child is hospitalised, child can be managed with normal saline depending on the severity. For example: mild dehydration 30-50 ml/kg, moderate dehydration 50-70ml/kg This deficit is to be combined with administration of maintenance fluid simultaneously and given over 24-48 hrs.

EUVOLEMIC/HYPERVOLEMIC DEHYDRATION

In the presence of symptomatic hyponatremia, hypertonic saline (3% sodium chloride) 5- 6 mL/kg is preferred.

Example: A 10 kg child will require 60 mL 3%saline infusion over 30 – 60 mins (depending on the urgency). This will not cause volume overload. ▪ How much sodium this will provide? 60 mL of 3% saline will provide 30 mEq (1 mL of 3% saline gives 0.5 mEq of sodium) How much sodium is needed to raise the serum level by 1 mEq? Eg. Baby weight 10 kg. 10 x 0.6 x1 = 6 mEq. Hence when we provide 30 mEq, it will raise the serum level by 5 mEq.

Hypovolemic Hyponatremia	Euvolemic Hyponatremia	Hypervolemic Hyponatremia
Dehydration present Causes 1.Extra renal loss – GI -Vomiting, diarrhea - significant nasogastric aspirate 2. Renal Loss -Renal Tubular Acidosis (RTA), osmotic diuresis (Diabetic ketoacidosis), diuretic therapy, adrenal insufficiency If history does not point toward GI or renal loss – consider cutaneous loss ask for excessive sweating/ manifesting in summer. 3. Cerebral salt wasting syndrome Investigation Urine Na >20mEq/L– Renal cause Urine Na < 20 mEq/L- Non Renal ↓Na ↓K ↑ cl – RTA ↓Na ↑K ↓glucose-Adrenal insufficiency	**No Dehydration no edema** Causes 1. Water intoxication (Use of 5% Dextrose in post operative Period). 2.Psychogenic water drinking 3.SIADH Investigation Urine Na > 20 mEq/L – SIADH Cerebral salt wasting Urine Na< 20 mEq/L – water intoxication Psychogenic water drinking	**Edema Present** Causes 1. Renal failure 2. Nephrotic syndrome 3. Congestive heart failure 4. Protein energy malnutrition 5. Cirrhosis liver Investigation Urine Na > 20 mEq/L – Renal failure Urine Na < 20 mEq – all

Most of the time hyponatremia is managed with clinical decisions supported by basic investigations.

Case Scenario 1

A 1-year-old developmentally normal, previously healthy baby boy is admitted with Lobar Pneumonia with fever, cough and tachypnea. CxR confirms Pneumonia. Baby is started on IV Ceftriaxone and IV maintenance fluids. On day 2 of admission, baby has decreased urine output (0.4 ml/kg/hr) for last 24 hours. Clinically perfusion is normal with no signs of dehydration and no h/o of vomiting/ diarrhoea. There is no edema/ hypertension. Urinary bladder is not distended. Rest of the examination is unremarkable apart from respiratory signs of Pneumonia. He has normal sensorium with no neurological deficit.

Lab Results:

Serum studies

Sodium 126 mEq/L BUN 4 mg/dL
Chloride 98 mEq/L Creatinine 0.4 mg/dL
Potassium 3.7 mEq/L Glucose 129 mg/dL
Bicarbonate 25 mEq/L

Urine studies
Specific gravity 1.035

Ultrasound Abdomen (KUB)

Normal

1. What is the likely cause of oliguria and hyponatremia?
2. What test will you do to confirm the diagnosis?
3. How will you manage the child further?

In spite of starting the correct management, baby develops generalised tonic clonic seizures refractory to IV Lorazepam and IV Phenytoin. ABG done shows Sodium of 116.

1. What will be your immediate management?
2. How will you manage the baby further after seizure stops?
3. What will you monitor (clinical and lab)?

What are the clinical features of the dreaded complication that can happen if you correct very fast?

Case scenario 2

3 year old female, weighing 10kg was brought to with complaints of fever for 3 weeks associated with bifrontal headache and GTCS refractory to lorazepam and levetiracetam and fosphenytoin, hence she was intubated and mechanically ventilated. CSF study and MRI was suggestive of Tubercular Meningitis. Antituberculosis treatment (ATT) along with intravenous steroids were started. Ventriculoperitoneal (VP) shunt was placed in view of obstructive hydrocephalus. Her admission serum sodium -132. On day 2 serum sodium -121meq/l). vitals HR-100/min, Spo2-99%, ABP-100/76 mmHg, UO-2.8ml/kg/hr.

Q: How will you approach this low sodium? What is your immediate management?

Case scenario progresses:

Fluid restriction was done to 2/3rd maintenance and 3% saline was continued at 1ml/kg/hr to maintain normal serum sodium levels as a part of neuroprotective care. EEG monitoring revealed no seizures. Serum sodium was monitored 6hrly and Na transiently improved to 125 meq/l, but subsequently by day 4, the serum sodium gradually reduced to 123, 121 and 119 meq/l?

Q: What is the reason for hyponatremia despite 3% saline? What additional test will you do to confirm your diagnosis?

Q: Based on reports, How will you calculate fluid prescription for this child weighing 10kg to correct hyponatremia?

Q: What will you need to monitor?

Case scenario progression: She continued to have persistent hyponatremia with polyuria despite sodium replacement

Q: How will you manage refractory hyponatremia in this specific scenario?

Case progression:

After 10 days of hospitalisation, polyuria improved though serum sodium levels showed fluctuations requiring further fluid and medication adjustment. The child finally improved after 24days of treatment and got discharged.

Case scenario 3

A 5-year-old female child, known case of Steroid dependent nephrotic syndrome, on mycophenolate mofetil, presented with edema. Parents had stopped medication on their own for last 1 month. No e/o infection.

On examination, child irritable and anxious with strangers. Height - 108 cm(25-50 th centile), weight - 27 kg(> 97th centile), dry weight – 23 kg , BP - 114/84mmHg (95th centile), HR - 74 bpm, CFT < 2 sec, pulses well felt, RR - 33/min.

There is generalised anasarca. Respiratory system exam reveals reduced air entry on the right side. There is free fluid in the abdomen. Other systems are normal.

Investigations done on admission:

S.Creatinine	0.4
B urea	23
S. Sodium	28
S. Potassium	4.1
S. Chloride	102
S. Bicarbonate	22
S albumin	2.1
S. cholesterol	343
CBG	85
CBC	Normal

Q1. What is the metabolic abnormality in this child?

Q2. What further investigations will you order?

Q3. What are the steps in the management?

FLUIDS IN SPECIAL SITUATIONS

Contributors: Dr Thangavelu Dr Sudarsan K, Dr Murali T, Dr Chidhambharam L

Essential facts

- Fluid therapy is a dynamic process on constant flux
- Monitoring at the bedside and constant adjustments are necessary especiallyin a sick child
- Resuscitation is based on intravascular fluid status
- Restoration to baseline is based on ECF status and finally total body water

What is different in fluid Mx in SAM?

- Recognizing signs of dehydration
- Calculating volume of fluid to be replaced
- Determining the best electrolyte composition
- Associated comorbidities

STEP 1

Assessment of fluid status

- Change in weight if available is the best
- Clinical assessment
- Input / output charts
- Measurement of ongoing losses (Urine, drains)

If hypotensive → Resuscitation

STEP 2

Calculation of deficit

Determines Volume of replacement

- Expressed as percentage of body weight
- Based on all parameters in step 1
- Can add anticipated losses if deemed necessary

STEP 3

Identify associated electrolyte disturbance
Determines composition of replacement fluid

- Most important is sodium
- Potassium , Magnesium
- Phosphate

STEP 4

Attention to co morbidity / disease pathology
Determines rate of correction of replacement fluid

- Anemia
- Severe acute malnutrition (SAM)
- Cardiac function
- Renal function
- Cerebral edema
- Sepsis / Capillary leak / vasoplegia

STEP 5

Prescription based on all 3 above Volume, composition, rate

STEP 1: Assessment of fluid status

- Weight difference
- Calculate input and output meticulously
- Do not forget ongoing losses, losses through drains, urine
- Thorough clinical examination, frequently re-assess

Remember, in SAM.

- ✓ Edema may mask dehydration
- ✓ Altered skin turgor in v/o SAM
- ✓ Irritability, lethargy per se due to SAM

In a SAM child, Diarrhea + 2 of lethargy/sunken eyes/very slow skin pinch suggests **severe** dehydration

STEP 2: Calculating deficit

- % change in body weight
- Input-Output difference, estimate of dehydration, electrolyte changes
- Ensure all losses are taken into account

- Both over and under estimation of severity common

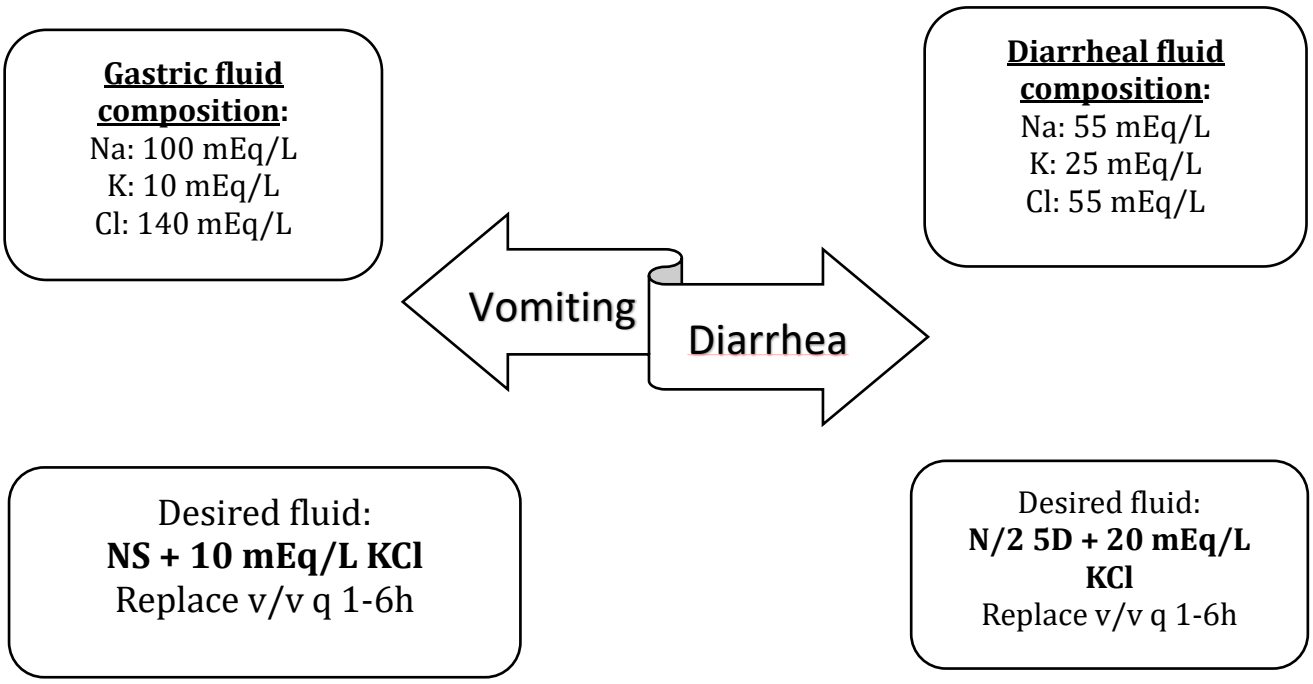
STEP 3: Identify electrolyte disturbances

- Actively look for electrolyte disturbances so that appropriate fluid can be chosen
    - ✓ Hypernatremia
    - ✓ Hypokalemia
    - ✓ Hypomagnesemia
    - ✓ Hypophosphatemia

Composition of commonly available fluids

IVF (/L)	Na (mEq/L)	Cl	K	Ca	Mg	Glucose(G/L)	Osm (mOsm/L)
NS	154	154	-	-	-	-	308
DNS	154	154	-	-	-	50	560
N/2S	77	77	-	-	-	-	155
N/2 5D	77	77	-	-	-	50	405
RL	130	109	4	3	-	-	273
Plasmalyte	140	98	5	0	3	-	294
Isolyte P	23	29	20	-	3	50	340
ORS	75	65	20	-	-	75	245
ReSoMak	45	70	40	-	3	25	300

Choice of replacement fluid



STEP 4: Associated comorbidities

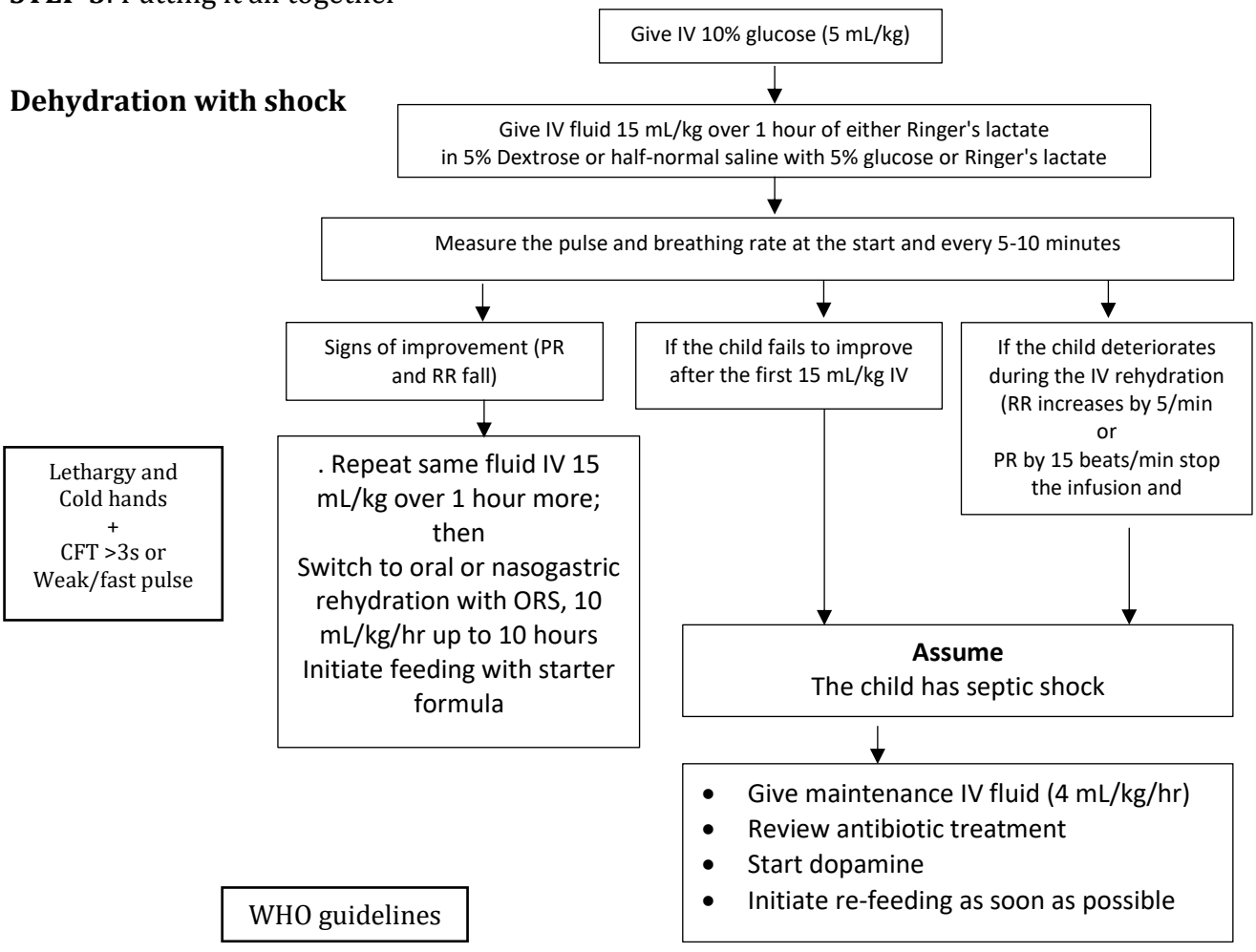
- Help determine the rate of correction
- Caution if associated
- Severe anemia
- CCF
- Renal dysfunction
- Cerebral edema
- Capillary leak

Evaluate for

- ✓ Hypoglycemia
- ✓ Hypothermia
- ✓ Infections

STEP 5: Putting it all together

Dehydration with shock



Dehydration with shock

- Empirical Abx: Ceftriaxone/Cefotaxime for 7-14d
- KCl: 3–4 mEq/kg/d for 14 days
- $MgSO_4$: 0.3 mL/kg (max 2 mL) im once then 0.2-0.3 mL/kg orally for 2 wks
- Food without added salt to avoid Na
- Do not treat edema with diuretics
- Multivitamin, Vit A, Zinc, Folate, Iron
- Feeding advise (F75 → F100)

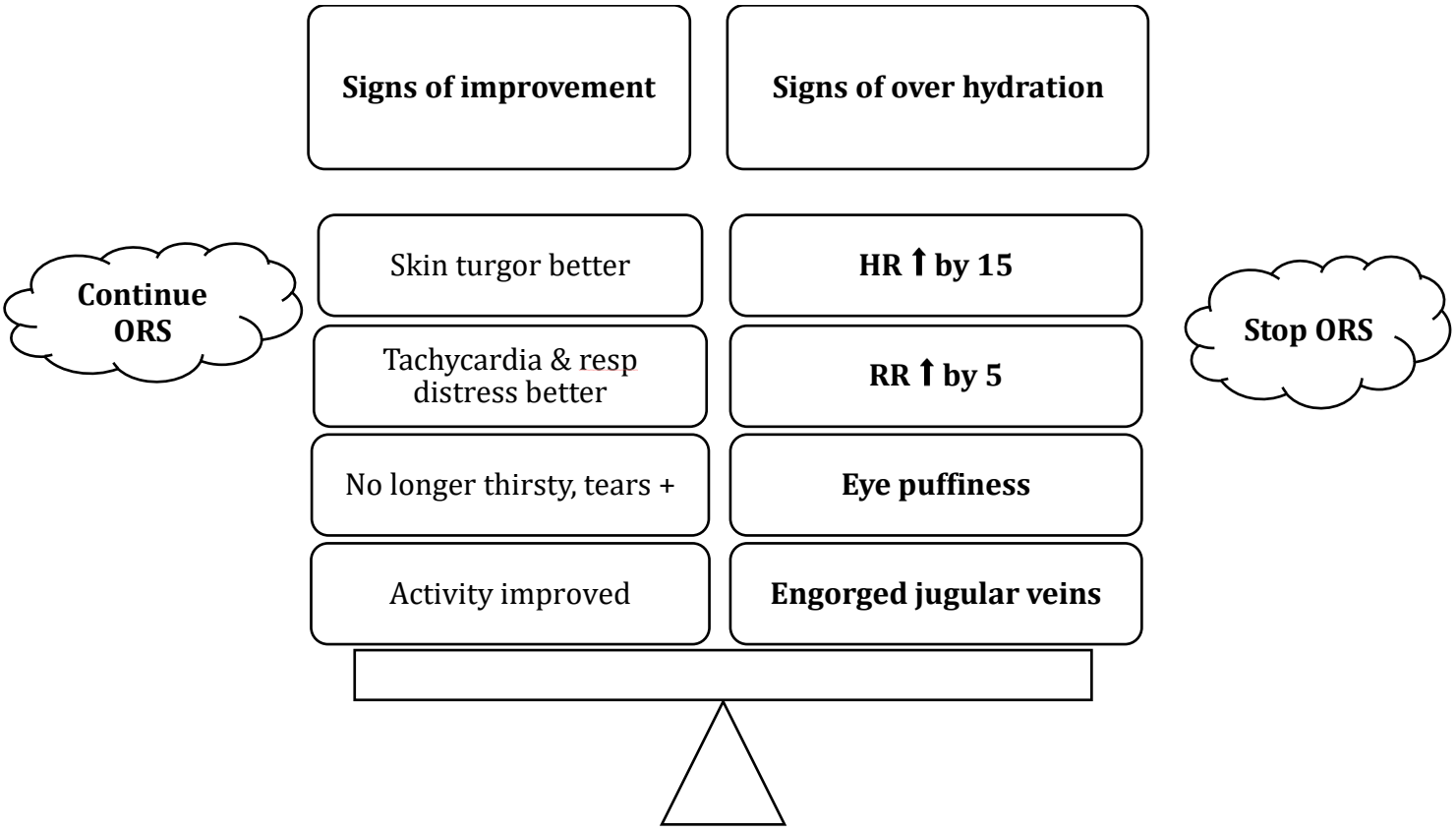
Dehydration without shock

- ORS 5 mL/kg q 30 min for first 2h f/b
- ORS 5-10 mL/kg q2h till rehydrated (max 10 h)
- Add 20 mEq/L (15 mL) KCl to 1L ORS
- Replace ongoing loss (30-50/100 mL per stool in <2/>2y)
- Continue breast feeding, start F-75 diet simultaneously

Home made ReSoMal
1 packet ORS (has 20 mEq K)
2L water
45 ml KCl syp (60 mEq K)

Monitoring

- Every 30 min initially till stabilized then q1-2h



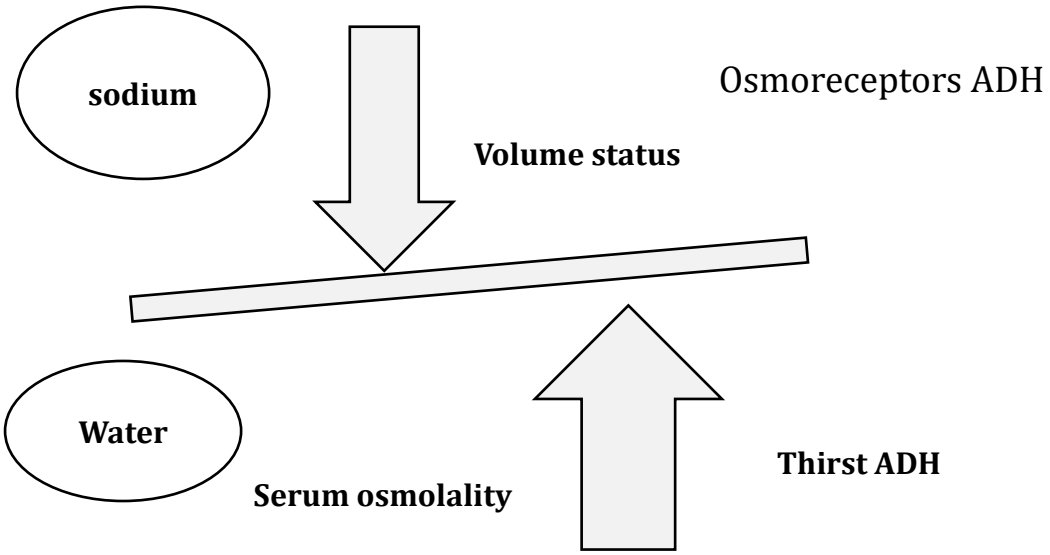
Case scenario

- 15 mo old Ramu is brought to OPD with diarrhea for the last 3 days- watery, 10 episodes/day, not blood stained. Mother says he has been less active. O/E: sunken eyes, cold peripheries, HR 172/min, CFT 4s. He has lustre less hair with protuberant abdomen and visible wasting
- Diagnosis with severity?
- Management?

Tips and tricks

- Presume severe dehydration even if moderate dehydration clinically in a SAM child
- Over and under estimation common; reassess frequently
- Give smaller volumes
- Correct slowly
- Prefer oral route
- Beware of electrolyte changes
- Continuous ongoing monitoring is vital

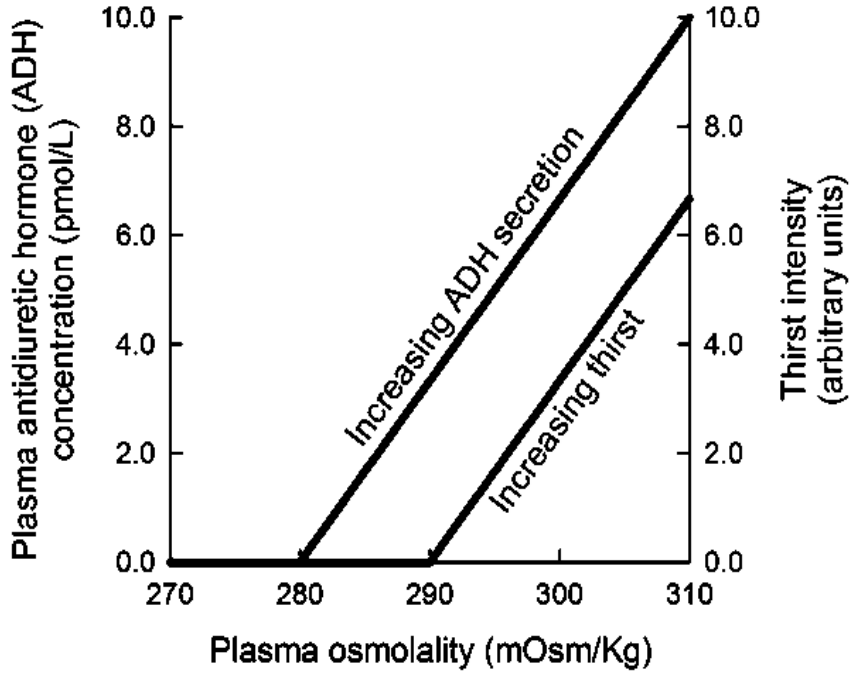
Hydration/ water homeostasis

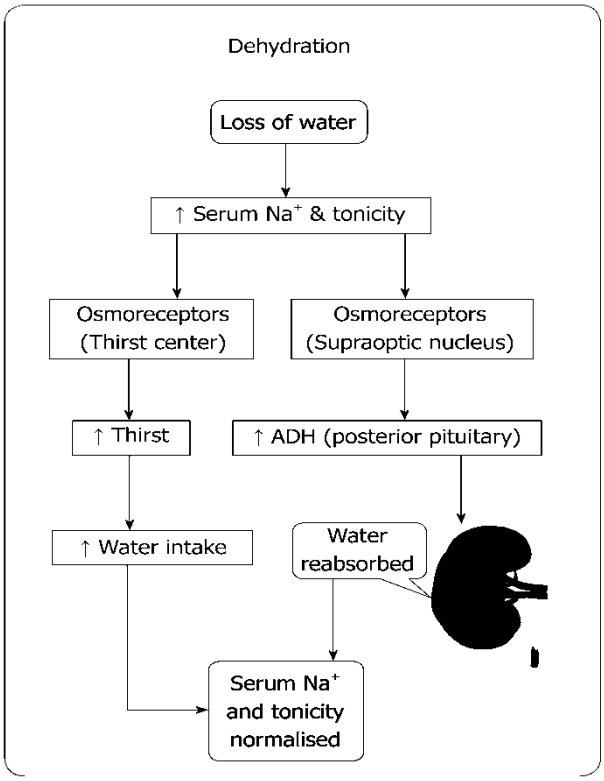


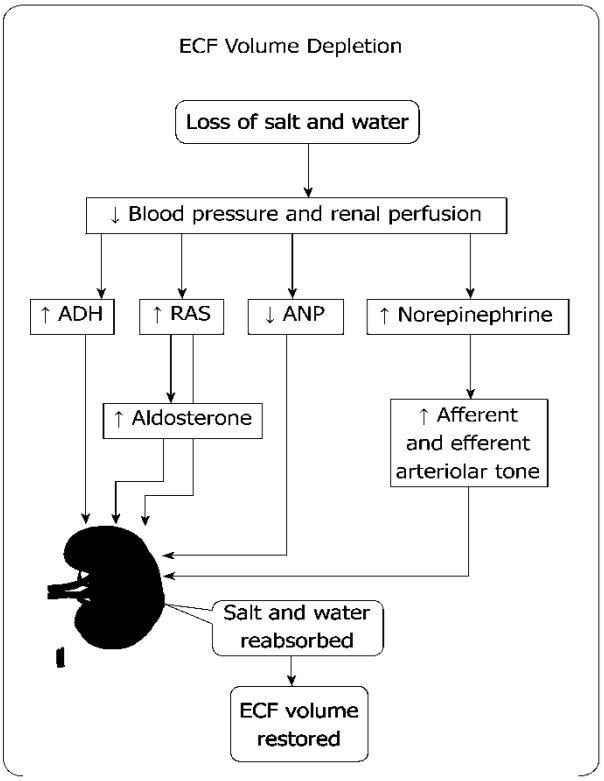
Dehydration

- Loss of normal fluid and electrolyte homeostasis

- Due to rapid and excessive fluid loss gastrointestinal tract (diarrhea and vomiting), skin (fever, sweat, burns), urine(glycosuria, diuretic therapy, obstructive uropathies, interstitial disease, neurogenic and nephrogenic diabetes insipidus).


Plasma antidiuretic hormone (ADH) concentration (pmol/L)
10.0
8.0
6.0
4.0
2.0
0.0
Increasing ADH secretion
Increasing thirst
Thirst intensity (arbitrary units)
270
280
290
300
310
Plasma osmolality (mOsm/Kg)


Dehydration
Loss of water
↑ Serum Na+ & tonicity
Osmoreceptors (Thirst center)
Osmoreceptors (Supraoptic nucleus)
↑ Thirst
↑ ADH (posterior pituitary)
↑ Water intake
Water reabsorbed
Serum Na+ and tonicity normalised


ECF Volume Depletion
Loss of salt and water
↓ Blood pressure and renal perfusion
↑ ADH
↑ RAS
↓ ANP
↑ Norepinephrine
↑ Aldosterone
↑ Afferent and efferent arteriolar tone
Salt and water reabsorbed
ECF volume restored

Isonatremic

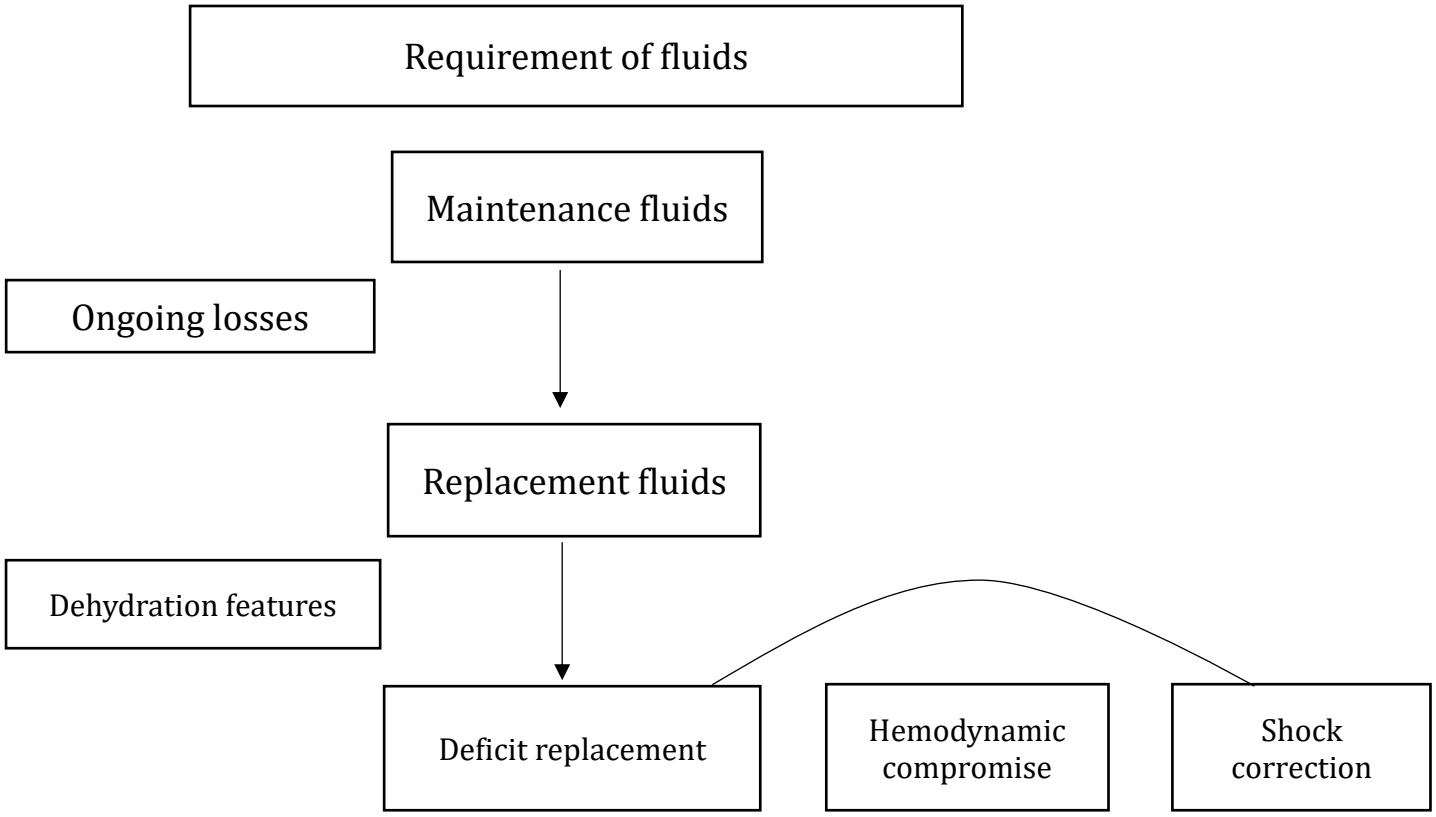
- Replace with isotonic Fluids – Rapid replacement

Hyponatremic

- Replace with isotonic fluids. Slow replacement (24 hrs)
- (Na < 120 – seizures – volume bolus – isotonic enough – hypertonic – Na overshoot)
- Post volume bolus – hypotonic fluids (N/2) to prevent rapid rise in Na

Hypernatremic

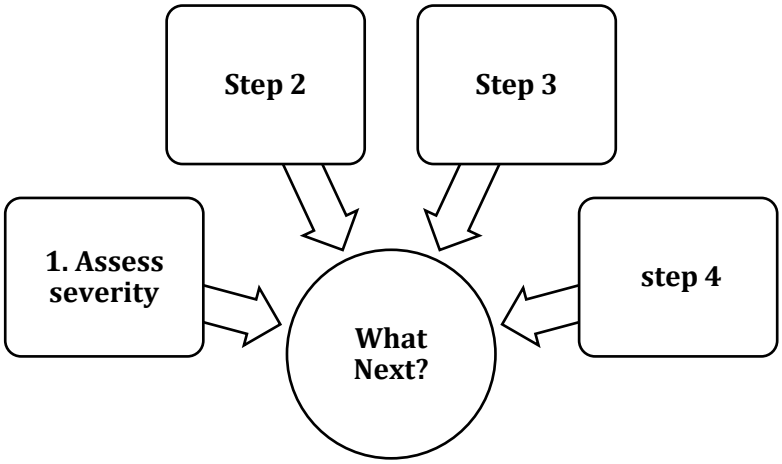
- Replace with isotonic fluids (to prevent rapid fall) . Slow replacement (24 hrs – 48 hours)
- If Na not falling with isotonic fluids as expected can use hypotonic fluids



CASE 1

- 6 years old
- Fever, vomiting 8-10 episodes
- Loose stools watery 5-6 episodes
- Poor oral intake, lethargic, urine output 2-3 times in last 10 hours
- Hr – 130 / min , BP – 100/80 , Radial pulse felt , RR – 20 / min, sats – 96% , afebrile
- CFT – 2 secs

What next?

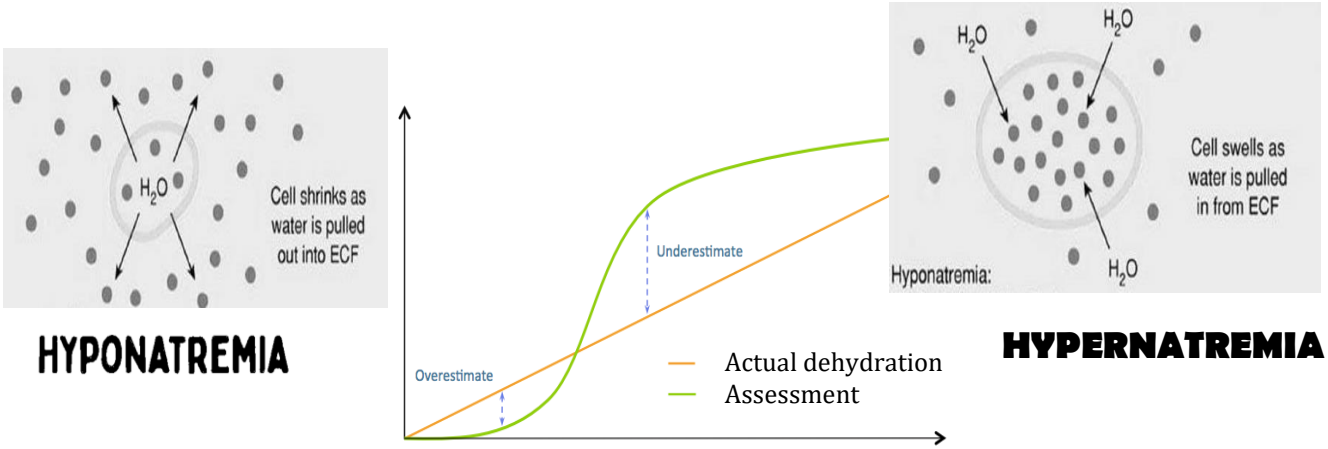


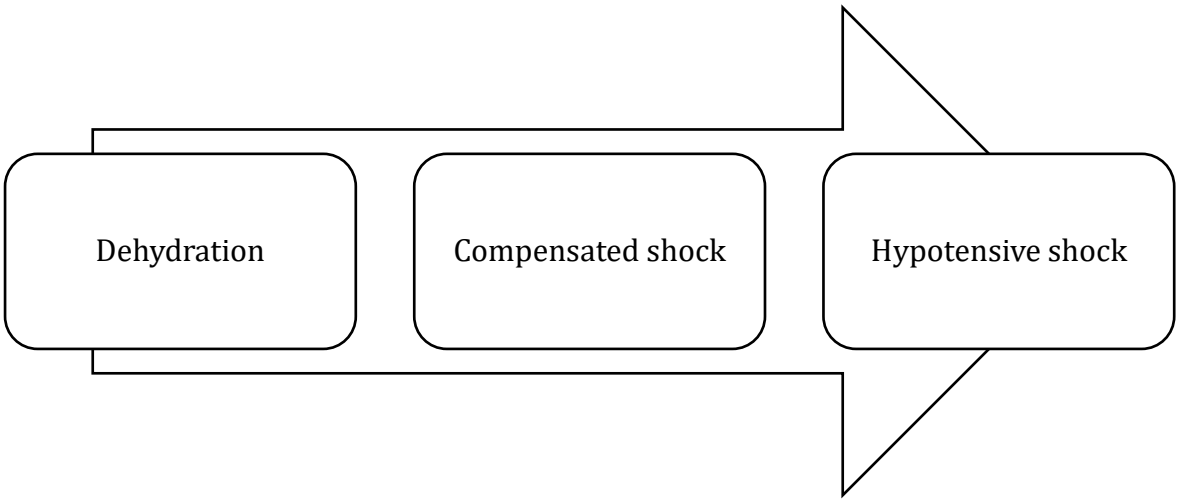
Step 1. Assess severity

Table 1. Degree of Fluid Deficit & Clinical Symptoms Associated with Dehydration

	Mild Dehydration	Moderate Dehydration	Severe Dehydration
Weight Loss Older child Infant	 3% (30 ml/kg) 5% (50 ml/kg)	 6% (60 ml/kg) 10% (100 ml/kg)	 9% (90 ml/kg) 15% (150 ml/kg)
Heart rate	Normal	Mildly increased	Marked tachycardia
Distal pulses	Normal	Slightly diminished	Weak, thready
Capillary refill	Normal	Approx. 2 seconds	>3 seconds
Urine output	Normal	Decreased	Anuria
Fontanelle	Flat	Soft	Sunken
Eyes	Normal	Normal	Sunken
Tearing	Normal	Diminished	Absent
Mucosa	Normal	Dry	Parched

Adapted from Gunn VL, Nechyba C. The Harriet Lane Handbook, 16th edition. 2002.

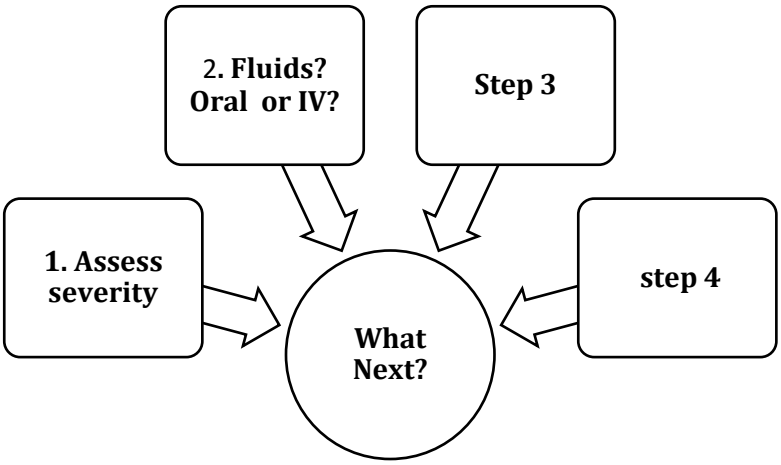




The index case

- Airway Stable
- Circulation: Tachycardic, perfusion good, Liver span N, BP normal, narrow pulse pressure
- Disability: lethargic
- Dehydration - moderate
- CBG: 62mg/dl
- Serum Na – 135

What Next?



Oral/ Intravenous?

1. SHOCK: Isotonic fluid IVF
2. MODERATE DEHYDRATION:
    - ORS
    - IVF as second choice.
    - Isotonic fluid throughout
3. NO/MILD: ORT
4. On admission– Check electrolytes
    - HCO3 < 16, hyponatremia, hypoglycemia
    - In hyperosmolar dehydration (DKA, Hypernatremia) signs of dehydration are absent, because dehydration is intracellular

Fluid replacement calculation for dehydration

Step 1: Deficit

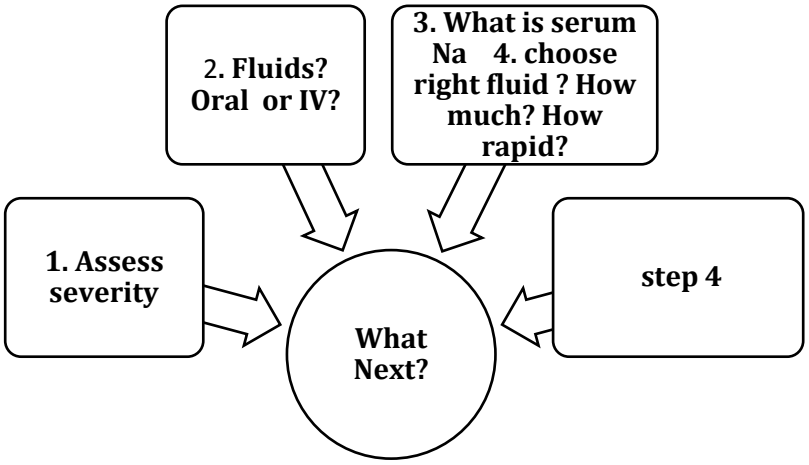
- Mild dehydration: 30-50ml/kg
- Moderate dehydration: 50-75ml/kg
- Severe dehydration: 70-100ml/kg

Step 2: Ongoing losses:

- replace one milliliter of fluid for every gram of output, stool, emesis, or urine.
- If measurements are not available, replacing 10 mL/kg body weight for each watery stool or 2 mL/kg body weight for each episode of emesis

Step 3: Maintenance

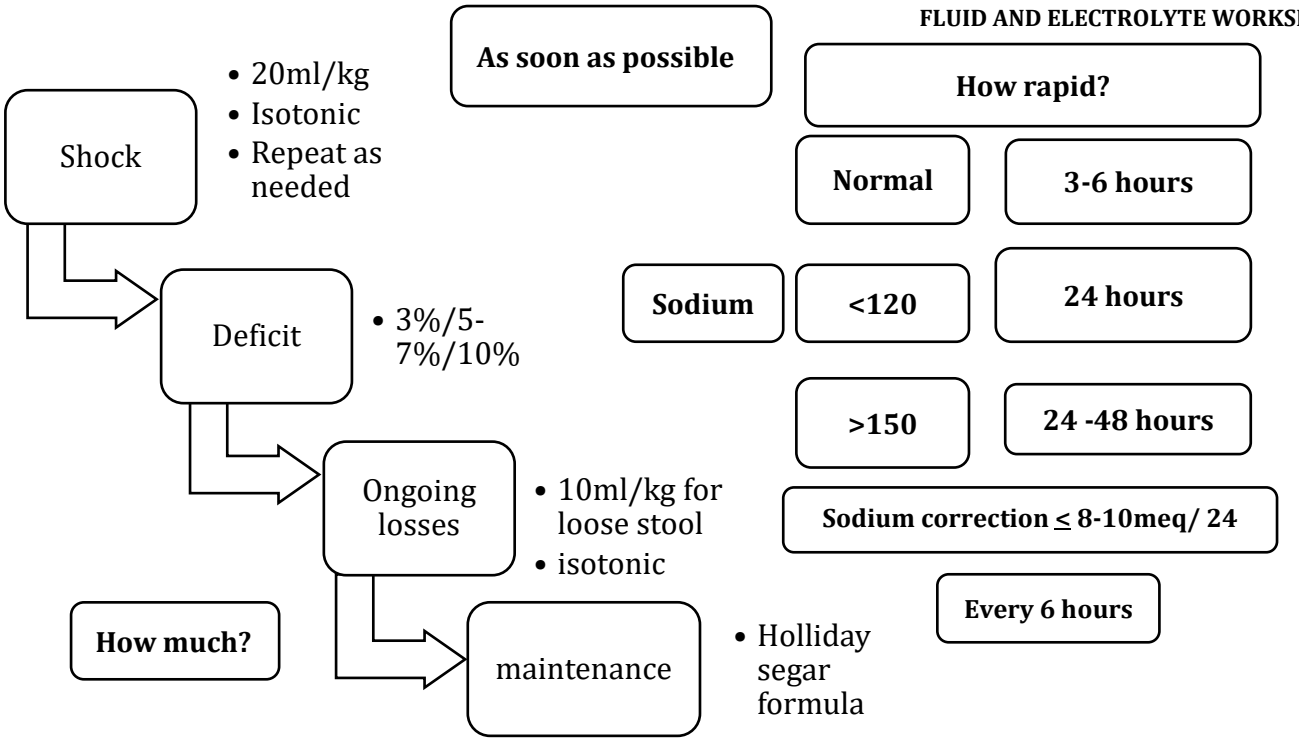
What next?



COMMON NAME	Normal Saline[1]	Hartmann's[2]	Plasma-Lyte[3]	D5W[4]	D10W	0.9% Saline with 5% Glucose	0.45% Saline with 5% Glucose	0.18% Saline with 4% Glucose	3% Saline
CHEMICAL NAME	0.9% Sodium Chloride	Compound Sodium Lactate	PL 148	5% Dextrose	10% Dextrose				
Na	154	129	140	0	0	154	77	31	513
K	0	5	5	0	0	0	0	0	0
Cl	154	109	98	0	0	0	77	31	513
Ca	0	2	0	0	0	0	0	0	0
Mg	0	0	1.5	0	0	0	0	0	0
Bic	0	29 (as lactate)	27 (acetate) 23 (gluconate)	0	0	0	0	0	0
Gluc	0	0	0	50 g	100g	50 g	50 g	40 g	0

What fluid-RL/NS

- Numerous normal saline fluid boluses may result in a hyperchloremic non-anion gap metabolic acidosis, which may obscure acidosis secondary to poor tissue perfusion.
- Lactated Ringer's solution has the theoretical benefit of producing bicarbonate from lactate, provided that liver function is normal



IAP – STG Watery diarrhea(isonatremic dehydration)

Table 1: Rehydration therapy in acute diarrhea

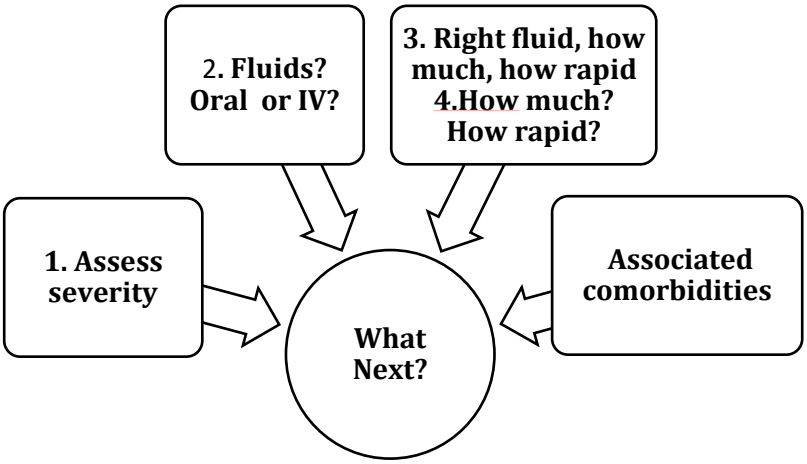
Treatment Plan	**Plan – A**	**Plan – B**	**Plan – C**
State of hydration	No dehydration	Some dehydration	**Severe dehydration**
Percentage of body weight loss	<5	5-10	>10
Estimated fluid deficit (mL/kg)	<50	50- 100	>100
Goals of management	Replacement of ongoing losses of fluid and electrolytes	Correction of existing deflicts of fluid and electrolytes	Urgent replacement of existing deflcits of fluid and electrolytes
Fluid therapy	Maintenance (oral)	Rehydration (oral)	Rehydration (intravenous (IV))
Treatment facility	Home	Health facility	Health facility
Rehydration fluid	Oral rehydration solution (ORS)/homemade solutions	ORS	RL*
Amount of rehydration fluid	For every loose stool: 10mL/kg Age up to 2 months- 5 teaspoons/ purge 2 months to < 2 years- 50 – 100 ml Older child: As much as desired Plus Free access to drinking water	75 mL/kg Over 4 hours Plus Non- breastfed infants <6 months- 100-200mL of clean drinking water. Older Children and adults: Freeaccess to plain water in addition to ORS	IV Fluid Infants 30ml/kg over 1hour 70ml/kg over 5 hours Age>1 year 30 ml/kg over ½ hour 70ml/kg over 2 ½ hours Plus ORS (5 ml/kg/h) start orally as soon as child is able to frink
Monitoring	Watch for vommiting, early signs of dehydration, blood in stools, etc	Monitor every hour and reassess after 4 hours • If still in plan B repeat as above • If rehydration, shift to plan A	Monitor ½ hourly and reassess after 6 hours(infants) 3 hours(older children) • If still in plan C, repeat as above • If rehydrated , shift to plan B/A

Normal saline (0.9% NacL) or half strength Darrow's solution may be used if Ringer Lactate (RL) is not available. Severely malnourished children rehydration slowly over 6- 12 hours.
In children who fail on oral rehydration administration of rehydration fluids either by nasogastric(NG) tube or intravenously (IV) is effective and recommended

Maintenance fluids

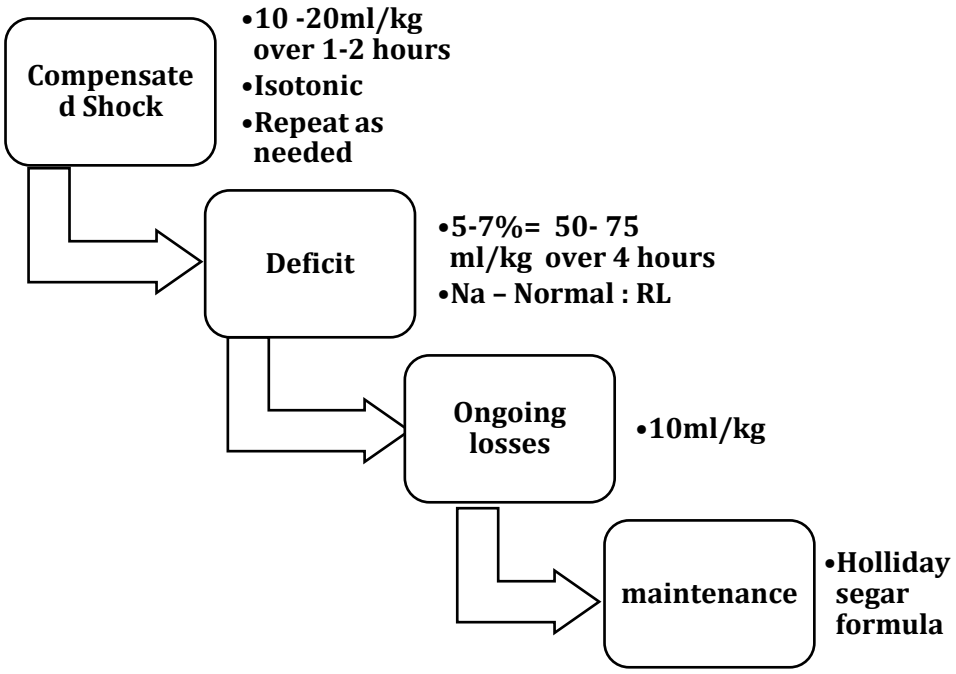
Body weight	Fluid per day
0-10kg	100ml/kg
11-20kg	1000ml+50ml/kg for each kg>10kg
>20kg	1500ml+ 20ml/kg for each kg>20kg

Body weight	Fluid per day
0-10kg	4ml/kg/hr
11-20kg	40ml/hr+2ml/kg/hr x (wt-10 kg)
>20kg	60ml/hr+ 1 ml/kg/hr x (wt-20kg)



Associated co-morbidities

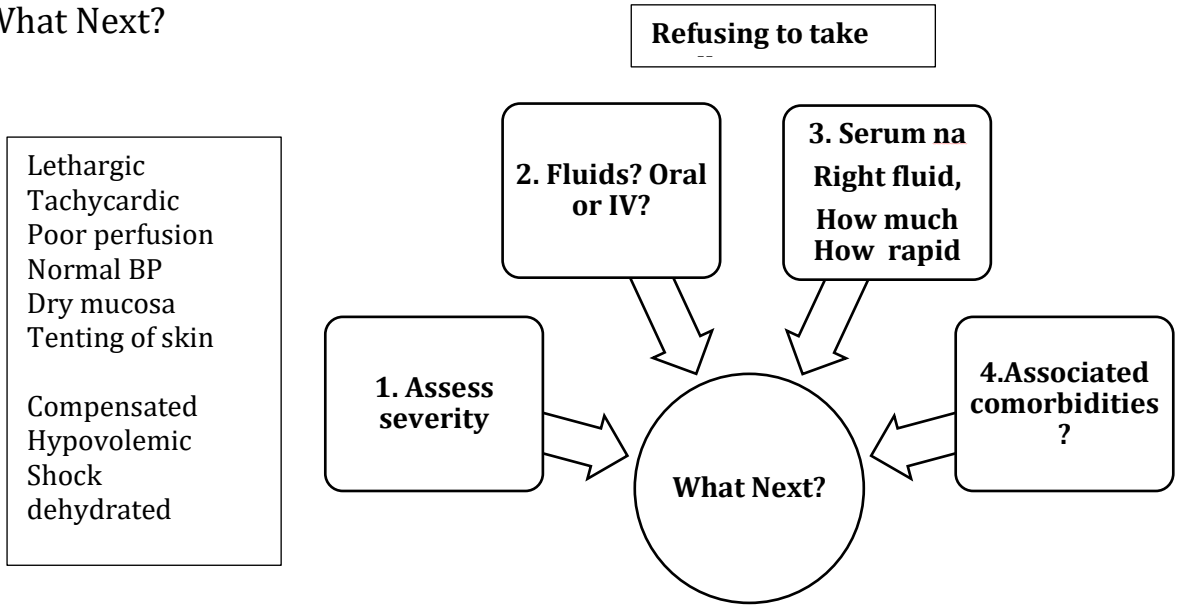
- Look for sepsis
- Adequacy of fluids
- Calculative errors
- Failure to thrive
- CNS abnormalities

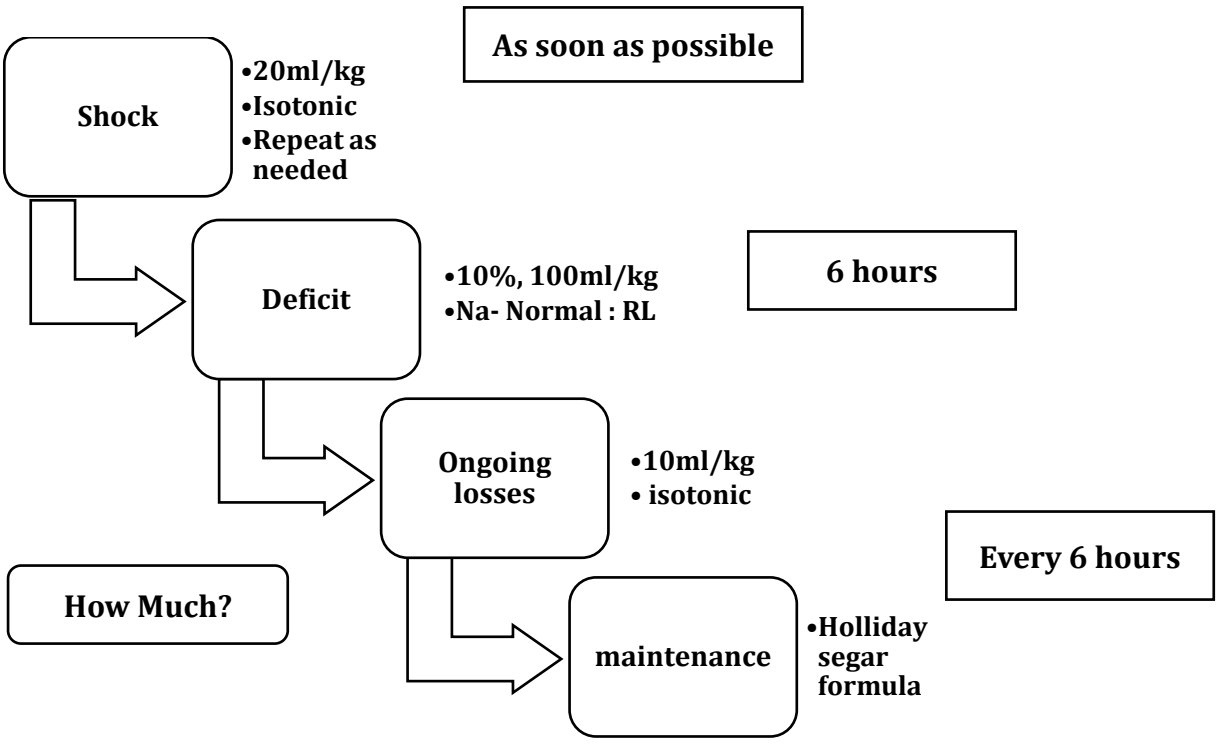


Case 2

A 10-month-old infant presents to the emergency department wita 4-day history of frequent watery stools. He is now refusing to drink. He is listless in his mother's arms. On physical examination, his mucous membranes are dry and the skin on his abdomen is tenting. His heart rate is 160 beats/min and blood pressure is 80/40 mm Hg. His current weight is 9 kg. One weck ago, when he was seen in clinic for a routine examination, he weighed 10 kg. His serum sodium measures 138 mEq/dL (138 mmol/L). After failing a trial of oral therapy, intravenous access is obtained and he is given 20 mL./kg (200 mL) of normal saline. Following the infusion, his heart rate, perfusion, and mental status improve.

What Next?

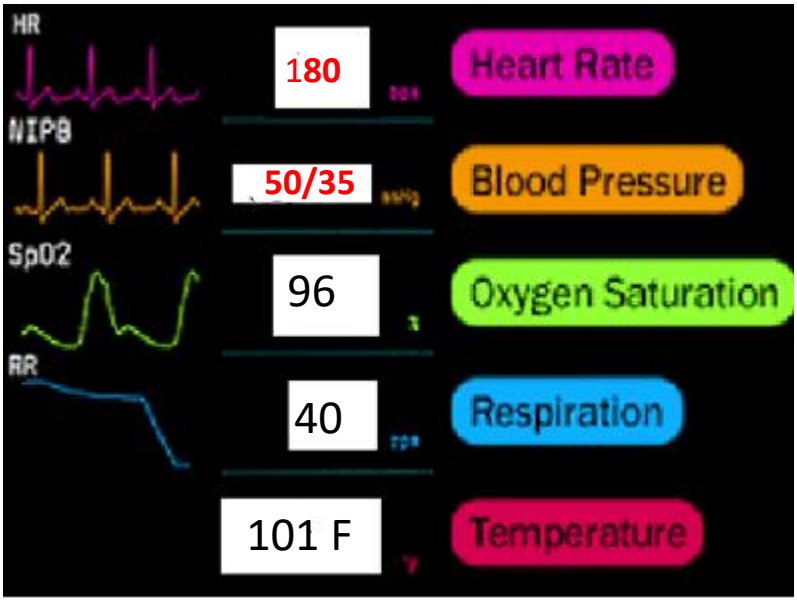




Case 3

8 Month male infant history of fever, loose stools, weight loss, posturing, irritability, reduced urine output

Irritable, bulging anterior fontanelle, intermittent posturing, doughy skin, systematic examinaton-normal.



Mother Revealed improper mixing of 2gm ORS packet in 200 ml water

Diagnosis : Hypernatremic dehydration , in shock , with altered sensorium ? CNS bleed

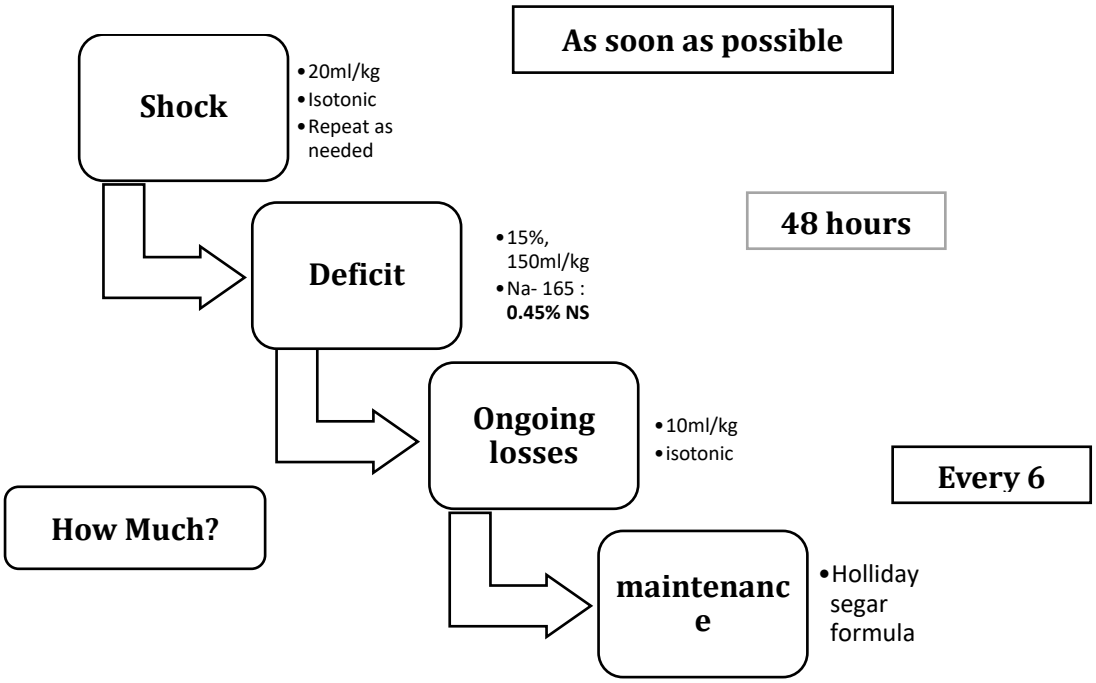
CBC : HB/TLC/PLATELET	**14/17700/3 LAKH**
Serum Sodium / K	**165 / 3**
Blood cultures sent	
INR/APTT	**1.3, 34/27**
Urea/ Creatinine	**60/0.5**

Weight at last vaccine visit : 10 kg

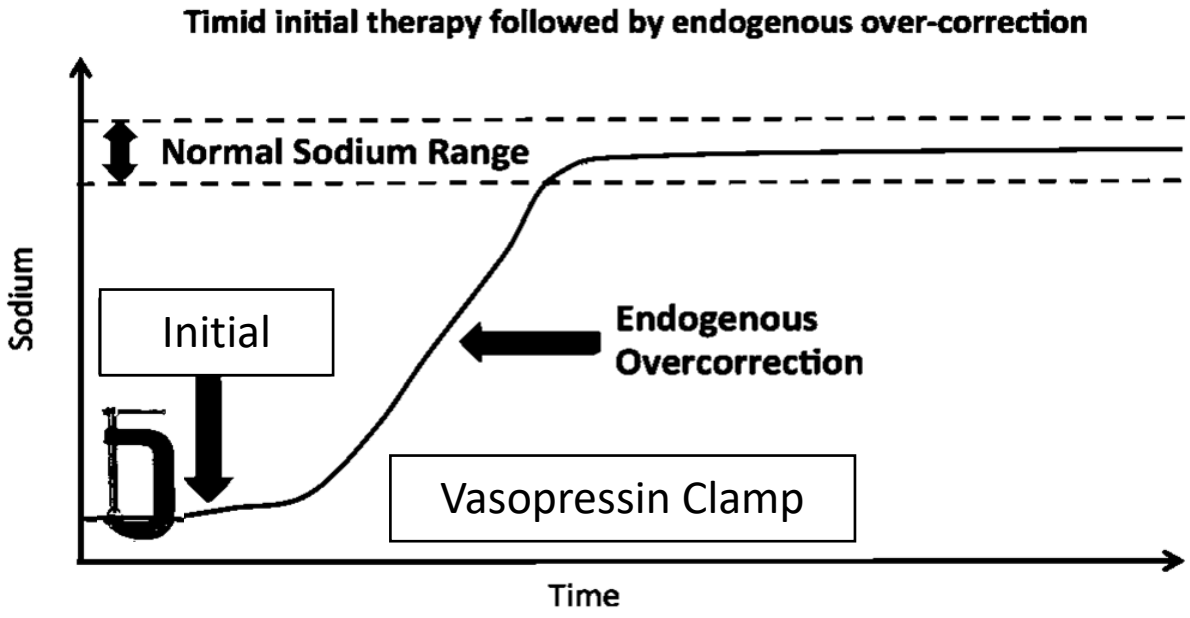
8 Month infant 10 Kg

RATE OF FLUID ADMINISTRATION

- Total fluid requirement = deficit and maintenance fluid , and expected drop of Na per day
- deficit = 15 % Severe Dehydration (because infant in shock) = 150*10 = 1500 over 48 hours
- Maintenance = 1000*2 = 2000 ml over 48 hours
- Total = 3.5 L – bolus 200 ml = 3.3 L over 48 hrs = 69 ml/hr



Endogenous overcorrection of Hyponatremia in hypovolemic hyponatremia



METABOLIC ACIDOSIS

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A fall in pH is termed acidemia, and the underlying disorders that lead to acidemia is acidosis. A primary metabolic acidosis is a pathophysiologic state characterized by an arterial pH of less than 7.35 (acidemia) in the absence of an elevated PaCO2.

Traditional Henderson-Hasselbalch theory - [H+] = 24 x PaCO2/[HCO3 -]. a change in either HCO3 - or PaCO2 changes the other variable in the same direction (compensation) within certain limits. Limitations of this approach:

- Though it does show the change that occurs in Paco2 and Hco3 it does not necessarily state that they are the cause of the underlying acid base abnormality.

- The role of plasma proteins, specifically albumin, in acid–base balance is neglected.

The Modern Stewart Approach – The modern physical- chemical approach introduced in 1980 by Peter Stewart states that there are only 3 independent variables controlling H+ concentration and that changes in Hco3 and Paco2 are the consequence of these in an attempt at maintain pH in the normal range .

- PaCo2

- SID- Strong Ion Difference (strong cations – strong anions)
  (Na+K+Ca+ Mg) – (Cl+lactate) Normal – 40 mmol/L
- Narrowing of SID causes Acidosis and Widening of SID causes Alkalosis

- Atot – weak acids (albumin, phosphate)
  Albumin and phosphate act as weak acids the latter contributing to acidosis in renal failure. Hypoproteinemia causes a base excess.

Eg: Metabolic Acidosis occurring with large volume saline administration is because of excess chloride administration and narrowing of SID. When large volumes of saline are administered it has a proportionally greater effect on total body chloride than on sodium.

Metabolic Alkalosis with Vomiting occurs due to loss of Chloride. Replacement with Saline or Ringers Lactate corrects its

Classification of Lactic Acidosis (Cohen & Woods):

TYPE A: It occurs in hypoperfusion and hypoxia.

- Tissue hypoxia is seen in carbon monoxide poisoning, severe asthma and severe anemia.
- Hypoperfusion occurs in state of shock- cardiogenic, hemorrhagic, septic, regional

  (mesentric , limb) ischemia) , cardiac arrest

TYPE B: It occurs when there is NO clinical evidence of hypoperfusion.

It is further subdivided into 3 subtypes:-

- **B1 -** Acquired diseases - diabetes mellitus, seizures, ARDS , sepsis, malignancies, pheochromocytoma, post cardiopulmonary bypass, renal failure, thiamine deficiency, thyroid storm (all causing increased production)hepatic failure, (decreased clearance) etc.
- **B2 -** Medications and Toxins - acetaminophen, epinephrine, isoniazid, nitroprusside etc.
- **B3** - is due to Inborn errors of metabolism

Laboratory assays estimate only L- lactic acidosis. D-lactic acidosis is rare and is caused by d-stereo isomer of lactic acid which is synthesized by pathological gut flora

In Metabolic Acidosis, check for Anion Gap, Delta Gap, Osmolar Gap

Anion Gap (correct for low albumin)

NAGMA - Normal Anion gap acidosis (Cl high)

(diarrhoea, renal tubular acidosis, saline, acetazolamide)

HAGMA -Wide Anion Gap acidosis > 12 (Cl -N)

GOLDMARK mnemonic G- glycols,O- oxoproline, L- lactic acidosis, D- D lactate , Mmethanol, A-aspirin, R-renal failure, K-Ketoacids, Oxoproline - Acetaminophen use

Low Albumin - a correction factor of 2.5 must be multiplied to every 1mg/dl reduction of albumin below 4 mg/dl and this added to Anion Gap (AG) to get the **True anion gap.**

eg- Albumin – 1.6 mg/dl and Anion Gap - 12

Corrected (True) AG = (4 - 1.6) × 2.5 + AG = 6 +12 = 19

Another formula- Na – (Chloride + Bicarbonate) + 2.5 (4 – Sr.albumin)

When the anion gap is not corrected in hypoalbuminemic pts, abnormally elevated anion gaps could be missed.

DELTA RATIO & DELTA GAP

Universal rule- The increment in anion gap (AG-12) = decrease in bicarbonate (24- NaHco3)

DELTA RATIO. (Delta AG / Delta HCo3)

(AG – 12 / 24 - NaHCo3)

Metabolic Alkalosis

Change in **AG** > drop in **HCO3** (24 - NaHco3)

(For the given anion gap increase , bicarbonate did not fall as much)

N anion gap metabolic acidosis

Change in AG < drop in HCO3 (For the given anion gap increase , bicarbonate fell much more)

Values -

< 0.4 - NAGMA
1.4-0.8 – NAGMA + HAGMA
1- 2 - HAGMA
>2 - HAGMA + Metabolic Alkalosis

DELTA GAP = (AG - 12) + HCo3

If Delta Gap < 18 = Non Anion Gap Metabolic Acidosis
If Delta Gap > 30 = Metabolic Alkalosis

OSMOLAR GAP

Osmolar Gap = Measured Osmolarity – Calculated Osmolarity. (Normal = < 10 meq/L)
Calculated Osmolarity = 2xNa + Glucose/ 18 + Urea/ 6

Treatment of Metabolic Acidosis –

Correction of acidosis with bicarbonate may be warranted in patients of myocardial dysfunction as acidosis can cause catecholamine refractoriness. Adverse effects of bicarbonate can be reduced by giving slow infusions in preference to rapid boluses, by correcting hypocalcemia and ensuring adequate ventilation

Bicarbonate side effects

- Hypernatremia, Hyperosmolality (osmolality is 2,000 mOsm/L equal to 5.8% NaCl.
- Impaired oxygen unloading due to left shift of the oxyhaemoglobin dissociation curve
- Hypercapnia with paradoxical intracellular & CSF acidosis -Ventilation must be adequate to eliminate CO2 produced from. HCo3
- Ionized hypocalcemia & Low K due to alkalosis causing shift into cells decreasing myocardial contractility.

Always treat the underlying cause

- Shock - Restore perfusion with fluids and adequate tissue oxygenation / ventilation, vasoactives, early antibiotic treatment, source control (surgical debridement , central line removal , ischemic gut)

- Status asthmaticus - taper high dose of beta 2 agonist to reduce lactate levels

- Changing from Normal Saline to Balanced fluids (Ringer Lactate, PlasmalyteA) to reduce hyperchloremic normal anion gap acidosis. Normal Saline- Na- 154 meq/l, Cl- 154meq/l Ringer Lactate – Na-130 meq/l, Cl- 110 meq/l

- Antidotes for toxins, drugs (Paracetamol even in normal doses can be toxic in hepatic dysfunction).

- Institute dialysis early in Renal failure for persistent acidosis

Analysis with ABG

Measured values - pH, paCo2 , paO2, tCO2 : **Calculated values –** Hco3, BE, SBE

1. History & Physical. gives an idea of what acid base disorder might be present

2. Look at the pH

   • If pH < 7.35, then academia
   • if pH > 7.45, then alkalemia
   • pH may be normal in the presence of a mixed acid base disorder, particularly if other parameters of the ABG (PCo2, HCo3)are abnormal.

3. Look at PCO2, HCO3-. What is the acid base process (alkalosis vs acidosis) leading to the abnormal pH? Are both values normal or abnormal?

   - One abnormal value will be the initial change (side of the pH change) and the other will be the compensatory response.
   - The direction of compensatory variable is on the same side as the primary variable.
   - Remember compensation never over shoots the pH.

4. If respiratory process, is it acute or chronic?

   - To assess if acute or chronic, determine the extent of compensation.
     10 mmHg change in PaCo2 – Bicarbonate changes by 1 (Acute)
     10 mmHg change in PaCo2 – Bicarbonate changes by 4 (Chronic)

5. If metabolic process, is degree of compensation adequate?

   - Calculate the estimated PCO2, this will help to determine if a separate respiratory disorder is present. In a primary metabolic acidosis, the degree of acute respiratory compensation (pCo2 rise) can be predicted by the following relationship:

     Expected PaCO2 = (1.5 X [HCO3-]) + 8 ± 2 Winters Formula

     If the measured PaCO2 is higher than the expected PaCO2, a concomitant respiratory acidosis is also present. Another formula.....

     1 mEq/L change in HCo3 – PaCo2 changes by 1 (Acute)
     1 mEq/L change in HCo3 – PaCo2 changes by 4 (Chronic)

6. If metabolic acidosis, then look at the Anion Gap.
   - If elevated (> 12), then acidosis due to. (Ketoacidosis, Uremia, Lactic acidosis, Toxins)
   - If anion gap is normal, then acidosis likely due to diarrhea, RTA, saline

7. If anion gap is elevated, then calculate the Delta-Ratio (Δ/Δ) to assess for other disorders.

- Δ/Δ compares the change in the anion gap to the change in bicarbonate.
- If ratio between 1 and 2, then only wide anion gap acidosis
- If < 1, then there is a coexistent Normal anion gap acidosis
- if > 2, then there is a coexistent Metabolic alkalosis present (or rarely a compensated chronic respiratory acidosis.)

8. If normal anion gap and cause is unknown, then calculate the Urine Anion Gap (UAG).

- In RTA, UAG is positive.
- In diarrhea and other causes of metabolic acidosis, the UAG is negative. (neGUTive in diarrhea)

Metabolic acidosis is the pathological state with an arterial pH of less than 7.35 in the absence of an elevated PaCO2
Traditional Henderson- Hasselbalch theory $H^+ = 24 \times PaCO_2 / HCO_3$. Change in any one variable changes the other variable within limits. However They do not state the cause of the underlying abnormality. This does not consider the role of albumin.
The modern Stewart approach is based on the 3 independent variables which control the H^+ concentration to maintain the pH. Partial pressure of CO2, the strong-ion difference (SID), and the total amount of weak acids. SID is the difference between strong cations and anions. (Na+K+Ca+Mg)– (Cl+ lactate) Normal – 38-42 mEq/L. Narrowing is acidosis and widening is alkalosis. Weak acids are Albumin and phosphate A tot- total concentration of weak acids. increase in ToT is metabolic acidosis and decrease results in metabolic alkalosis.

Approach to Acid base analysis

1. What is the pH? 7.35-7.45 normal but check pCO_2 and Base excess
   pH <7.35 acidemia
   pH >7.45 alkalemia

2. What is the primary disorder?
   In acidosis check for low HCO3 (metabolic) or High $PaCO_2$(respiratory)
   In alkalosis check for high HCO3 (metabolic) or low $PaCO_2$ (respiratory)
   pCO_2 and pH move in the opposite directions in respiratory and in the same direction in metabolic

3. Look for compensation in metabolic events
   Metabolic acidosis - winters formula to know the $PaCO_2$ compensation
   1.5 (HCO_3) +8 ± 2 or 40 ± SBE
   Metabolic alkalosis - pCO_2 changes by 0.7 for every1 mEq/L HCO3

4. Compensation in respiratory events

Acute respiratory acidosis Hco3 changes by 1 for every 10 change in $PaCO_2$
pH changes by 0.08 for every 10 change in $PaCO_2$
Chronic respiratory acidosis Hco3 changes by 3 for every 10 change in $PaCO_2$
pH changes by 0.03 for every 10 change in $PaCO_2$
Acute respiratory alkalosis Hco3 changes by 2 for every 10 change in $PaCO_2$
pH changes by 0.08 for every 10 change in $PaCO_2$
Chronic respiratory alkalosis Hco3 changes by 4 for every 10 change in $PaCO_2$
pH changes by 0.03 for every 10 change in $PaCO_2$

5. Check for anion gap (AG).
AG = (Na+ K)– (Cl+HCO_3) =12 ± 2 mEq/L
Correct for low albumin= observed AG + 2.5(4 - albumin in g/dL)

6. Delta Gap Increment in anion gap should be the same as decrement in bicarbonate Delta ratio is Delta AG/Delta HCO_3
When change in AG is more it is metabolic alkalosis
When change in HCO_3 is more it is non anion gap metabolic acidosis.
if <.4 NAGMA
1-2 HAGMA
1.4-1.8 NAGMA+HAGMA
>2 HAGMA + metabolic Alkalosis
Delta Gap – AG-12 +HCO_3 <18 non anion gap metabolic acidosis
>30 metabolic alkalosis
Osmolar Gap=measured osmolality –calculated osmolality (n =<10mEq/L)

7. Non anion gap metabolic acidosis (Normal anionic gap metabolic acidosis)
Calculate urine anionic gap (UAG) = (urinary Na + Urinary K)- urinary chloride
If positive UAG: Renal etiology (Type I, II, IV renal tubular acidosis)
Urinary pH>6: Type I RTA
Urinary pH <5.5: Hypokalemia: Type II RTA, Hyperkalemia: Type IV RTA
if negative UAG: Extra renal etiology

Lactic acidosis–Cohen and woods classification.

Type A in tissue hypoperfusion and hypoxia

Type B in situations without tissue hypoperfusion

B1 – acquired conditions-Sepsis, seizures, Diabetes, ARDS, renal failure, malignancy, thyroid storm, post cardio pulmonary by-pass (all with excess production) Liver failure (decreased excretion)
B2 medications - Epinephrine, acetaminophen, isoniazid, nitroprusside.

B3-IEM related

Management of metabolic acidosis:

Correction is warranted if myocardial dysfunction is encountered

Given as slow infusions / Correct hypocalcaemia/Ensure adequate ventilation

Causes of metabolic acidosis

Anion gap acidosis	Non -Anion Gap Acidosis
Lactic acidosis DKA Aki IEM Tumour lysis Rhabdomyolysis TPN Exogenous sources Poisoning – methanol, Glycols, Ethanol, Salicylates	Hyperchloremic acidosis TPN GI loss Renal causes Drug induced tubulopathies

Approach to metabolic acidosis:

1. History- GI loss, medications, renal issues
2. Examination – for aetiology dehydration in DKA, hyperventilation
3. ABG confirmation – to know metabolic acidosis ± respiratory acidosis
4. Anion gap – look for normal and high anion gap
5. Check compensation by winters formula
6. Look for additional metabolic disturbances by Delta gap
7. Treat the underlying cause /bicarbonate therapy/ dialysis

DKA- Insulin and fluids
Distal RTA – bicarbonate and citrate
CKD-oral sodium bicarbonate
Methanol. Ethanol poisoning - Fomepizole
Sepsis – fluid resuscitation and electrolyte correction
Sodium bicarbonate increases the arterial pH only if there is adequate alveolar ventilation

Bicarbonate replacement is done using SBE or bicarbonate levels
SBE x body weight in Kg x 0.3
HCO_3 deficit (mEq/L) = 0.3 x bodyweight in Kg x HCO_3(Expected – Observed)
Adverse effects of sodium Bicarbonate
Hypervolemia, hyperosmolarity, hypernatremia, hypocalcaemia
Bicarbonate may worsen lactic acidosis
Can decrease blood pressure and cause raised ICP due to hypertonicity

References:

1.Nichols DG & Shaffner DH. Rogers text book of pediatric Intensive care (2016)
2. Robert M, Kliegman & Joseph W. St Geme III.Nelson Textbook of Pediatrics International Edition 21st edition
3.Zimmerman J.J Clark R.S.B, Fuhrman B.P, Rotta A.T, Kudchadkar S.R, Relvas M.S & Tobias J.D. Fuhrman & Zimmerman's Pediatric Critical Care (Sixth edition)
4. Sood P, Puri S. Interpretation of arterial blood gas. Indian J Crit Care Med 2010; 14 (2):57-64.

1. 1year male child (6 Kg) with acute watery diarrhoea 10-12 episodes /day, lethargy, vomiting and seizures Treated with IVF outside. Clinical examination revealed verbal responsive, sunken eyes, dry tongue and mucosa, pallor, increased skin turgor. Heart rate was 160/mt. RR49/mt. ++/+ prolonged CRT, BP 80/66mm Hg. Cool below ankle SpO_2 96% in room air. urine output is 4ml/kg/hr. Blood glucose was 35 mg/ dl. ABG showed the following –pH 7.2, pCO_2 35 HCo3 14 BE -7

   Na 122 K 2 Cl 96 lactate 3.6
   - What is the physiological status?
   - Interpret the ABG
   - Outline the fluid therapy and management?

2. 3month male child admitted with persistent vomiting and seizures. History revealed previous sib death at 3 months of age. examination revealed lethargy, tachypnoea, Dusky extremities. Primary assessment revealed stable airway, RR 60/mt, no retractions, bil air entry, no added sounds. HR 160.mt +++/+ Poor distal pulses, CRT >3 seconds, cool below knee, BP 70/? Verbal responsive, PERRL. CBG was 40mg/dl,
   ABG pH 6.9 Pco2 25 Hco3 10 BE -8 lactate 6 Na 130 K 3 CL 100

   - What is the physiological status?
   - Interpret the ABG
   - Discuss the investigations and management

3. 10 year old female child was admitted with altered sensorium and pain abdomenhematemesis. She was lethargic, and pink. Primary assessment revealed the following maintainable airway, RR of 40/mt, bil air entry was equal, no retractions, no added sounds, saturation was 96% in room air. HR was 140/mt, central and peripheral pulses were +++/+, CRT >3 seconds, cool below knee, BP 80/40mm Hg.GCS 10. PERRL. Head to foot examination was not contributory. Her urine was red coloured.

   CBG was 250mg/dl. Venous blood gas revealed the following pH 6.8Pa02 85 Paco2 28 Hco3 7 Na 140 K 5.0Cl 100 BE -20 lactate 3

   - What is the physiological status

- Interpret the VBG
- Anion gap and delta gap
- What are the possible diagnosis?

4. 2year female child weighing 14 kg was admitted with history of fever vomiting 5 days afebrile since morning. History of facial puffiness and rashes over the body. She was breathless and lethargic with reduced urine output. Treated with paracetamol and ceftriaxone. Assessment revealed the following stable airway, RR5/mt bil air entry no added sounds, no retractions, HR 160/mt ++/0 BP not recordable. Cool below knee CRT > 3 sec anuric for 4 hours. GCS 8 PERRL. Petechial rashes and ecchymosis all over the body with distended abdomen.

   BG was 40mg/dl. Na 128 K 5 Cl 90 lactate was 3.6 mmol VBG showed the following pH7.0 HCo3 12 PCo2 18 Po2 80 BE -6 lactate 3
   - What is the physiological status?
   - Interpret the ABG
   - Likely diagnosis investigations and management

5. 8-year-old female child (16kg) with vomiting, breathlessness, lethargy and pain abdomen. Treated outside as wheeze with nebulisation for 2 days. history revealed recent weight loss. She was lethargic but responsive to commands, dehydrated, pink. Airway was stable, RR36/mt, no retractions, bil airentry normal, no added sounds.HR 120/mt ++/+ cool below knee, CRT 3 seconds unequal pupils, BP90/60 mmHg, sats 96% room air Urinary Catheter revealed 120 ml urine output.

   Her CBG was 350mg/dl. Ph 7.104 Pco2 18.5 po2 60.5 Hco35.7 BE -23.9NA 154 K 3 .29 Ca 1.09 Cl 128 Hb 18.2 A gap 23.9lac 2.55
   - What is the physiological status
   - Interpret the ABG
   - Outline the management

6. 1 year boy child with cyanosis. Airway- maintainable. Breathing - RR 30/min, WOB Normal, No added sounds, Cyanosis present, SPO2 83% with O2 NRM. Circulation – HR 156/min, NIBP – 92/66 Perfusion good. Disability – unresponsive, Exposure – Temp – 98 F, No abnormal smell, Central Cyanosis present

   ABG -pH 7.2 Pco2 28.7 o2 167 Hco3 14 BE -1.2 HCt 40Na 142 k 4 ca 1.0 cl 109sO2 99 FO2HB 63.2 FCOHB 0.8 FMetHB 53.5 Lactate5 Gl200

   - What is the physiological status
   - Interpret the ABG Calculate Delta Gap
   - Write the Management
   - List the likely causes for this scenario

7. 10-year female kid with history of vomiting, lethargy and pain abdomen. Treated outside with normal saline boluses as acute abdomen. Referred for surgical opinion. She is lethargic /Primary assessment showed maintainable airway, RR 40/mt, no retractions, no added sounds, bill air entry saturation with room air 99/Hr 120.mt, +++/++ peripheries warm, CRT <3 sec BP 100/70. DEM intact PERRL.

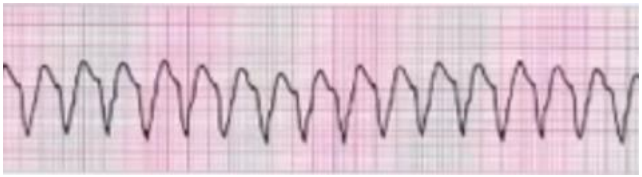
   ABG pH 6.99 Hco3 4 Pco2 30 Po2 97 CBG 300 Na 121 K 5.6 Cl 108 lactate 2

   - Interpret the ABG
   - What is the fluid of choice
   - How to treat acidosis
   - After 8 hours of therapy the ABG
   - pH 7.23 Pco2 35 Hco3 18 Po2 100 Na 146 K 4 CL 128 BE - 3
   - What is your interpretation of ABG
   - Management strategy?

8. 2year old female child weighing 7 kg admitted with fever loose stools and vomiting 3 days Breathlessness one day. Wt for age and Wt for HT below -3SD She is lethargic, dehydrated, acidotic breathing. RR40/mt bil air entry equal no added sounds mild Subcostal retractions saturation 96% with NRM HR 160 central pulses good peripheral pulses weak CRT> 3 sec Cool below knee Bp 78/50. Received NS bolus outside

   CBG 50mg/dl ABG Ph 7.1 Hco3 10 Pco2 38 Po2 160 Na 130 K3.5 CL 112 SGOT 50 SGPT 35 Bil 0.3 Albumin 2.

   - Interpret the ABG calculate the anion gap
   - What is the fluid management

9. 5yr female child brought to the emergency department, afebrile, Unresponsive HR 200/mt, BP120/80mmHg, Seizures at ER, Dilated pupils, sluggish reaction. No significant history. No previous medical illness.
   ABG Ph 7.1 Pco2 28 HCo3 12 Po2 90 Na 135 K 4 Cl 110 BG 100
   ECG 

   - Interpret the ECG and Blood gases
   - What is the likely diagnosis?
   - What is the management?

10. 10 months female with history of fever breathlessness vomiting loose stools

    Lethargic, responsive to calls, RR 65/mt retractions, bil equal air entry, no added sounds, sats at 96% with NRM HR 170/mt ++/+ cool below knees BP not recordable. catheter showed 20 ml clear urine DEM intact PERRL.
    ABG Ph 7.2 Paco2 50 Pao2 79 Na 139 K 4. Cl 110 Hco3 10
    - What is the physiological status
    - Interpret the ABG
    - Management

11. 6year boy with disorientation and drowsy for 2 hours. Was playing at the Garage with the father. Later brought by the neighbour as found alone and drowsy in the car. Examination revealed drowsy child GCS 6/15 , no evidence of trauma pallor or cyanosis or fang mark or bite marks. No shock No history of previous seizures. Intubated in view of low GCS.
    Post intubation Blood gases are as follows -pH 7.3 Po2 110 Pco2 18 HCO3 18 BE -11 Lac 4 Na 140 K 4.5 CL 110 BG 100 serum osmolarity 311.

- Interpret the ABG
- Calculate the AG delta Gap and osmolar Gap
- What are the underlying causes you would think in this type of ABG

HYPERNATREMIA

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Definition: Serum Na > 145 mmol/ L or mEq/L. Some references mention as > 150 mEq/L

Salt and water physiology

60% of body weight is constituted by water. Between extracellular fluid (ECF) and intracellular fluid (ICF) is the cell membrane. Only water permeates through the cell membrane. This transport is from lower tonicity to higher tonicity which means in hypernatremia it is from intracellular to extracellular compartment. The electrolyte composition of ECF and ICF has almost equal osmolality but electrolyte concentration is different. ECF: Na 135-145 mEq/L K 3.5 -4.5 mEq/L and ICF: Na 10-20 mEq/L K 120 - 150 mEq/L. Sodium is closely related to water balance. Thirst and ADH release are the major defences associated with hypernatremia. Threshold for thirst begins at 5-10 mosm/kg higher than that for ADH release

Causes of hypernatremia (Table 1)

Hypernatremia develops only by two mechanisms

1. Loss of free water (most common) – could be as loss of water or hypotonic fluids leading to hypovolemic hypernatremia

2. Gain of sodium (less common) – mostly iatrogenic; rarely accidental leading to hypervolemic hypernatremia

Table 1 showing the causes for hypernatremia

Hypotonic fluid or electrolyte free water loss	Excess salt or gain of salt
GIT : Diarrhea	Improper ORS or formulae
Renal: osmotic agents Diabetes Insipidus Chronic kidney disease Acute tubular necrosis	Iatrogenic Bicarbonate or hypertonic saline
Skin :Burns , increased sweating	Salt poisoning Child abuse Salt with water instead of sugar Pica Hyperaldosteronism

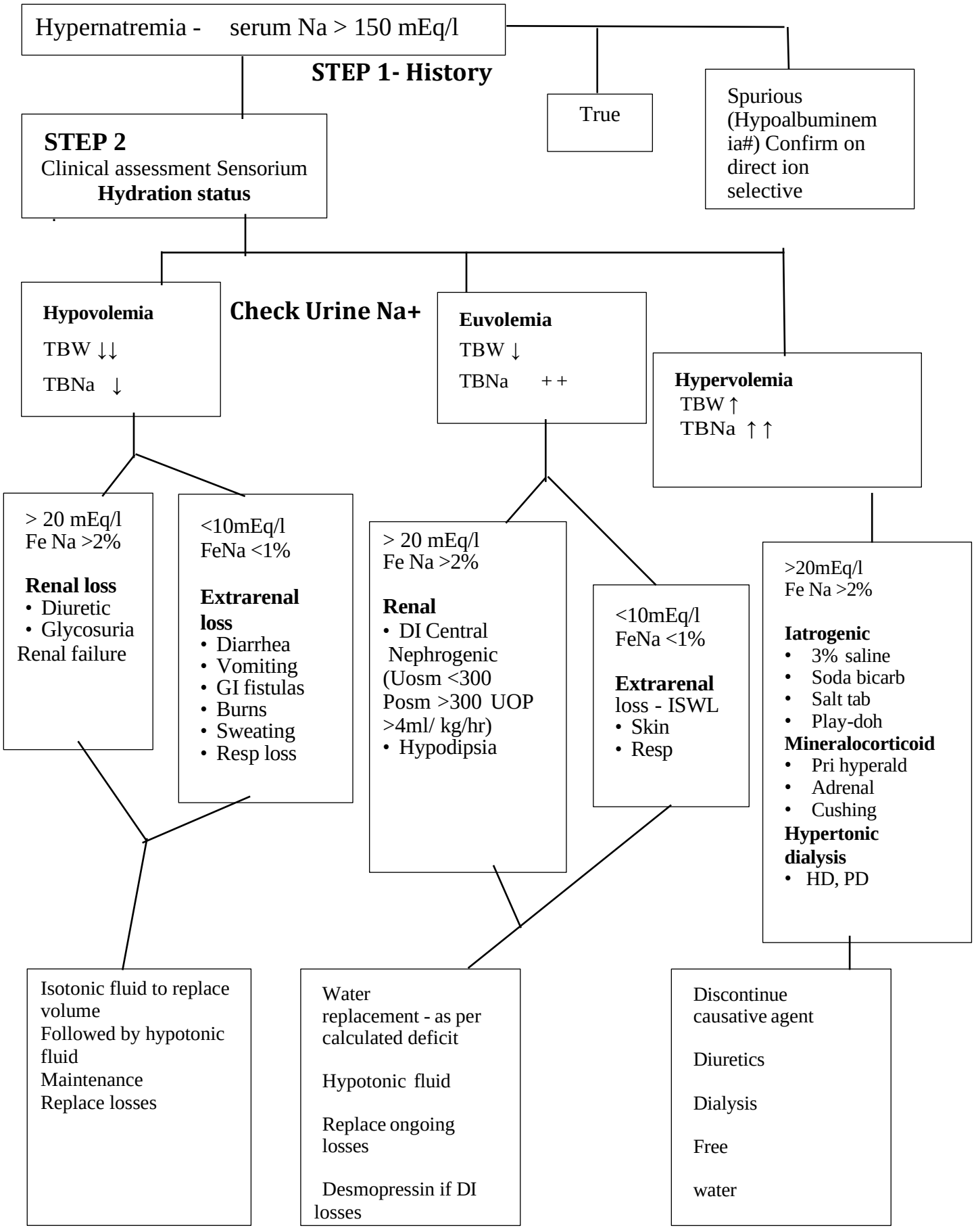
Clinical features

1. Dehydration and shock: Not obvious as ECF water content is near normal. Subtle findings – thirst and "doughy" skin, tachycardia, wt loss
2. CNS symptoms: Convulsions, irritability, high-pitched cry and. Some alert infants are very thirsty.

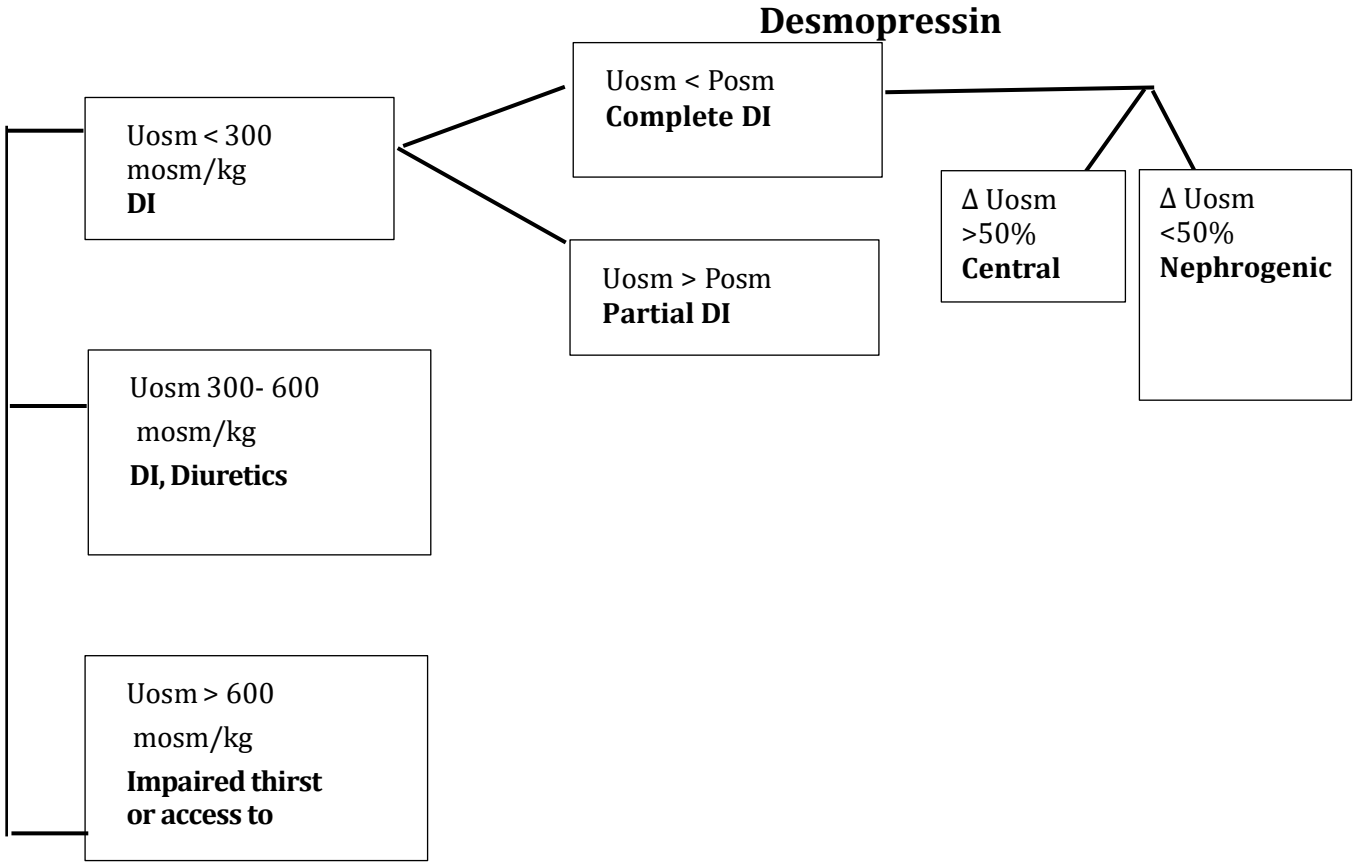
   a) Brain haemorrhage : Brain shrinks, results in tearing of bridging blood vessels - subarachnoid, subdural, parenchymal bleed .
   b) Thrombosis: Stroke, dural sinus thrombosis, peripheral thrombosis, and renal vein thrombosis - possibly due to hypercoagulability.

3. Lab investigations

- CBC: high HCT favours dehydration
- CXR: Can identify volume overload-pulmonary congestion, pleural fluid USG Lungs: presence of B lines. IVC filling will indicate the volume status
- Urine Sodium: < 10 favours dehydration > 20 – Salt excess or renal losses FENA: < 1.0 – hypovolemia > 2.0 Salt excess and hypervolemia
- Blood sugar, urea, creatine, other electrolytes, calcium and magnesium. High serum chloride – Salt excess
- Serum and urine osmolarity
- Serum AVP level and response to AVP
- Neuroimaging: For cause in DI and CNS complications
- ABG: In a setting of edema, hypertension, hypokalemia, hypernatremia and metabolic alkalosis – hyperaldosteronism


Hypernatremia - serum Na > 150 mEq/l
STEP 1- History
True
Spurious (Hypoalbuminemia#) Confirm on direct ion selective
STEP 2
Clinical assessment Sensorium
Hydration status
Check Urine Na+
Hypovolemia
TBW ↓↓
TBNa ↓
Euvolemia
TBW ↓
TBNa + +
Hypervolemia
TBW ↑
TBNa ↑↑
> 20 mEq/l
Fe Na >2%
Renal loss
• Diuretic
• Glycosuria
Renal failure
<10mEq/l
FeNa <1%
Extrarenal loss
• Diarrhea
• Vomiting
• GI fistulas
• Burns
• Sweating
• Resp loss
> 20 mEq/l
Fe Na >2%
Renal
• DI Central Nephrogenic (Uosm <300 Posm >300 UOP >4ml/ kg/hr)
• Hypodipsia
<10mEq/l
FeNa <1%
Extrarenal loss - ISWL
• Skin
• Resp
>20mEq/l
Fe Na >2%
Iatrogenic
• 3% saline
• Soda bicarb
• Salt tab
• Play-doh
Mineralocorticoid
• Pri hyperald
• Adrenal
• Cushing
Hypertonic dialysis
• HD, PD
Isotonic fluid to replace volume
Followed by hypotonic fluid
Maintenance
Replace losses
Water replacement - as per calculated deficit
Hypotonic fluid
Replace ongoing losses
Desmopressin if DI losses
Discontinue causative agent
Diuretics
Dialysis
Free water

STEP 5- Check urine osmolality



- Useful to do UEC, calcium, magnesium, phosphate and glucose. These may need concurrent management
- In the presence of hypoalbuminaemia (albumin <30 g/L), a blood gas sodium level is more reliable
- Initial paired serum and urine sodium, creatinine and osmolality is ideal, but if results will be delayed, a urine dipstick for specific gravity will give an indication of urinary concentration and treatment should not be delayed

Acute hypernatremia, of < 48 hours duration and symptomatic, is managed to achieve a rise in Na of 3-5 mEq/l immediately with a rise of 10-12 mEq/l in 24 hours
Chronic hypernatremia, of > 48 hours duration is corrected more gradually, with a rate of rise of not more than 0.5 per hour or 8-10 mEq/l per day.

Free water deficit in milliliters = Current total body water x ([current plasma Na/140] - 1)
Free water deficit in milliliters = (4 mL/kg) x (weight in kg) x (desired change in plasma Na)
Adrogue Madias formula predicts the change in Na achieved with 1 litre of chosen fluid

Change in serum (Na^+)

$$= \frac{\text{infusate } (Na^+) + \text{infusate}((K^+) - \text{serum } (Na^+)}{\text{Total body water}+1}$$

Case scenario

A late preterm neonate born at 36 + 3 weeks, B wt – 2.48 kg with uneventful antenatal and early neonatal period. Brought for first postnatal review only on D 18 with weight of 1.573kg, decreased urine output, loose stools-watery and foul smelling. He was exclusively breast fed. On admission he was dull and lethargic with sunken eyes and depressed AF. Systemic examination revealed HR of 180/min, doughy feel of skin, proximal and distal pulses equally felt, legs a little cold to touch. There was 36.8 % weight loss.Systolic BP – 60 (NIBP). Septic work up done. Treatment initiated USG abdomen- bilateral renal cortical echoes, echogenic medullary pyramids, no hydronephrosis What are the salient points in the history? What may be the cause? What tests would you like to order? What is the probable diagnosis? Outline the management

Investigations done on admission:

S.Creatinine	2.7
B urea	217
S. Sodium	180
S. Potassium	5.8
S. Chloride	102
S. Bicarbonate	22
CBG	85
CBC	Normal

Case history:

11 months old female infant weighing 10 kg was brought to ER with acute watery diarrhoea and vomiting of 2 days duration. She also had an episode of sudden vacant stare followed by up rolling of eyeball yesterday which lasted for a period 2 minutes. Child had fever for which she was treated with ORS and some medications On assessment at your ED on arrival

- Found to be pain responsive. febrile. weight -9kg
- RR 40/m9n, no increased WOB, BAE: equal, SpO2 of 98-99% in room air
- HR – 162/min, BP- 70/48 mm Hg, CFT- >3s. Weak peripheral pulses. Normal urine output
- POCT: RBS-295mg%, BLOOD Gas electrolytes: Na- 156, K- 4.2, Cl – 125, HCO3 – 17

Discuss the following questions and write your management plan.

Questions

1. What is your diagnosis?
2. What are the principles in management in this child?
3. List the various steps in management in order of priority.
4. What is the underlying mechanism of hypernatremia based on history and volume status? What etiological factors have contributed to hypernatremia?
5. What is the duration over which the correction of sodium levels should be done based on current serum sodium values?
6. How will you calculate the maintenance fluid requirement in this child?
7. How will you estimate the electrolyte free water loss in this child?
8. What will be the final fluid prescription after correction of shock? Choice of fluids & rate of correction?
9. How will you address the ongoing losses?

Case scenario:

A 10-year-old boy weighing 30 kg is undergoing treatment for severe traumatic brain injury after a road traffic accident in the PICU (day 5 of PICU stay). He had severe cerebral edema and underwent decompressive craniectomy on day 2 of admission. There is ongoing discussion regarding poor neuroprognosis given the CT Brain and clinical features such as non-reactive pupils (4 mm each). He has no response to pain, absent deep tendon reflexes. He is invasively ventilated and on ketamine and midazolam infusions. His vitals are as follows:

- HR 150/min, BP 86/44 (55), SpO2 98% (FiO2 30%.
- His peripheral perfusion is poor and CVP is 2 mmHg.
- He is on 3% saline infusion at 30 ml/hr. A routine review of charts shows increasing sodium trends over the past 24 hours as follows:

- Na (in mmol/L) every 6 hours: 145 – 150 – 153 – 164
- Other labs: K 4 mmol/L, HCO3 – 24 mmol/L, Cl- 110 mmol/L, Urea 30 mg/dl, Creatinine 0.6 mg/dl
- Are you concerned about the electrolyte trends?
- Could 3% saline be the cause of this rising sodium trends?
- What is the one clinical parameter that will guide you to the possible diagnosis?
- How will you approach this situation?

Hypocalcemia/ Hypomagnesemia

Contributors: Dr Shanthi S, Dr Mani Kumar S, Dr Anita Tarigopula, Dr Mituna Shree J

Calcium is essential for nerve conduction, muscle contractility and coagulation.

Normal values of calcium:

Ionized calcium – 4.65 to 5.25 mg/dL (1.2 to 1.3 mmol/L) (1 mg/dL = 0.25 mmol/L).

Total calcium – 8.5 to 10.5 mg/dL (2.12 to 2.62 mmol/L)

Hypocalcemia is defined as corrected serum total calcium levels <2.12 mmol/l (8.5 mg/dl).

The serum calcium falls by 0.8 mg/dL (0.2 mmol/L) for every 1 g/dL (10 g/L) fall in the serum albumin concentration

The formula for albumin-corrected serum calcium is as follows:

total serum Ca concentration (mg/dL) + 0.8 × [4 – serum albumin concentration (g/dL)

Ionised calcium is not affected by albumin levels. However, it can be affected by change in pH. Alkalosis increases the amount of albumin-bound calcium and decreases the level of ionized calcium, in acute respiratory alkalosis, the level of ionized calcium falls to 0.16 mg/dL for each 0.1 unit increase in pH

Hypocalcemia in Newborns

1) For term infants or preterm infants weighing >1500 g at birth

   Total serum calcium <8 mg/dL (2 mmol/L) or ionized calcium <4.4 mg/dL (1.1 mmol/L)

2) For very low birth weight infants weighing <1500 g.

   Total serum calcium <7 mg/dL (1.75 mmol/L) or ionized calcium <4 mg/dL (1 mmol/L)

Etiology of Hypocalcemia

	Parathyroid mediated	**Non parathyroid mediated**
Genetic	• Familial isolated hypoparathyroidism • Syndromes associated with hypoparathyroidism: −22q11.2 deletion (DiGeorge) syndrome −Hypoparathyriodism, Sensory Neural Deafness, Renal Dysplasia Syndrome (HDR) −Kearns–Sayre syndrome −Kenny–Caffey syndrome type 1 and 2 −Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) syndrome −Sanjad Sakati syndrome (SSS) −Mitochondrial trifunctional protein (MTP) deficiency syndrome • Autosomal Dominant Hypocalcemia (ADH) 1 and 2 • Pseudohypoparathyroidism 1A and 1B • Wilson's disease • Hemochromatosis	• Vitamin D dependent rickets (VDDR) type 1 and 2 • Heriditary vitamin D-resistant rickets (HVDRR) • Osteopetrosis • Maternal hyperparathyroidism
Acquired	• Post-surgical hypoparathyroidism • Hypomagnesemia • Autoimmune polyendocrine syndrome type 1 (APS1) • Blood transfusion(haemosiderosis) • Radiation therapy • Sclerotic metastases	• Vitamin D deficiency • Malabsorption chronic kidney disease Hungry bone" syndrome End-stage liver disease • Critical illness • Acute pancreatitis Citrate (blood trasfusion) Drugs: −Loop diuretics −Phosphate −Foscarnet −EDTA −Anti-convulsants −Magnesium sulfate −Calcitonin, bisphosphonates −Cinacalcet

Adopted from Pepe, J., Colangelo, L., Biamonte, F., Sonato, C., Danese, V. C., Cecchetti, V., et.al

2020. *Diagnosis and management of hypocalcemia. Endocrine.*

Evaluation:

Obtain a complete history and physical examination to detect clinical features of hypocalcemia and findings that may help in identifying etiology.

History:

- Dietary history (particularly calcium, vitamin D intake)
- History of neck surgery/radiation
- Family history of calcium disorders
- Feeding problems, nausea, vomiting, delayed eruption of teeth
- Apnea, jitteriness, irritability
- Cardiac abnormalities or recurrent infections
- Muscle cramps, twitching, or spasms
- Circumoral or distal paresthesias
- Seizures

Suspect hypocalcemia when a child presents with any of the following features

- Numbness and tingling sensation in the circumoral region
- Paresthesias of the hands and feet, muscle cramps especially after exercise
- Carpopedal spasm (tetany). (Signs of latent tetany: Chvostek sign: twitching of the orbicularis oris muscle with light tapping of the facial nerve at the anterior external auditory meatus. Trousseau sign: carpopedal spasm when BP cuff maintained 20 mm Hg above SBP for 3 minutes)
- Laryngospasm with stridor
- Convulsions
- Features of Rickets: Widening at the wrists, knees, and/or ankles, bowing of the extremities

- Cardiovascular manifestations: hypotension, heart failure, arrhythmias
- ECG changes: prolonged QT interval

Diagnostic Tests:

Step 1: Check Total and ionized calcium levels – confirm hypocalcemia

Step 2: Check serum phosphorus, magnesium, alkaline phosphatase, creatinine

Step 3: Check Intact PTH level. If intact PTH is low, evaluate for hypoparathyroidism

Step 4: Assess Vitamin D status – check 25-hydroxyvitamin D level. If vitamin D level is in deficiency range, evaluate. Blood for 1,25 dihydroxy vitamin D should be stored before initiating treatment. 1,25 (OH)2 D levels will be needed to detect problems in Vitamin D metabolism. In Vitamin D dependent rickets type I levels are low and in Vitamin D dependent rickets type II levels are increased.

Step 5: Check urine calcium and creatinine. A timed 24hr urinary calcium excretion (collected in containers with hydrochloric acid to prevent precipitation of calcium salts) can be obtained in older children. Hypercalciuria is suggested by values greater than 0.1mmol/kg/day. Timed urinary collection may be difficult in young children and a random spot urine calcium creatinine ratio repeated on 2–3 occasions at the same time of day is the most appropriate way of assessing urine calcium excretion. The calcium creatinine ratio on the second voided urine sample of the day after an overnight fast is most closely related to 24-hour urine calcium level. In the presence of hypocalcaemia a urine calcium/creatinine ratio greater than 0.3 on spot samples suggests inappropriate excretion and indicates hypocalcemic hypercalciuria. This is due to activating mutations of the calcium sensing receptor which downshift the set point for calcium responsive PTH release.

Step 6: Hand/wrist/knee x-ray if rickets is suspected

Step 7: Measure maternal calcium and vitamin D levels in the case of hypocalcaemia in infancy because of the link with maternal vitamin D deficiency and hyperparathyroidism

Other investigations that may be needed for rare causes are karyotyping (22q11&10p13 deletion and chest radiograph for thymic hypoplasia (Di-George syndrome), renal ultrasonogram for nephrocalcinosis and renal dysplasia (syndrome of hypoparathyroidism, deafness, renal dysplasia HDR), assessment of autoantibodies (antiparathyroid antibodies) for autoimmune causes, hearing test for deafness. Maternal and family screening may be needed for familial forms of hypocalcemia. DNA testing may be necessary to identify genetic causes of hypocalcemia.

Treatment

- Acute symptomatic hypocalcemia should be treated immediately
- Calcium gluconate (preferred) 100 to 200 mg/kg/dose (max 1 to 2 g/dose) IV (0.5ml-1 ml/kg/dose) over 5 to 10 minutes with cardiac monitoring
- (Calcium chloride 20 mg/kg/dose (max 2 g/dose) can alternatively be given if readily available).
- Bolus should be immediately followed by a continuous infusion of calcium gluconate: 500 to 800 mg/kg/24 h or an intermittent infusion of calcium chloride of 10 to 20mg/kg/dose (max 1 g/dose) q4–6h PRN.

10% solution of calcium gluconate contains about 9.3 mg of elemental calcium / mL

- Calcium gluconate can be given via peripheral IV. It is diluted in equal amount of NaCl or 5%dextrose or distilled water and given over 10 minutes in children and

over 20 minutes in newborns. Calcium chloride should only be given via central line due to risk of tissue necrosis with extravasation.

- Continue the IV infusion or intermittent doses until patient is on an effective oral regimen.
- Oral calcium 25 to 50 mg/kg/24 h elemental calcium (max 1 g elemental calcium per 24 hours) divided 3 to 4 times daily. Calcium carbonate contains 40% of elemental

  calcium and is the drug of choice.
- For patients with hypoparathyroidism, calcitriol should be initiated as soon as possible:

  infants 0.04 to 0.08 mcg/kg/24 h divided twice daily, > 1 year 0.25 mcg/24 h and increase as needed up to a maximum of 2 mcg/24 h
- Magnesium supplements should be given as needed to correct hypomagnesemia.
- For patients with vitamin D deficiency, treat with high-dose oral cholecalciferol

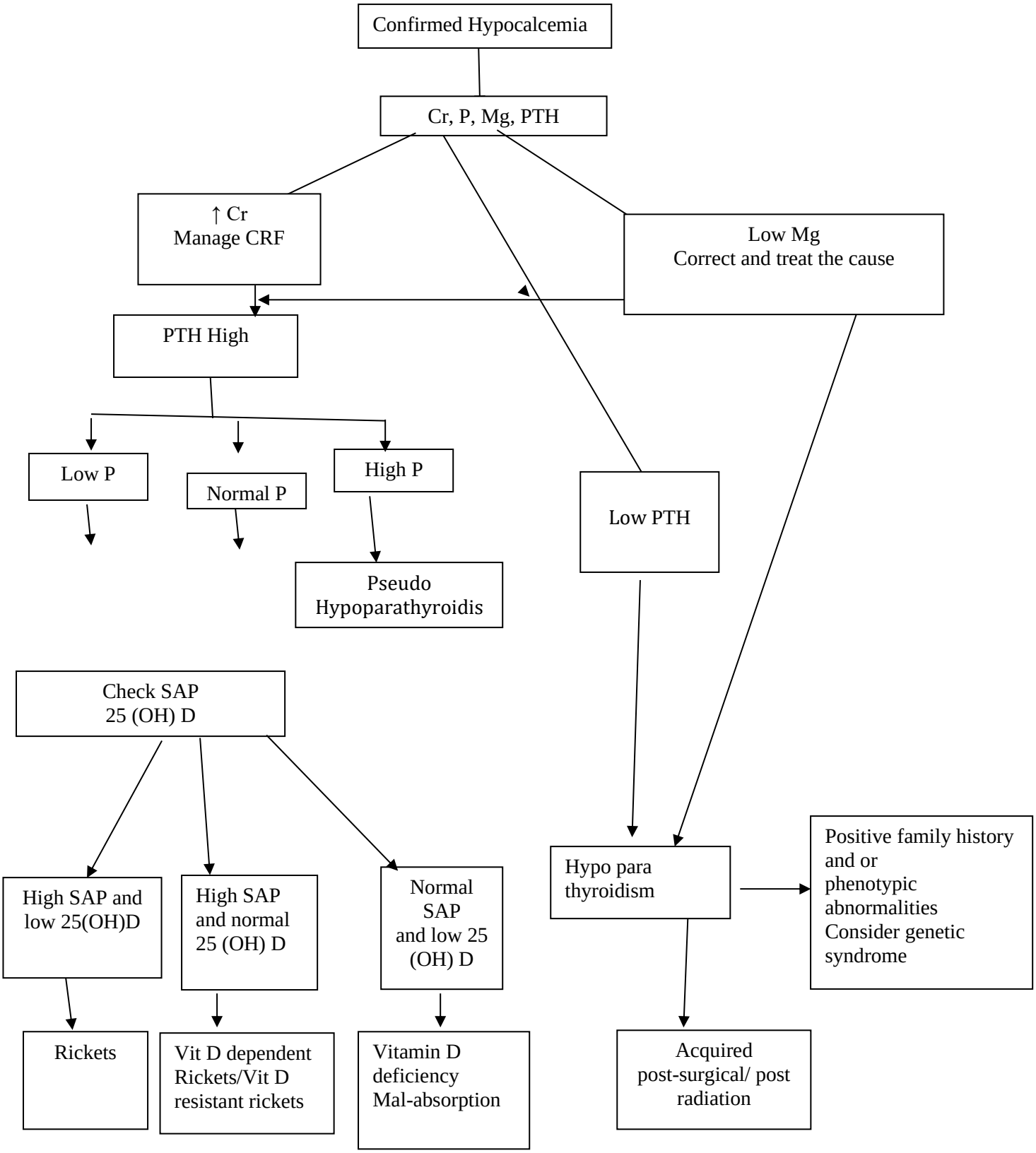
  (vitamin D 3) over 8 to 12 weeks (goal total of ~200,000 to 400,000 IU).

  Infants < 1 month: 1,000 IU daily

  Infants and children 1 month to 5 years: 1,000 to 2,000 IU daily

  Children 5 years to adult: 5,000 to 6,000 IU daily

IV Calcium is hyperosmolar and can cause severe tissue necrosis if extravasation occurs. Select a large vein. Monitor IV site frequently. Rapid IV administration can cause vasodilation, hypotension, bradycardia, syncope, cardiac arrhythmias, and cardiac arrest. Continuous cardiac monitoring is essential during infusion.



Modified from Pepe, J., Colangelo, L., Biamonte, F., Sonato, C., Danese, V. C., Cecchetti, V., Cipriani, C. et.al Diagnosis and management of hypocalcemia. Endocrine. 2020

CASE 1 :

A 2-year-old boy was brought because of absent teeth development and failure to walk. The patient appeared to be well nourished and content. His body mass index was 19.1 kg/m2 (90th percentile), he was 86 cm long (25th percentile) and he weighed 13.6 kg (75th percentile). Palpation of the patient's extremities revealed prominent, flared distal radii, humeri and femurs. The result of a total serum calcium test was 1.4 (normal 2.1–2.6) mmol/L

1.What further history should you elicit?

2.What are the investigations needed?

3.How will you manage this child?

CASE 2 :

13 days/male/ term/2.5 kg admitted with right focal seizures since 2 days.

Born to a 29 year old primi mother who had no pre-existing medical or surgical illness / drug intake. Spontaneous conception. Antenatal period was uneventful. Born by normal vaginal delivery at term. Birthweight was 2.5 kg. Apgar was 8/10 at one minute. Baby was discharged on second day of life. She is on exclusive breast feeds. Serum calcium was 3.6 mg/dL

1.What will be your initial management?

2. How will you clinically evaluate this child?

3. What other investigations will you do?

Hypomagnesemia

Magnesium is a co-factor in many biochemical reactions and essential for cellular function and nerve conduction. Magnesium also affects the electrical activity of the myocardium and vascular tone,
Normal serum magnesium levels are between 1.5 and 2.3 mg/dL(1.2- 1.9mEq/L).
Hypomagnesemia is serum magnesium less than 1.5 mg/dL. There may be variations among clinical laboratories

Etiology of hypomagnesemia

Gastrointestinal	Renal losses	Redistribution of magnesium from the extracellular to the intracellular space
Reduced intake Reduced absorption • Malabsorption • Short bowel syndrome Increased losses Chronic diarrhea Laxative abuse Excessive gastric suctioning or vomiting Hypomagnesemia with secondary hypocalcemia (HSH)	Inherited • Gitelman syndrome • Bartter syndrome Familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC) • Autosomal-dominant hypocalcemia with hypercalciuria (ADHH) • Isolated dominant hypomagnesemia (IDH) with hypocalciuria • Isolated recessive hypomagnesemia (IRH) with normocalcemia • Hypomagnesemia with secondary hypocalcemia (HSH)	• Hungry bone syndrome • Treatment of diabetic ketoacidosis • Refeeding syndrome • Acute pancreatitis
	Drugs: Loop diuretics,cisplatin, amphotericin B, cyclosporine, tacrolimus, and pentamidine,	
	Others Aldosterone excess Hypercalcemia Hypophosphatemia	

Hypomagnesemia is commonly seen in critically ill children often associated with other electrolyte abnormalities like acidosis, hypocalcemia and hypokalemia.

Clinical features include neuromuscular irritability(tremors,tetany, hyperreflexia seizures) and cardiac abnormalties(ventricular tachycardia, torsades de pointes)

Approach to hypomagnesemia includes a detailed history, clinical examination and relevant investigations. Since most patients are asymptomatic and magnesium is not included in routine electrolyte estimations, a high index of suspicion is needed. Consider hypomagnesemia in any child with refractory hypocalcemia or hypokalemia.

Invstigations

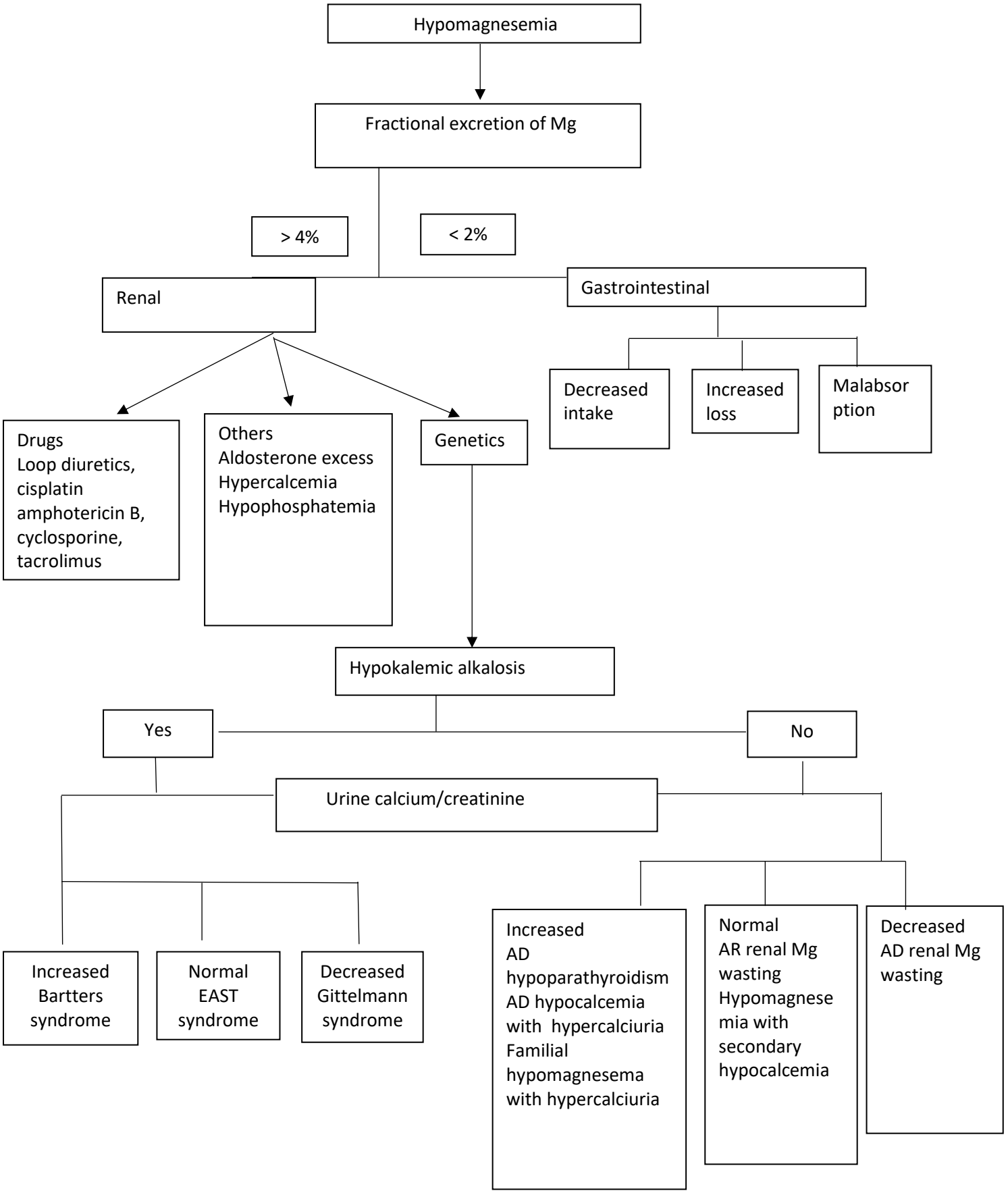
Serum Mg, Ca, Phosphate, sodium, potassium , bicarbonate, serum creatinine, fractional excretion of Mg, urine calcium, creatinine, ECG

FEMg = [(UMg x PCr) / (PMg x UCr x 0.7)] x 100 where UMg is urinary magnesium concentration, PCr is plasma creatinine concentration, PMg is plasma magnesium concentration and Ucr is urinary creatinine concentration. Plasma magnesium concentration is multiplied by 0.7 since 30% is bound to albumin and not filtered at the glomerulus.

Treatment

Severe hypomagnesemia is treated with IV magnesium sulphate at a dose of 25-50mg/kg(0.05 -0.1ml/kg of a 50% solution given slowly. The dose is repeated every 6 hours . After 2 or 3 doses Mg levels are rechecked. Rapid infusion can cause hypotension.The dose is reduced in renal insufficiency. 1ml of 50% MgSo4 contains 500mg of Mg

Long term therapy is often given orally. 10-20mg/kg given 3-4 times a day


Hypomagnesemia
Fractional excretion of Mg
> 4%
< 2%
Renal
Gastrointestinal
Decreased intake
Increased loss
Malabsorption
Drugs
Loop diuretics, cisplatin amphotericin B, cyclosporine, tacrolimus
Others
Aldosterone excess
Hypercalcemia
Hypophosphatemia
Genetics
Hypokalemic alkalosis
Yes
No
Urine calcium/creatinine
Increased
Bartters syndrome
Normal
EAST syndrome
Decreased
Gittelmann syndrome
Increased
AD hypoparathyroidism
AD hypocalcemia with hypercalciuria
Familial hypomagnesema with hypercalciuria
Normal
AR renal Mg wasting
Hypomagnesemia with secondary hypocalcemia
Decreased
AD renal Mg wasting

Hypo/ Hyperkalemia

Contributors: Dr Gowrishankar NC, Dr Prem Kumar L K, Dr Ekambaranath TS, Dr Venkateswari R

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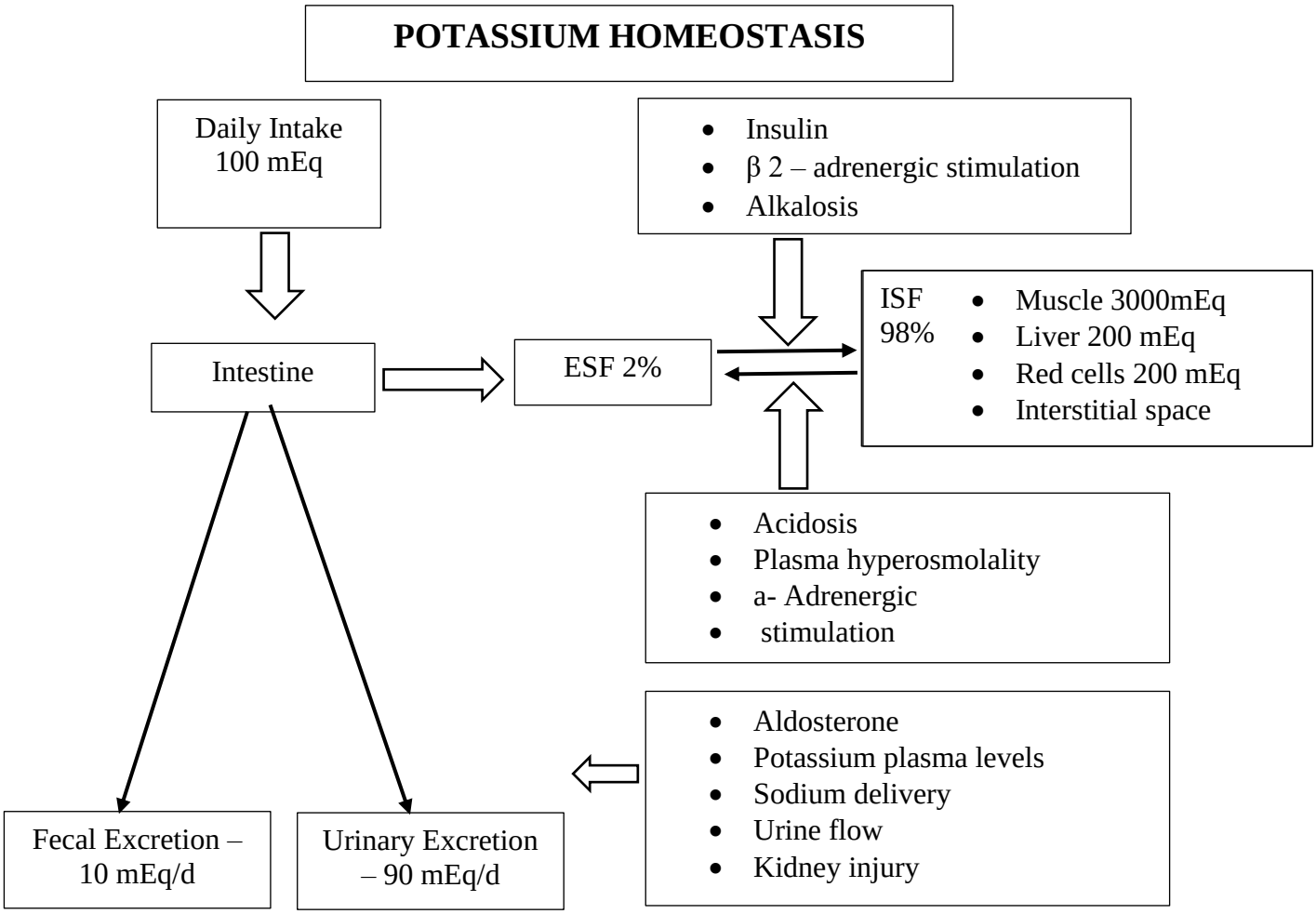


Potassium

- Total body K -50mEq/Kg. Predominantly an intracellular cation. 98% is in the intracellular compartment and majority in the skeletal muscle.
- The normal serum level is 3.5-5.5mEq/L. Higher levels may be seen in newborns and young infants.
- Potassium is essential for growth, to maintain the resting membrane potential of skeletal, smooth, cardiac muscle and nerves. It also helps to regulate cellular volume as well as intracellular calcium content.
- 90% excreted in urine and 10% GIT, sweat. Most of the filtered K is absorbed in the distal convoluted tubule and cortical collecting duct. K is secreted into the tubular lumen in exchange with Na and H ions.

Hyperkalemia

Definition: Serum or plasma concentration of K >5.5mEq/L; in neonates > 6mEq/L (serum K is 0.1-0.7 mmol/L higher)

- Mild hyperkalemia - 5.5-6 mEq/L.
- Moderate hyperkalemia - 6 -7 mEq/L.
- Severe hyperkalemia - >7 mEq/L and or presence of ECG changes

Causes of hyperkalemia

1. Increased K intake- IV/Oral, blood transfusions, parenteral nutrition
2. Increased production followed by transcellular shift-Tumor lysis syndrome, Excessive trauma, rhabdomyolysis, hemolysis, malignant hyperthermia
3. Transcellular shifts- metabolic acidosis, drugs-succinyl choline,beta blockers, digoxin, hyperosmolality(mannitol), hyperkalemic periodic paralysis

Symptoms

May be asymptomatic. Symptoms can range from muscle weakness to ascending flaccid paralysis, palpitations, syncope, arrhythmia and sudden cardiac arrest. Respiratory depression, ileus and paresthesia can occur

ECG changes include tall, peaked T waves, prolonged PR interval, progressive widening of QRS, Sine wave((fusion of QRS and T wave),VT, VF, asystole

A normal ECG does not exclude risk for arrhythmia, as life threatening arrhythmia can occur without warning

HYPOKALEMIA

Definition

- Severe hypokalemia – Potassium level less than 2.5 mEq/L
- Moderate hypokalemia – Potassium level between 2.5 and 3 mEq/L
- Mild hypokalemia – Potassium level between 3 and 3.5 mEq/L

Etiology of hypokalemia

Decreased intake	Increased intracellular uptake	Increased loss-extra renal	Increased Loss-renal	Endocrine
Severe acute malnutrition Anorexia	Metabolic alkalosis Insulin Beta adrenergic agents Heavy metals(barium) Anti -psychotic drugs Hypokalemic periodic paralysis	Diarrhea Emesis Cystic fibrosis	Diuretics DKA Tubulo interstitial disease Bartter syndrome Gitelman syndrome Renal tubular acidosis Amphotericin Liddle syndrome Hypomagnesemia	Aldosterone secreting adenoma Glucocorticoid remediable aldosteronism Apparent mineralocorticoid excess (AME) 11-beta-hydroxylase deficiency 17-alpha-hydroxylase deficiency Thyrotoxicosis

Clinical features

Many patients are asymptomatic. If severe hypokalemia, can present with muscle weakness (headlag, hypotonia, paralysis, respiratory failure, death) cramps, fasciculation and arrhythmias

ECG changes

PR prolongation, flattening of T waves, ST depression, U waves can emerge after the T waves (best seen in the precordial leads).

Management

Emergent treatment is needed in symptomatic patients, or those with ECG changes or severe hypokalemia

- Potassium chloride IV 0.5 to 1 mEq/kg of body weight per hour. The goal is to raise the potassium level by 0.3 to 0.5 mEq/L. May be associated with pain and phlebitis when administered through a peripheral vein. Choose a large vein . External jugular vein is a good option. Maximum adult dose is 40 mEq.

- Do NOT administer undiluted or by IV push . It must always be diluted in infusion fluid (RL or 0.9% sodium chloride).

- Rapid intravenous administration or overdose may cause cardiac arrest. Administer via an infusion pump.
- An infusion with a potassium concentration of no more than 40 mEq/L is given in most situations. Occasionally a higher concentration of 60mEq/L may be needed.
- When adding potassium chloride to an IV fluid bag, mix well by inverting the bag at least 10 times
- Clearly label all bags, syringes, pumps and lines that contain potassium to avoid inadvertent flushing
- Continuous ECG monitoring is needed.
- Serum concentrations should be evaluated 1 to 2 hours after completion of infusion
- May repeat dose as needed based on lab values
- Watch for rebound hyperkalemia
- Iv fluids should not contain dextrose as it can stimulate insulin secretion.

Note: 1 ml of KCl contains 2 mEq.

Asymptomatic patients

Stop diuretics/laxatives and drugs which result in hypokalemia. Use potassium-sparing diuretics if diuretic therapy is required. Treat underlying cause - Diarrhea or vomiting.
Replace ongoing excessive losses.

Moderate hypokalemia: Oral replacement. IV only for those who are unable to take oral medications.

Mild hypokalemia

Increase dietary potassium. Oral K supplements For those who are unable to take enteral potassium, the addition of a maintenance amount of potassium to IV fluids 20mEq/L is sufficient

In asymptomatic patients with chronic hypokalemia (RTA) potassium supplementation may be needed

Oral potassium is preferred over IV potassium in asymptomatic patients. Potassium chloride, phosphate, potassium acetate, potassium citrate-citric acid, and potassium bicarbonate are the various salts available. Potassium chloride is commonly used. Patients with acidosis can be given potassium acetate or citrate.

Dose:
Initial: 1-2 mEq/kg/day in divided doses. Titrate to desired clinical response. Usual range: 1 to 5 mEq/kg/day. Not to exceed 1 to 2 mEq/kg as a single dose up to 40 mEq/dose

Note:

- The strength of K in most commonly available potassium chloride syrup is 20 mEq in 15 ml
- Oral and parenteral potassium can safely be used simultaneously.
- Best taken with or soon after food to reduce gastrointestinal irritation.

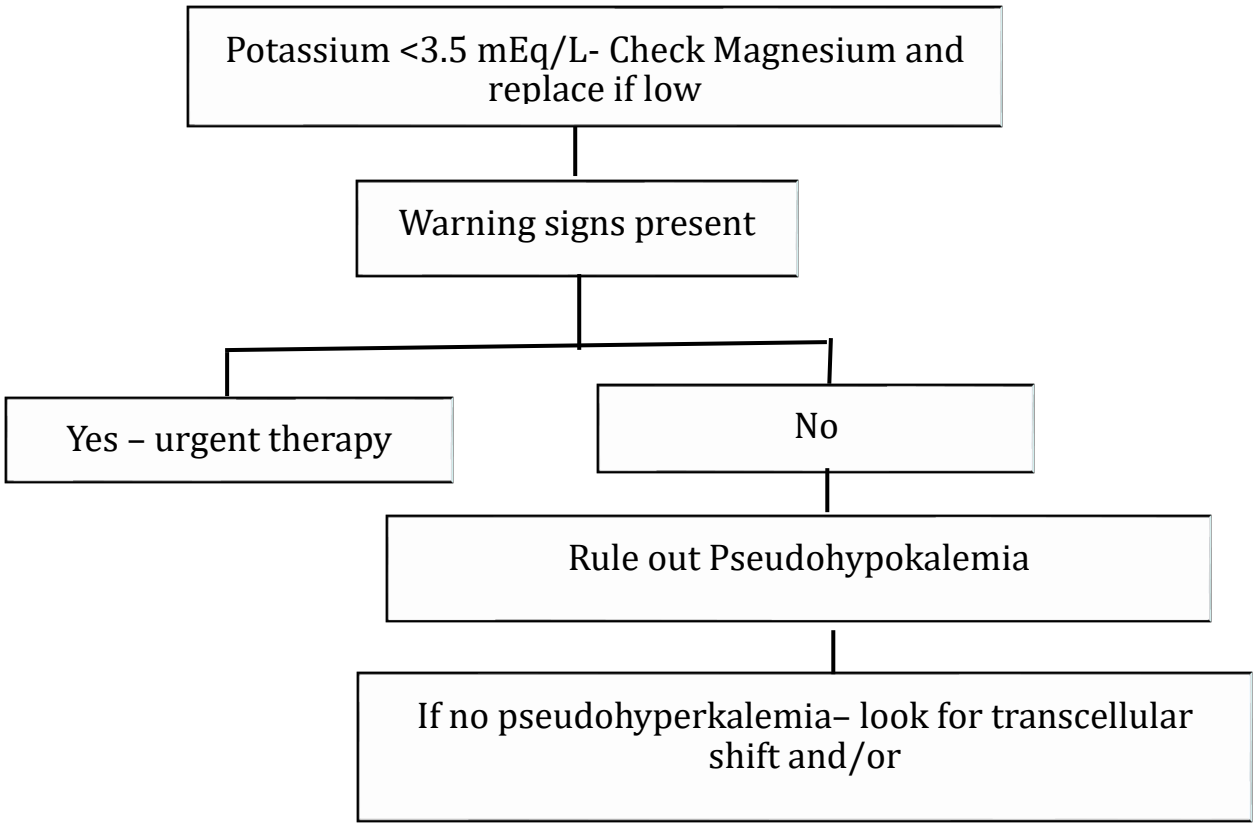
Other treatment:

Magnesium sulphate if hypomagnesemia is the cause.(25-50mg/kg IV over 30 minutes)

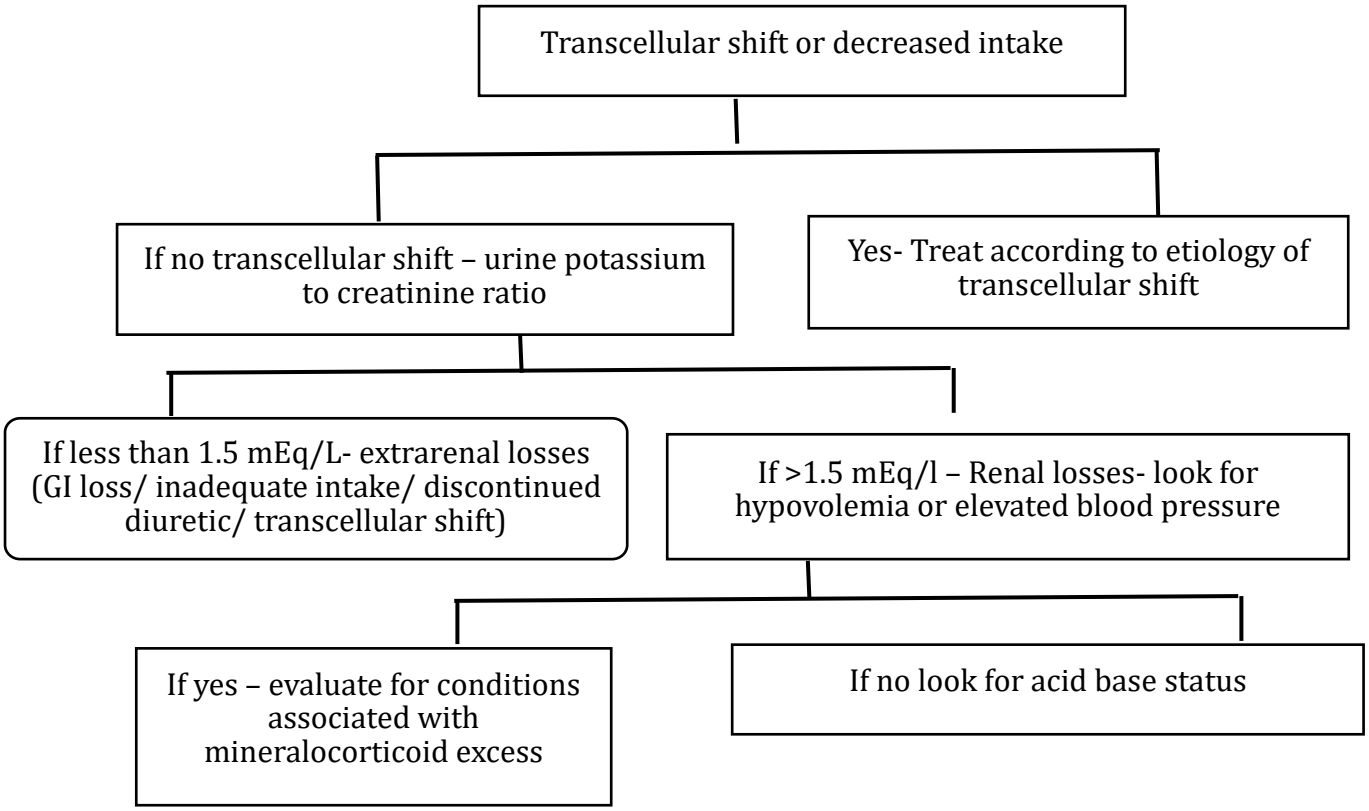
Potassium-sparing diuretic such as amiloride in Bartter, Gitelman

Spironolactone or eplerenone in hyperaldosteronism

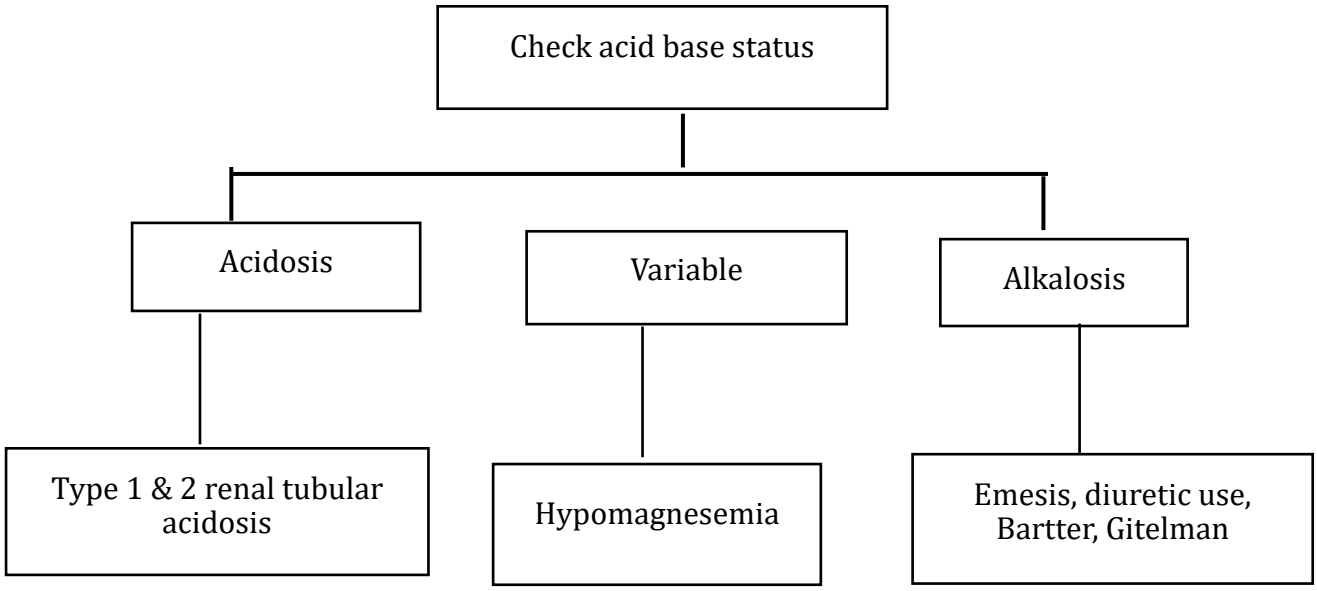
STEP 1- APPROACH TO HYPOKALEMIA



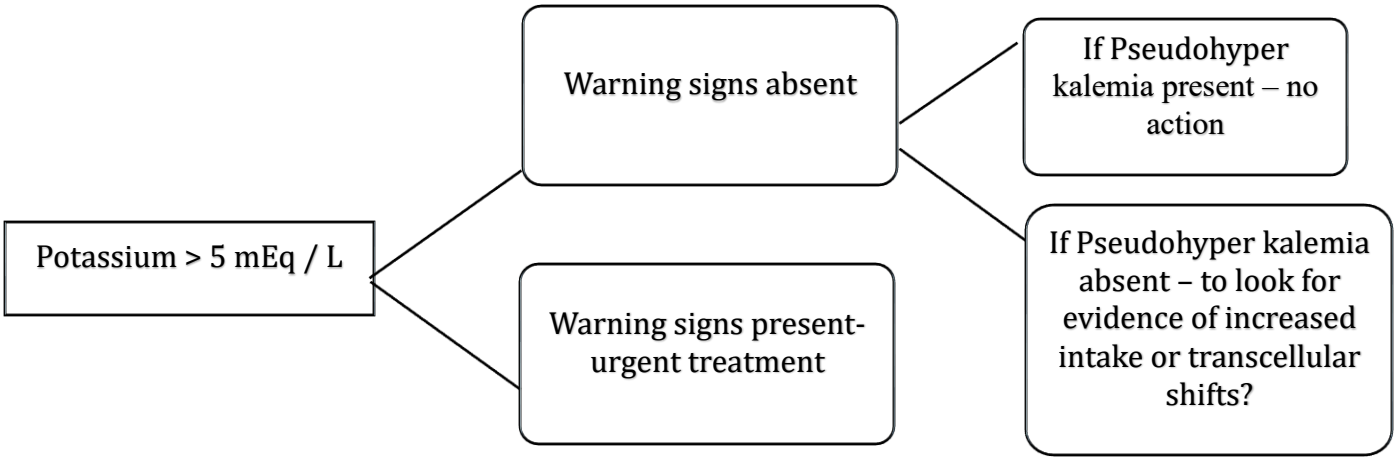
STEP 2- APPROACH TO HYPOKALEMIA



STEP 3- APPROACH TO HYPOKALEMIA



STEP 1- APPROACH TO HYPOKALEMIA



STEP 2- APPROACH TO HYPOKALEMIA