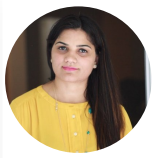


NSS

@SinghNisha9777

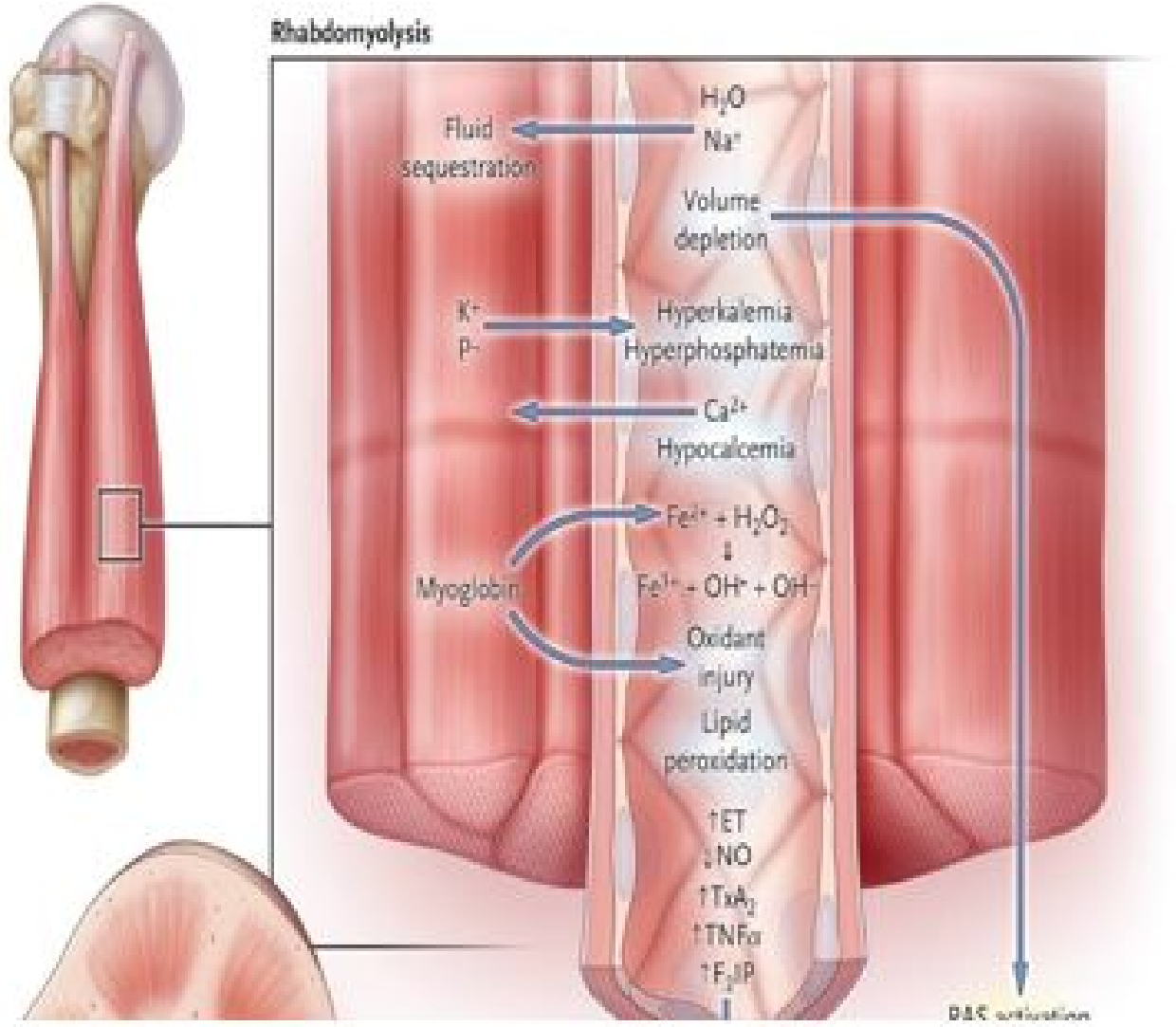
20 Tweets • 2020-11-21 02:30:40 UTC • See on Twitter

rattibha.com

1/ 📢Hello #MedTwitter

We recently had an interesting case-based discussion @ASPNeph pathology webinar.
Here’s what I learned about💥Rhabdomyolysis💥(RM) and AKI!
Let's begin with a poll:
Which one of these is true about RM?
#tweetorial #NephTwitter

2/ Ans: All the above.
💥Rhabdomyolysis💥
The disintegration of skeletal muscle→ release of intracellular constituents (myoglobin, electrolytes & Uric acid) into ECF & circulation



Bosh *et al* N Engl J Med 2009; 361:62-72

3/Let's review 💥pathophysiology💥:

📌Myoglobinemia→ intrarenal vasoconstriction→ direct and ischemic tubule injury

📌Myoglobinuria→ cast formation & tubular obstruction→ cast nephropathy

https://www.nejm.org/doi/10.1056/NEJMra0801327?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub

4/ 💥What are the causes of RM-
While the list is long, some common reasons include-
📌trauma
📌ischemia
📌drugs
📌toxins
📌metabolic disorders
📌infections (#COVID19, the new kid on the block)

Table 1. Major Categories and Commonly Reported Causes of Rhabdomyolysis.

Category	Commonly Reported Cause
Trauma	Crush syndrome
Exertion	Strenuous exercise, seizures, alcohol withdrawal syndrome
Muscle hypoxia	Limb compression by head or torso during prolonged immobilization or loss of consciousness,* major artery occlusion
Genetic defects	Disorders of glycolysis or glycogenolysis, including myophosphorylase (glycogenosis type V), phosphofructokinase (glycogenosis type VII), phosphorylase kinase (glycogenosis type VIII), phosphoglycerate kinase (glycogenosis type IX), phosphoglycerate mutase (glycogenosis type X), lactate dehydrogenase (glycogenosis type XI) Disorders of lipid metabolism, including carnitine palmitoyl transferase II, long-chain acyl-CoA dehydrogenase, short-chain L-3-hydroxyacyl-CoA dehydrogenase, medium-chain acyl-CoA dehydrogenase, very-long-chain acyl-CoA dehydrogenase, medium-chain 3-ketoacyl-CoA, thiolase† Mitochondrial disorders, including succinate dehydrogenase, cytochrome *c* oxidase, coenzyme Q10 Pentose phosphate pathway: glucose-6-phosphate dehydrogenase Purine nucleotide cycle: myoadenylate deaminase
Infections‡	Influenza A and B, coxsackievirus, Epstein–Barr virus, primary human immunodeficiency virus, legionella species *Streptococcus pyogenes, Staphylococcus aureus* (pyomyositis), clostridium
Body-temperature changes	Heat stroke, malignant hyperthermia, malignant neuroleptic syndrome, hypothermia
Metabolic and electrolyte disorders	Hypokalemia, hypophosphatemia, hypocalcemia, nonketotic hyperosmotic conditions, diabetic ketoacidosis
Drugs and toxins	Lipid-lowering drugs (fibrates, statins), alcohol, heroin, cocaine
Idiopathic (sometimes recurrent)	

5/ It is important to remember 💥medications💥.
Which of the following medications cause RM?

6/ All the above

💥Drugs like statins, anti-psychotics, antidepressants, particularly when used with drugs inhibiting CYP450 and CYP3A4 can lead to RM. Here's a quick review of drugs.

Medications causing Rhabdomyolysis

- Amino-caproid acid
- Antidepressants (Tricyclic antidepressants, Venlafaxine, Sertraline, Escitalopram)
- Anti-histaminics
- Anti-psychotics (Aripiprazole, Clozapine, Olanzapine, Risperidone, Olanzapine, Quetiapine)
- Anti-retrovirals (Tenofovir/Abacavir, Raltegravir)
- Colchicine
- Daptomycin
- Depakote
- Interferon alpha
- Lithium
- Ofloxacin/ Levofloxacin
- Statins (particularly in the setting of thyroid abnormalities, liver disease, diabetes, or with other medications metabolized by CYP450- CCBs, ART, macrolides, Amiodarone)

Nance et al. Diagnostic evaluation of rhabdomyolysis. *Muscle Nerve*. 2015

7/💥 Is AKI and CK levels related?!

The risk of AKI is low if CK level < 15,000 to 20,000 U/L

⚡exceptions are⚡

📌Sepsis

📌Dehydration

📌Acidosis

In these conditions, AKI is seen with CK levels as low as 5000 U/L

https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/610166

Cureus. 2019 Mar; 11(3): e4197.
Published online 2019 Mar 6. doi: 10.7759/cureus.4197
PMCID: PMC6504020
PMID: 31106097

A Late Presentation of Substance-related Rhabdomyolysis with Normal Serum Creatine Kinase Levels and Complicated with Acute Tubular Necrosis

Monitoring Editor: Alexander Muacevic and John R Adler

Asrar Ahmad,[1] Muhammad A Zain,[2] Ammar A Ashfaq,[1] and Waqas Ullah[1]

Author information ▸ Article notes ▸ Copyright and License information Disclaimer

8/💥 What are the initial complications of RM induced AKI? #boardreview @RoshanPGeorgeMD

9/ Ans-Hypocalcemia

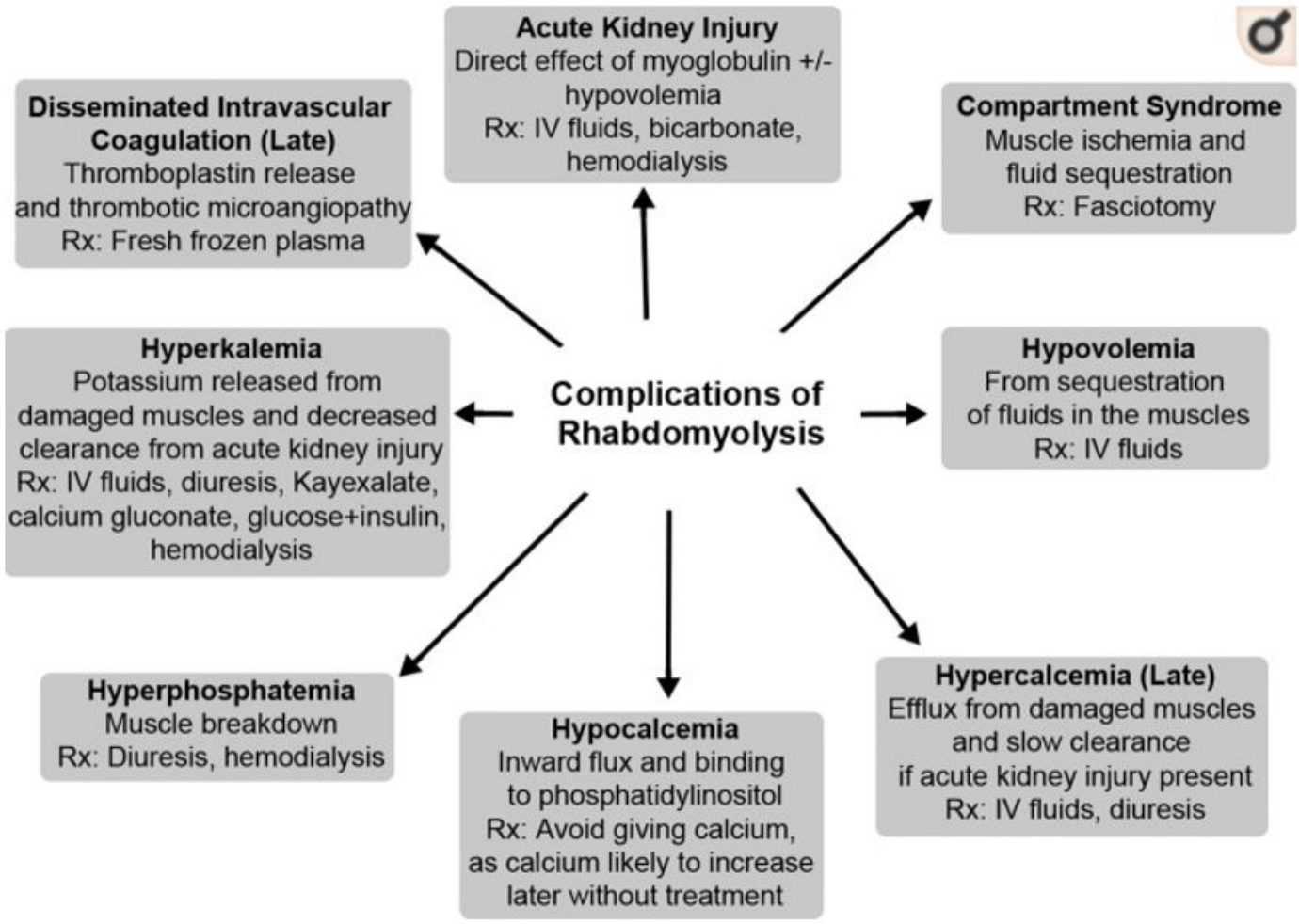
💥Complications💥 of RM

📌↓Ca: entry of Ca into ischemic muscle cells & precipitation of Ca-Phos

📌↑Ca (during recovery): mobilized from the muscles cell

📌↑K, Phos, Uric acid & Mg: released from damaged cells, ↓ clearance if AKI

📌HAGMA (if AKI present)



Elsayed EF, Reilly RF. Rhabdomyolysis: a review, with emphasis on the pediatric population. Pediatr Nephrol. 2010. PMID: 19529963

10/ 💥Diagnosis💥

📌📝History

📌UA: myoglobinuria → ➕heme (dipstick)

📌🔬microscopy: ➕myoglobin casts, ➖ RBC

📌🧪Labs: ↑creatinine, ↑CK & dyselectrolytemias

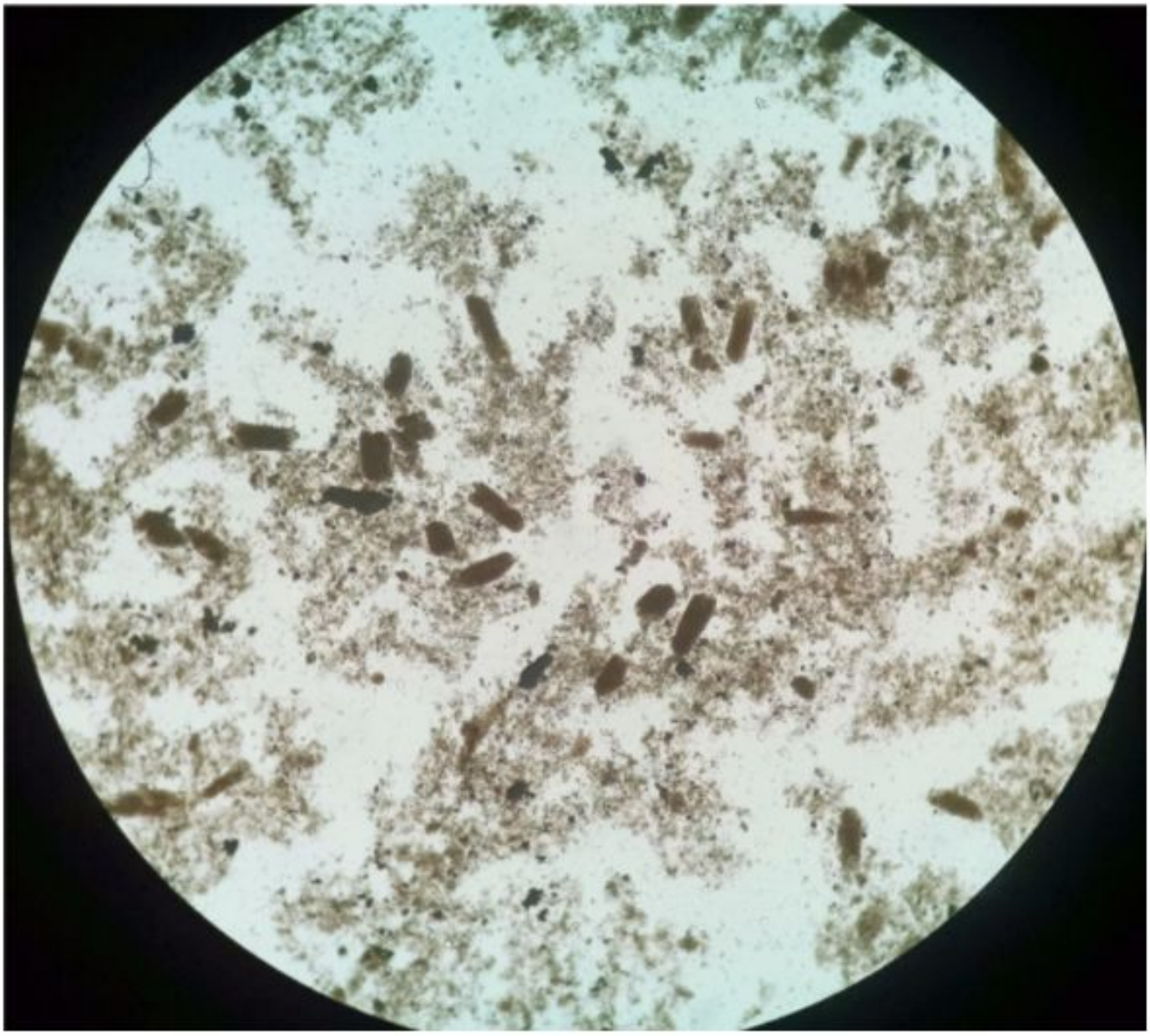


Figure 5. Myoglobin casts. Fresh and unstained urine sediment. Original magnification 100x. Bright field microscopy. Courtesy: José A. T. Poloni.

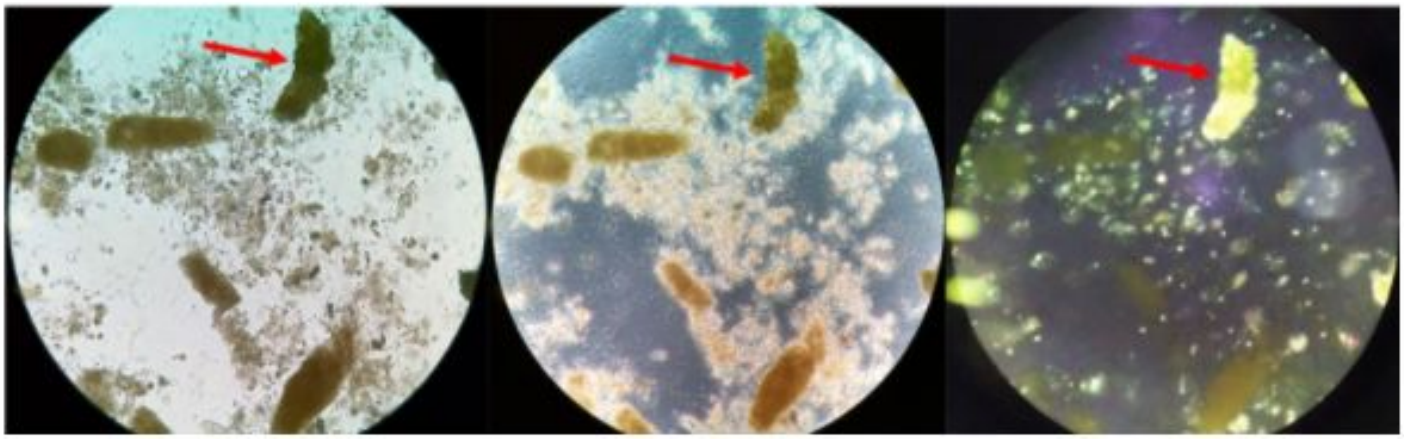
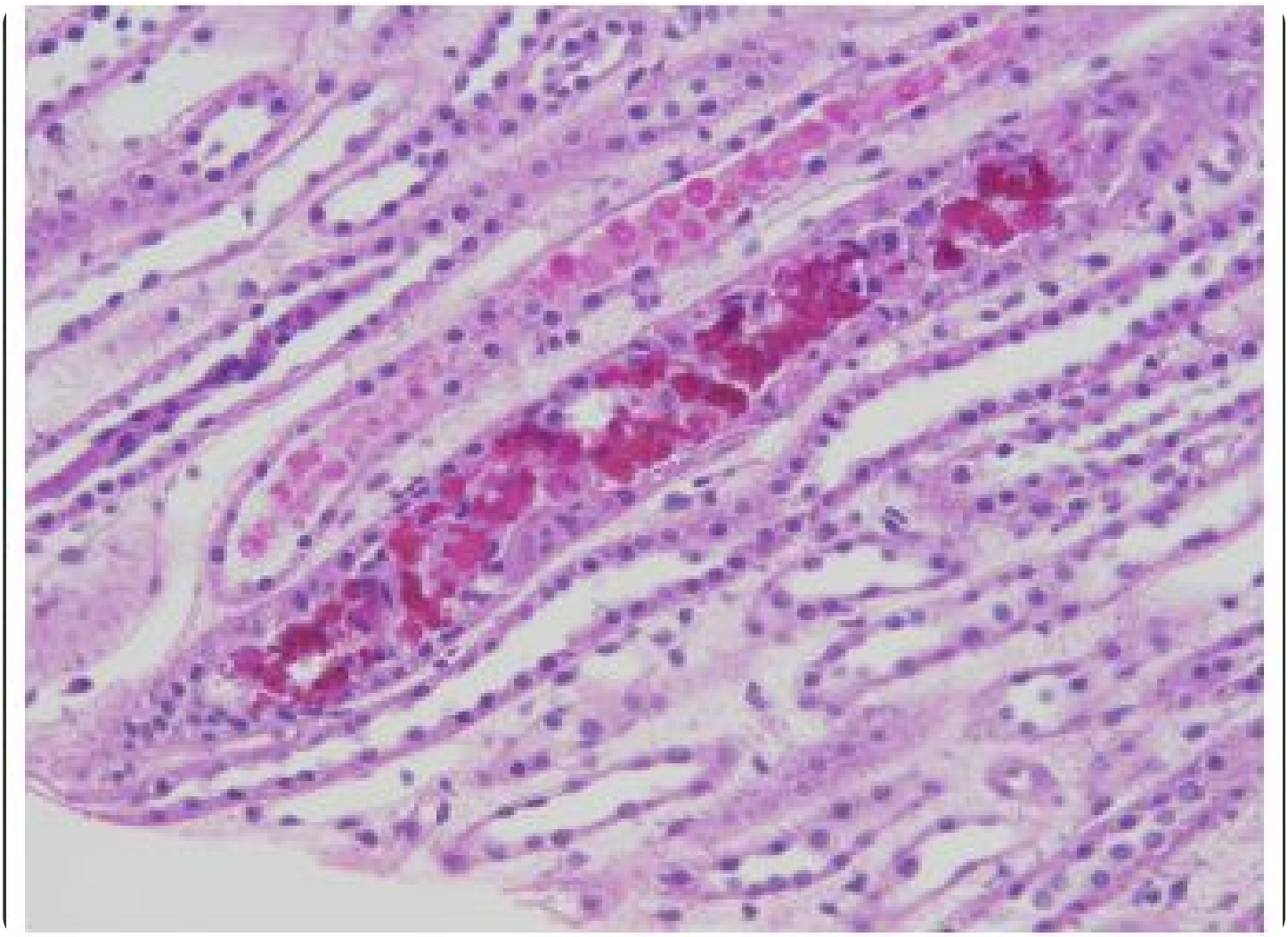


Figure 6. Myoglobin casts and urate/uric acid crystals cast (arrow). Fresh and unstained urine sediment. Original magnification 400x. Left: Bright field microscopy; Center: Phase contrast microscopy; Right: Polarized light microscopy. Tesser Poloni JA, Perazella MA. Am J Med Sci. 2018.

11/ 💥Biopsy is not usually necessary, but when performed shows-
⚡myoglobin cast nephropathy⚡
reddish globular casts in distal tubule with associated acute tubular injury (H&E stain)

https://www.ajkd.org/article/S0272-6386(16)30648-5/fulltext



12/💥 Main treatment approach to prevent AKI is 🌊🥤Hydration 💧💦

📌Isotonic fluids are preferred
📌hydrate to maintain a urine output of at least 200 mL/h
📌hydrate until CK level below 1000 U/L

13/💥 Is alkalinization of urine recommended?

Well, data is inconsistent and conflicting!

⚡Alkalinisation⚡ of urine →

📌↓cast formation by ↑excretion of myoglobin,

📌stabilizes myoglobin- Ferrin complex (↓oxidative damage)

📌↓renal vasoconstriction

📌↓risk of hyper K

14/ 💥RCTs are needed to determine if the addition of bicarbonate and mannitol therapy is of any benefit.

Here are some studies that looked into it-

Table 4. Comparative Studies on Preventive and Therapeutic Regimens in Rhabdomyolysis.

Study	Study Design	Patient Group	No. in Sample	Therapeutic Strategy	Outcome in Patients with Acute Kidney Injury
Shimazu et al.[34]	Retrospective	Patients with the crush syndrome	14	Late vs. early initiation of therapy; high (>10 liters for 48 hours) vs. low volume of hydration	Better if therapy initiated early; high volume of hydration better
Gunal et al.[35]	Retrospective	Patients with the crush syndrome	16	Early vs. late treatment with normal saline followed immediately by bicarbonate	Better if treatment initiated early
Homsi et al.[36]	Retrospective	Patients in the intensive care unit	24	Normal saline vs. normal saline plus bicarbonate and mannitol	No difference
Brown et al.[37]	Retrospective	Patients with trauma	2083	Normal saline vs. bicarbonate plus mannitol	No difference
Cho et al.[38]	Prospective, randomized	Patients with intoxication from doxylamine	28	Ringer's lactate vs. normal saline; bicarbonate if urine pH is <6.5	No effect on peak creatine kinase level or recovery with Ringer's lactate as compared with normal saline; more bicarbonate needed with normal saline than with Ringer's lactate

Bosh *et al* N Engl J Med 2009; 361:62-72

15/ When is dialysis/ KRT recommended?

📌Resistant symptomatic hyperkalemia (>6.5 mEq/L) or rapidly rising serum K

📌Oliguria (<0.5 mL/Kg for 12 hours) or, anuria +/- volume overload

📌Resistant metabolic acidosis (pH<7.1)

17/ 💥What's a better modality in removing myoglobin from circulation?

📌iHD- does not remove myoglobin

📌CRRT (CVVHF and CVVHDF)- super high-flux filters & high volumes of ultrafiltration (convection) can remove myoglobin

📌Plasmapheresis: not effective

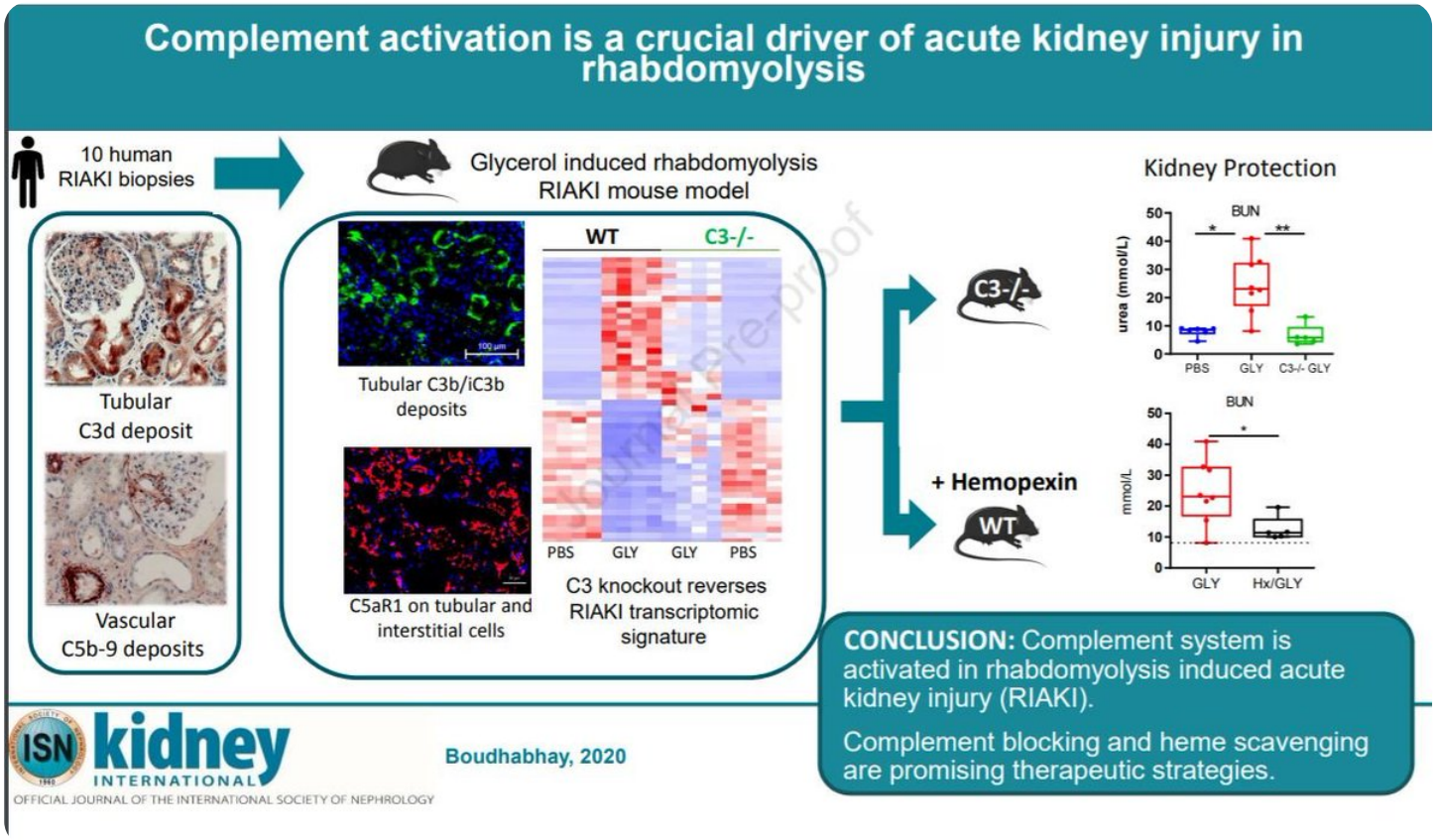
https://www.karger.com/Article/Abstract/343564

18/ 💥Newer therapies💥

📌Antioxidants (pentoxifylline, Vit E, & Vit C)→ possibly ↓tubular free radical injury

📌Acetaminophen- ↓free radical formation (Boutaud 2010)

📌Recently, complement activation was shown as🔑driver of AKI, with complement blocking as a potential Rx



19/ 💥Prognosis of AKI:
In ICU patients,
📌59% mortality when AKI is present
Versus
📌22% when no AKI.

https://www.nejm.org/doi/full/10.1056/nejmra0801327

20/ 💥Thank you for scrolling till the end!
That's all for today, let's end with a quick poll.
At what point would you admit a patient with isolated RM for hydration?

21/ Until next time...
@AsphNeph
#FellowFOAMgroup
@CaoimheCostigan @RoshanPGeorgeMD @drM_sudha
@pedsnephrology @kidnyhealth

contents of this publication.