Rhabdomyolysis

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Connecticut Children's

What is a Clinical Pathway?

An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

Objectives of Pathway

- To establish appropriate admission and discharge criteria for rhabdomyolysis
- To standardize inpatient management of rhabdomyolysis
- To decrease the rate of acute renal failure secondary to rhabdomyolysis

What is Rhabdomyolysis?

- Syndrome characterized by the breakdown of skeletal muscle leading to the release of intracellular muscle constituents, including CK and myoglobin, into circulation
- Most common etiologies in children are viral illnesses, exercise, and trauma

Why is Pathway Necessary?

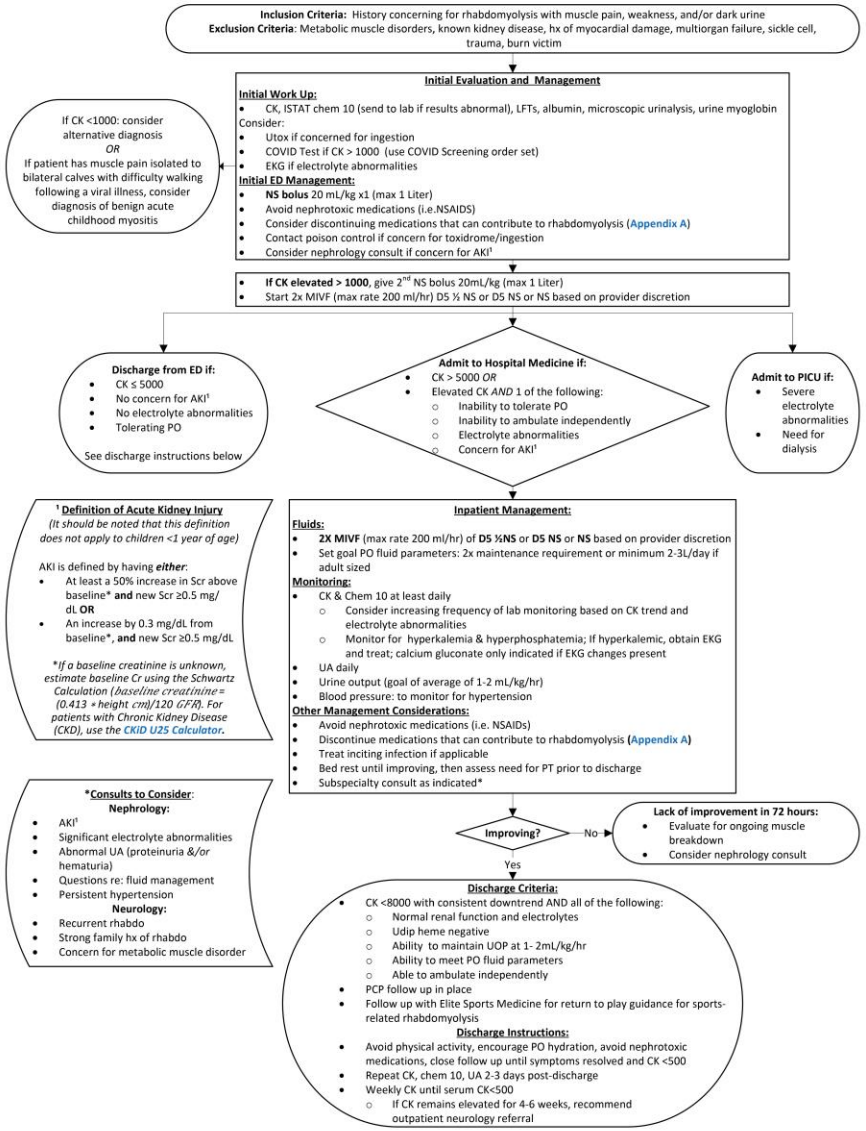
- Rhabdomyolysis severity can range from mild elevation in muscle enzymes to life threatening disease secondary to electrolyte imbalance and acute kidney injury, or even acute renal failure.
- Data for pediatric patients with rhabdomyolysis is limited, however the mainstays of treatment are prompt fluid resuscitation and minimizing further muscle damage.
- Prior to this pathway, Connecticut Children's had no standardized approach for the evaluation in the emergency room, admission criteria, inpatient management, discharge criteria, or post-discharge counseling and follow up recommendations for children presenting with rhabdomyolysis.

This is the Rhabdomyolysis Clinical Pathway.

We will be reviewing each component in the following slides.

CLINICAL PATHWAY:
Rhabdomyolysis

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



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Inclusion Criteria: History concerning for rhabdomyolysis with muscle pain, weakness, and/or dark urine
Exclusion Criteria: Metabolic muscle disorders, known kidney disease, hx of myocardial damage, multiorgan failure, sickle cell, trauma, burn victim

If CK <1000: consider alternative diagnosis
OR
If patient has muscle pain isolated to bilateral calves with difficulty walking following a viral illness, consider diagnosis of benign acute childhood myositis

Initial Evaluation and Management

Initial Work Up:
- CK, ISTAT chem 10 (send to lab if results abnormal), LFTs, albumin, microscopic urinalysis, urine myoglobin

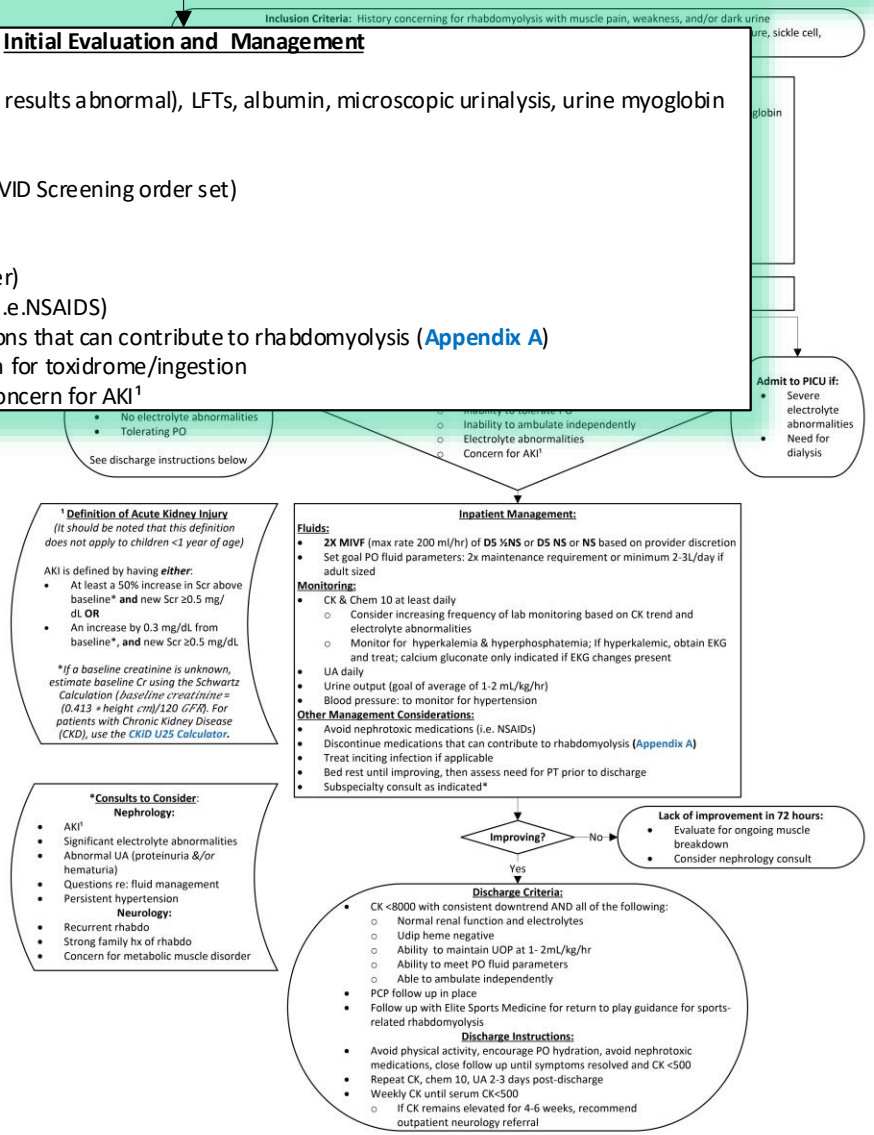
Consider:
- Utox if concerned for ingestion
- COVID Test if CK > 1000 (use COVID Screening order set)
- EKG if electrolyte abnormalities

Initial ED Management:
- **NS bolus** 20 mL/kg x1 (max 1 Liter)
- Avoid nephrotoxic medications (i.e.NSAIDS)
- Consider discontinuing medications that can contribute to rhabdomyolysis (**Appendix A**)
- Contact poison control if concern for toxidrome/ingestion
- Consider nephrology consult if concern for AKI[1]

Inclusion and Exclusion criteria:

- Consider common causes when obtaining the history
- Viral infection, overexertion, trauma, ingestion, underlying inherited metabolic

The most common presentation of Rhabdo in children is muscle pain, fever, symptoms of a viral infection, and muscle weakness.
- Dark urine is present <5% of children at presentation



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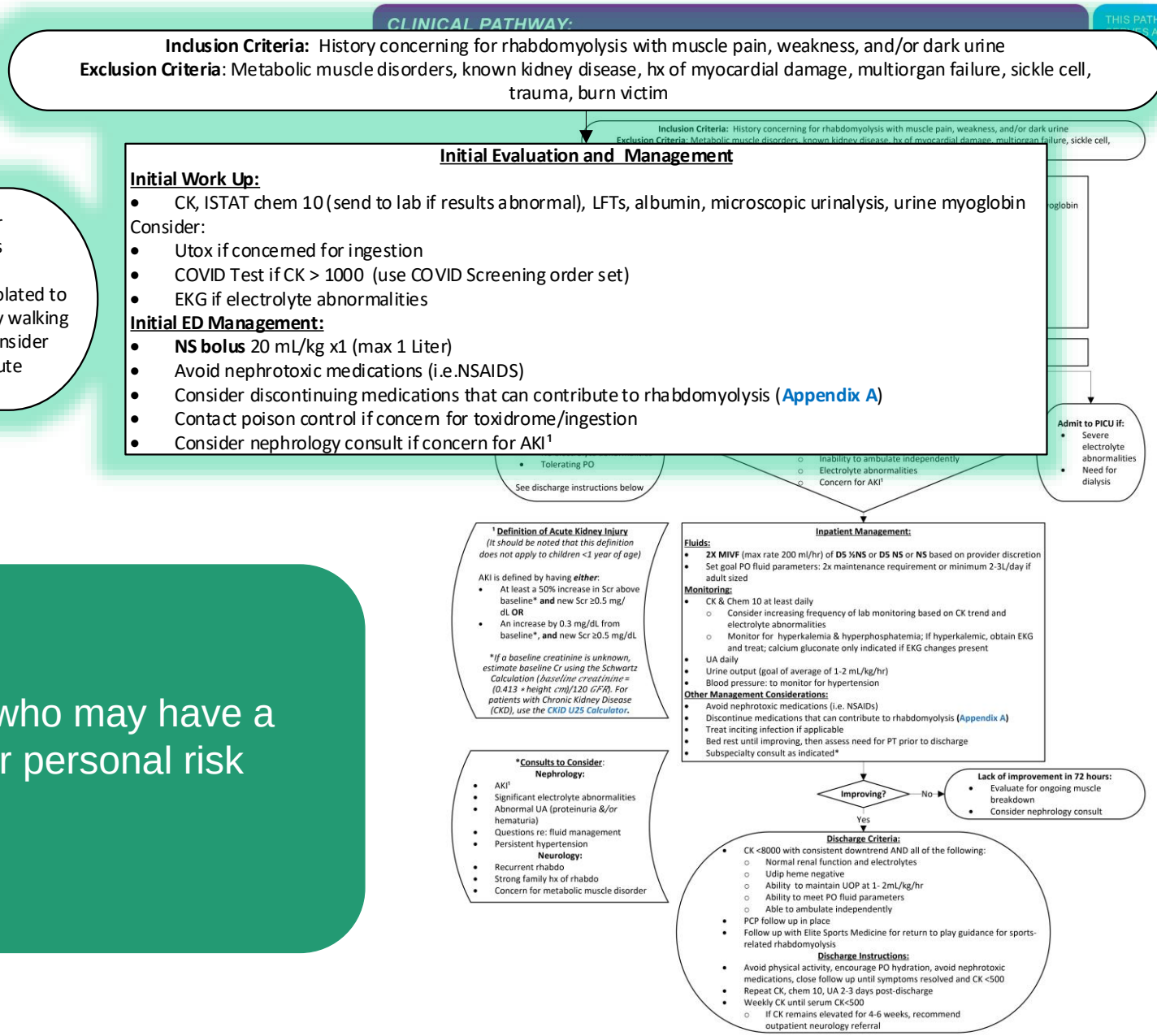
Consider Benign Acute Childhood Myositis if pain is limited to bilateral calves with difficulty walking following a viral illness.

- Child will have elevated CK but no myoglobulinuria

If CK <1000: consider alternative diagnosis
OR
If patient has muscle pain isolated to bilateral calves with difficulty walking following a viral illness, consider diagnosis of benign acute childhood myositis

Inclusion and Exclusion criteria:

- Exclusion criteria include individuals who may have a different clinical course based on their personal risk factors
  - Should be managed off pathway



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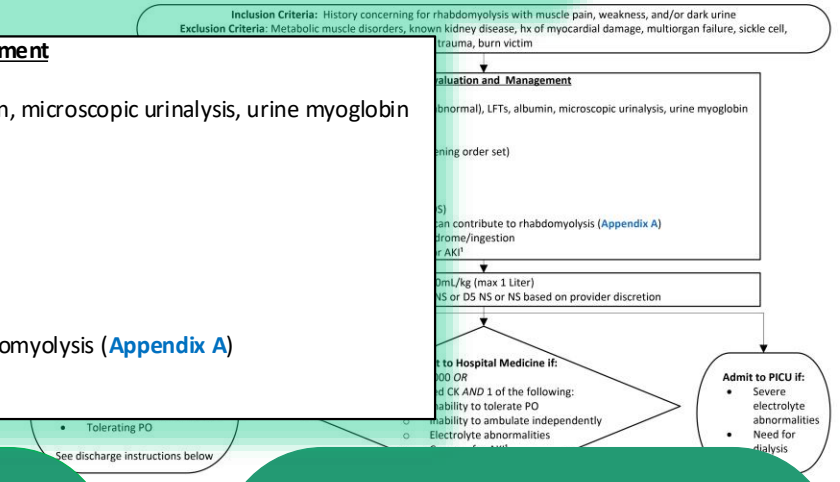


Common causes of Rhabdo:

- Cause often varies by age:
  - Younger children, viral is most common,
  - Adolescents, trauma is most common

Ingestion:

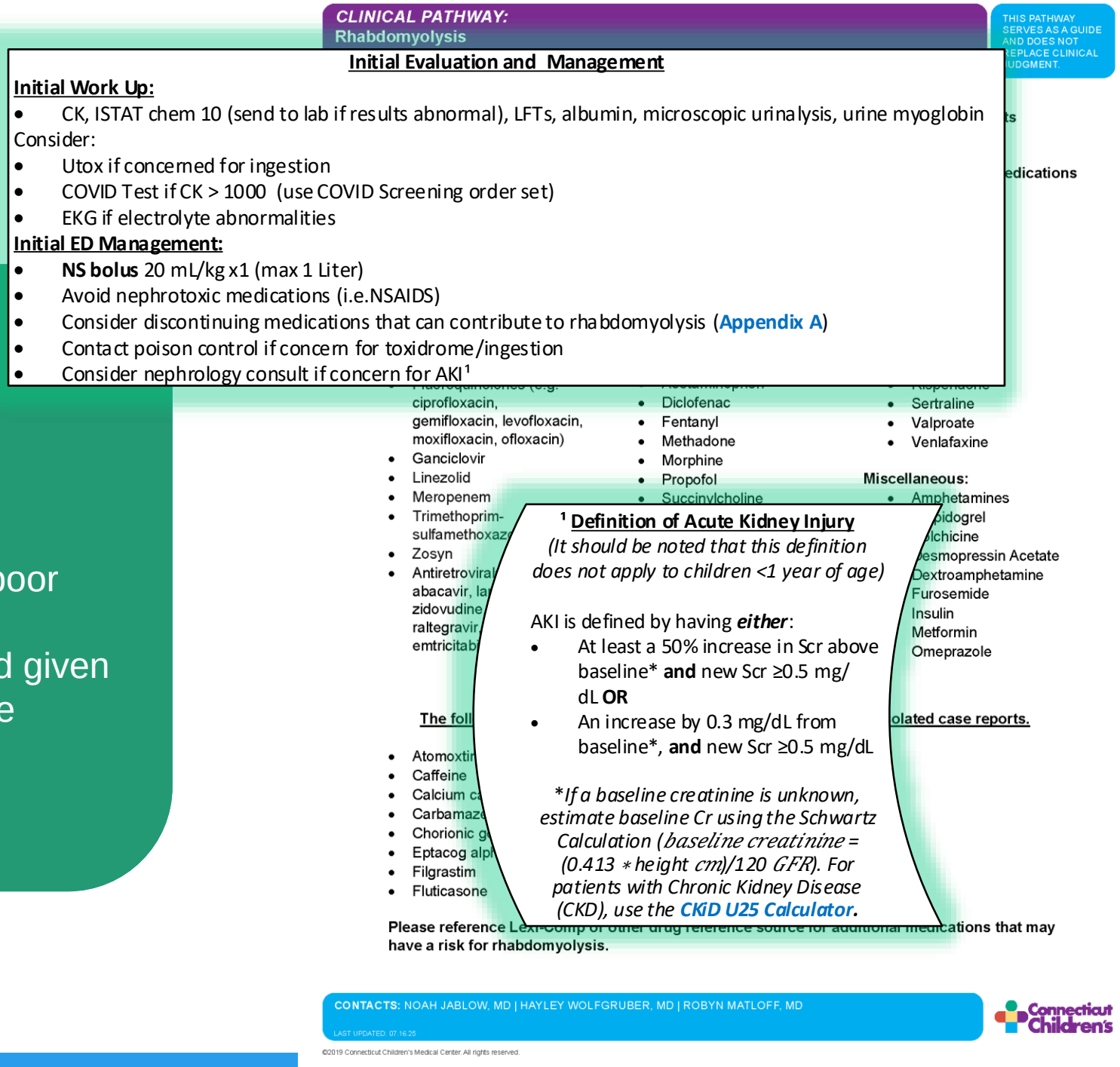
- Consider both prescribed medications (statins, antipsychotics) and illicit drugs (alcohol, cocaine, amphetamines)
  - See Appendix A

Overexertion:

- Risk factors include: inadequate hydration, extreme heat, unconditioned athlete, impaired sweating, concurrent supplement, NSAID, and/or statin use

Diagnosing Rhabdo:

- Albumin is helpful to know when administering large volume of fluid
- Urine myoglobin has high sensitivity, poor specificity
- Serum myoglobin is not recommended given its short half and thus high rate of false negatives



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ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, ofloxacin)
- Ganciclovir
- Linezolid
- Meropenem
- Trimethoprim-sulfamethoxaz
- Zosyn
- Antiretroviral abacavir, la zidovudine raltegravir emtricitab

- Diclofenac
- Fentanyl
- Methadone
- Morphine
- Propofol
- Succinylcholine

- Sertraline
- Valproate
- Venlafaxine

Miscellaneous:

- Amphetamines
- pidogrel
- lchicine
- esmopressin Acetate
- Dextroamphetamine
- Furosemide
- Insulin
- Metformin
- Omeprazole

The foll … **olated case reports.**

- Atomoxti
- Caffeine
- Calcium c
- Carbamaz
- Chorionic g
- Eptacog alp
- Filgrastim
- Fluticasone

Please reference Lexi-Comp or other drug reference source for additional medications that may have a risk for rhabdomyolysis.

[1] Definition of Acute Kidney Injury

(It should be noted that this definition does not apply to children <1 year of age)

AKI is defined by having ***either***:

- At least a 50% increase in Scr above baseline* **and** new Scr ≥0.5 mg/dL **OR**
- An increase by 0.3 mg/dL from baseline*, **and** new Scr ≥0.5 mg/dL

If a baseline creatinine is unknown, estimate baseline Cr using the Schwartz Calculation (baseline creatinine = (0.413 ∗ height cm)/120 GFR). For patients with Chronic Kidney Disease (CKD), use the **CKiD U25 Calculator.*

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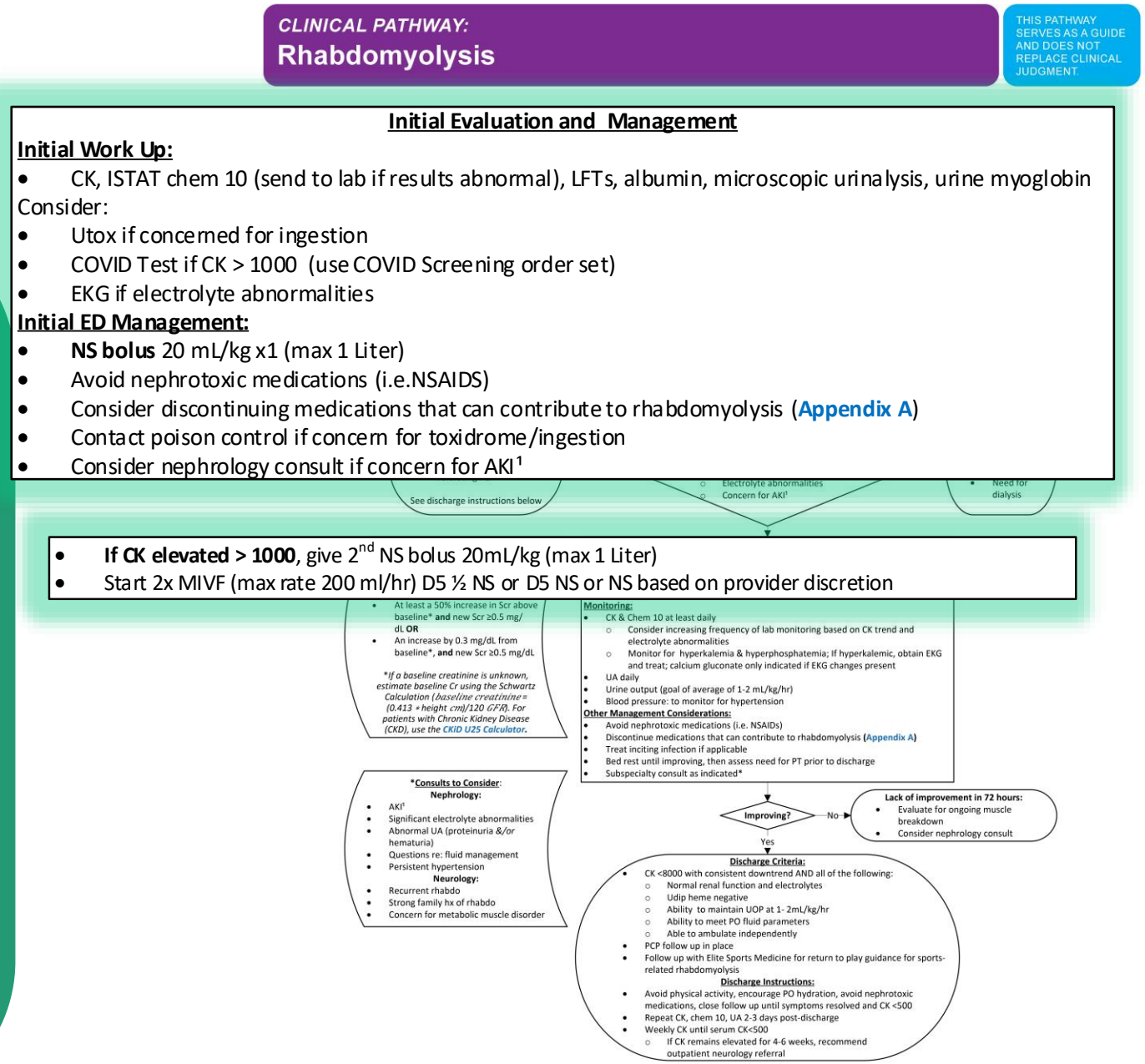
Initial management:

- Fluids are the mainstay of initial therapy
  - Begin with a 20mL/kg normal saline bolus
  - A patient may need a 2nd bolus if CK >1000K
  - Then start IVF at 2 x maintenance rate
- Consult Nephrology if acute kidney injury (AKI)
- Discontinue and avoid any nephrotoxic medications or medications that may contribute to rhabdomyolysis
  - Refer to Appendix A

***Note max bolus volumes and daily fluid goals



CLINICAL PATHWAY:
Rhabdomyolysis
Appendix A: Medications Associated with Rhabdomyolysis

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Anti-arrhythmic:
- Amiodarone
- Diltiazem

Anti-infectives:
- Amoxicillin
- Amphotericin-B
- Azithromycin
- Cefaclor
- Cefdinir
- Clarithromycin
- Daptomycin
- Erythromycin
- Fluconazole
- Fluoroquinolones (e.g. ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, ofloxacin)
- Ganciclovir
- Linezolid
- Meropenem
- Trimethoprim-sulfamethoxazole
- Zosyn
- Antiretrovirals (e.g. abacavir, lamivudine, zidovudine, tenofovir, raltegravir, efavirenz, emtricitabine)

Anti-Lipemics:
- Atorvastatin
- Ezetimibe
- Fenofibrate
- Fluvastatin
- Gemfibrozil
- Lovastatin
- Pitavastatin
- Pravastatin
- Rosuvastatin
- Simvastatin

Anesthetics/Pain Control/Paralytics:
- Acetaminophen
- Diclofenac
- Fentanyl
- Methadone
- Morphine
- Propofol
- Succinylcholine
- Rocuronium

Anti-hypertensive
- Amlodipine
- Candesartan
- Losartan
- Ramipril

Immunosuppressants
- Cyclosporine

Neuro/Psychiatric Medications
- Aripiprazole
- Citalopram
- Clozapine
- Escitalopram
- Haloperidol
- Lamotrigine
- Olanzapine
- Paroxetine
- Pregabalin
- Quetiapine
- Risperidone
- Sertraline
- Valproate
- Venlafaxine

Miscellaneous:
- Amphetamines
- Clopidogrel
- Colchicine
- Desmopressin Acetate
- Dextroamphetamine
- Furosemide
- Insulin
- Metformin
- Omeprazole

The following medications are linked to rhabdomyolysis in small, isolated case reports. Clinical discretion is advised.

- Atomoxtine
- Caffeine
- Calcium carbonate
- Carbamazepine
- Chorionic gonadotrophin
- Eptacog alpha
- Filgrastim
- Fluticasone
- Ganciclovir
- Itraconazole
- Montelukast
- Mycophenolate
- Oseltamivir
- Tacrolimus
- Vecuronium

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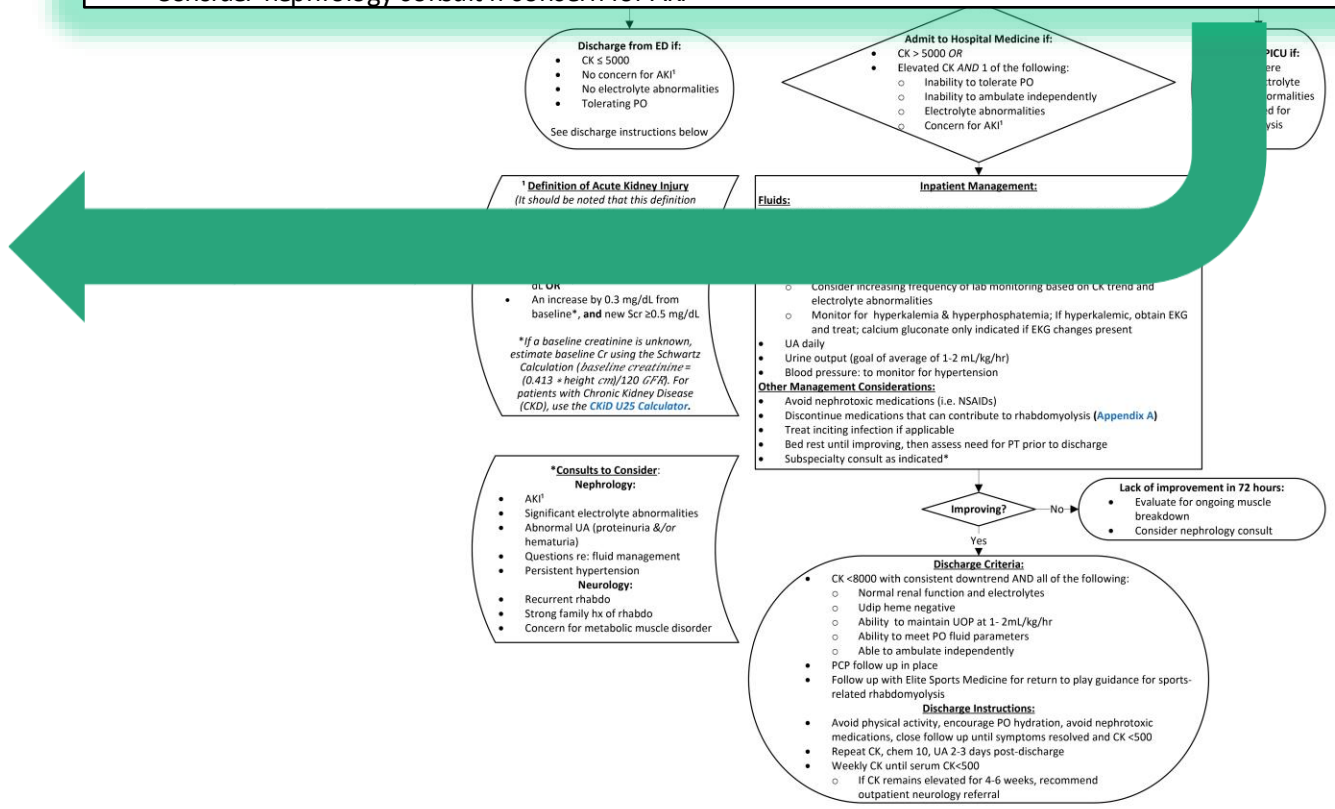

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CLINICAL PATHWAY:

Rhabdomyolysis

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Discharge from ED if:

- CK ≤ 5000
- No concern for AKI[1]
- No electrolyte abnormalities
- Tolerating PO

See discharge instructions below

Admit to Hospital Medicine if:

- CK > 5000 *OR*
- Elevated CK *AND* 1 of the following:
  - Inability to tolerate PO
  - Inability to ambulate independently
  - Electrolyte abnormalities
  - Concern for AKI[1]

Admit to PICU if:

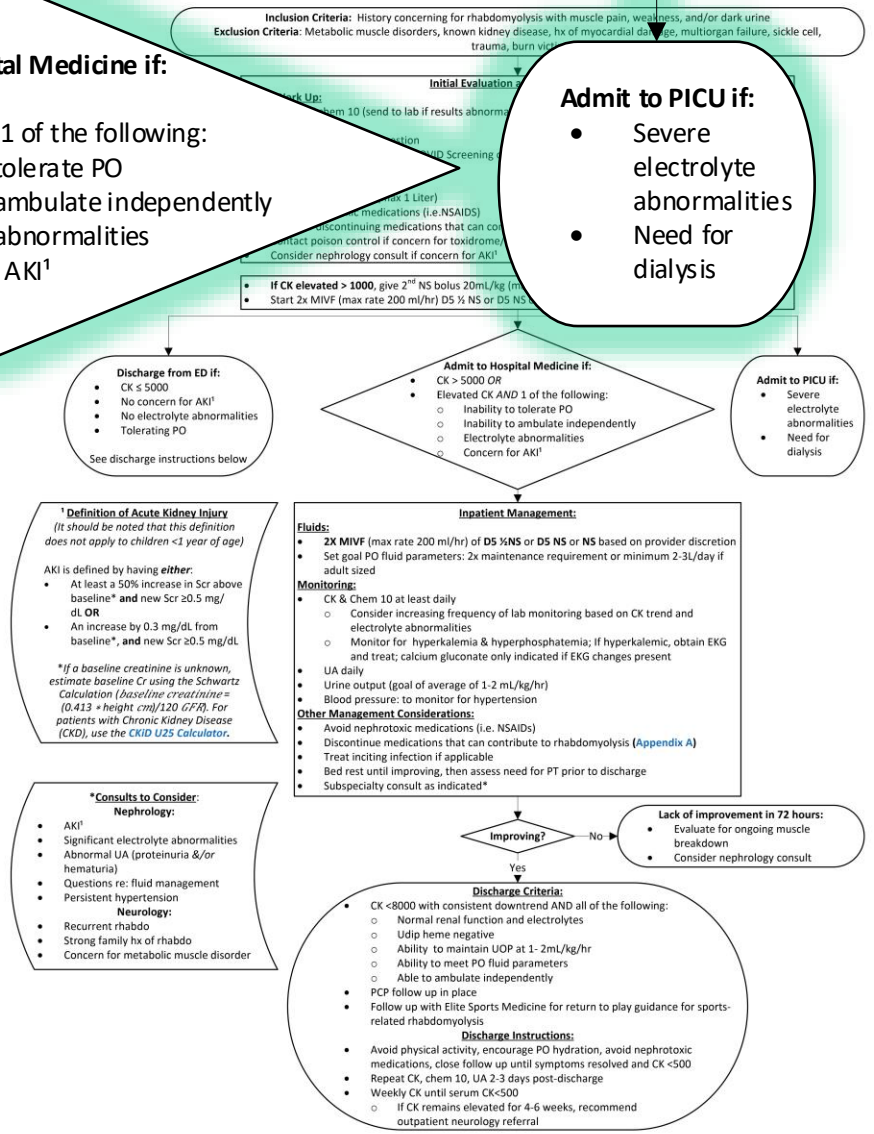
- Severe electrolyte abnormalities
- Need for dialysis

Admission Criteria:

- Patients require admission if CK is greater than 5000 or CK is elevated and has certain risk factors

If Discharging from the ED, provide education to:

1. Maintain adequate hydration (goal for an adult size patient is 2-3L)
2. Refrain from activity (provide school note if necessary)
3. Avoid nephrotoxic medications (such as ibuprofen)
4. Follow up with PCP in 24-48 hours for repeat lab work and serial monitoring of CK until < 500



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- Fluids:
  - D5 ½ NS or D5NS **without** Potassium
  - Fluids should run at 2 x maintenance
  - Watch for iatrogenic hyponatremia

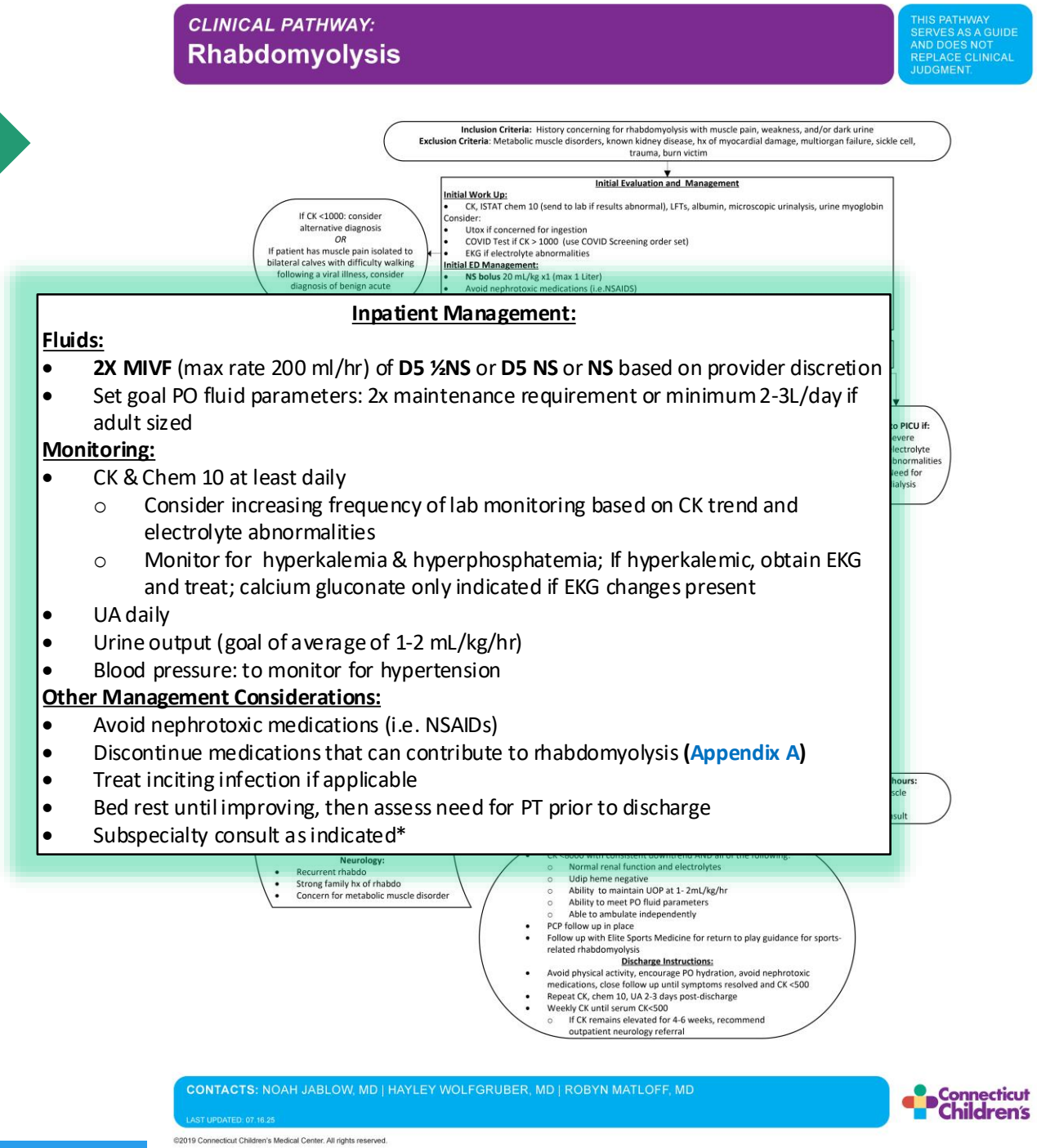
Monitor for hyperkalemia, hyperphosphatemia, metabolic acidosis and calcium (hypo early, hyper late)

Hyperphosphatemia typically does not require treatment unless patient is symptomatic

Avoid calcium supplementation unless treating hyperkalemia with EKG changes or severe hypocalcemia

- it may increase risk of muscle injury and lead to hypercalcemia following fluid resuscitation as Ca reenters the blood stream

Avoid nephrotoxic medications



Treatment goals:

- Monitor for complications:
  - AKI, arrhythmias secondary to electrolyte abnormalities, compartment syndrome
- Bicarbonate (to alkalize the urine), mannitol, and diuretics are NOT recommended for routine care
- Trending the CK is recommended, however the clinical status is the best method for evaluating improvement

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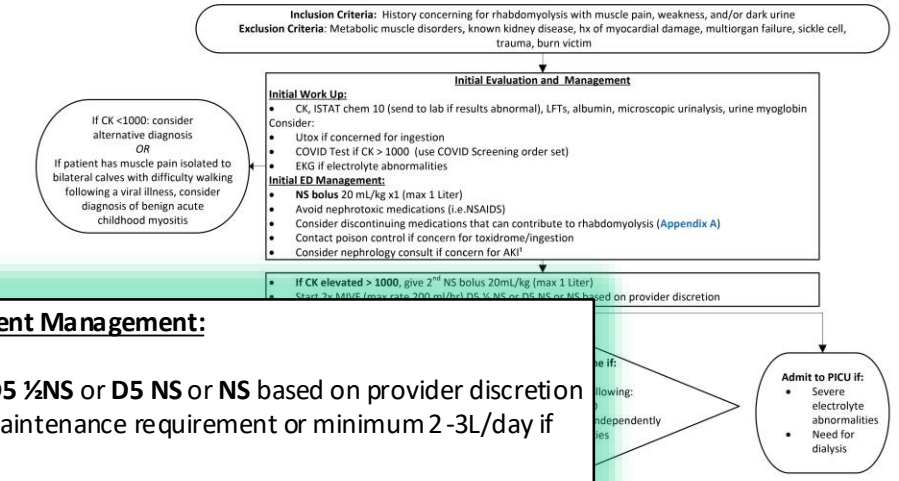

Inpatient Management:

Fluids:

- **2X MIVF** (max rate 200 ml/hr) of **D5 ½NS** or **D5 NS** or **NS** based on provider discretion
- Set goal PO fluid parameters: 2x maintenance requirement or minimum 2 -3L/day if adult sized

Monitoring:

- CK & Chem 10 at least daily
  - Consider increasing frequency of lab monitoring based on CK trend and electrolyte abnormalities
  - Monitor for hyperkalemia & hyperphosphatemia; If hyperkalemic, obtain EKG and treat; calcium gluconate only indicated if EKG changes present
- UA daily
- Urine output (goal of average of 1-2 mL/kg/hr)
- Blood pressure: to monitor for hypertension

Other Management Considerations:

- Avoid nephrotoxic medications (i.e. NSAIDs)
- Discontinue medications that can contribute to rhabdomyolysis **(Appendix A)**
- Treat inciting infection if applicable
- Bed rest until improving, then assess need for PT prior to discharge
- Subspecialty consult as indicated*

If CK not improved after 72h, consider continued muscle breakdown

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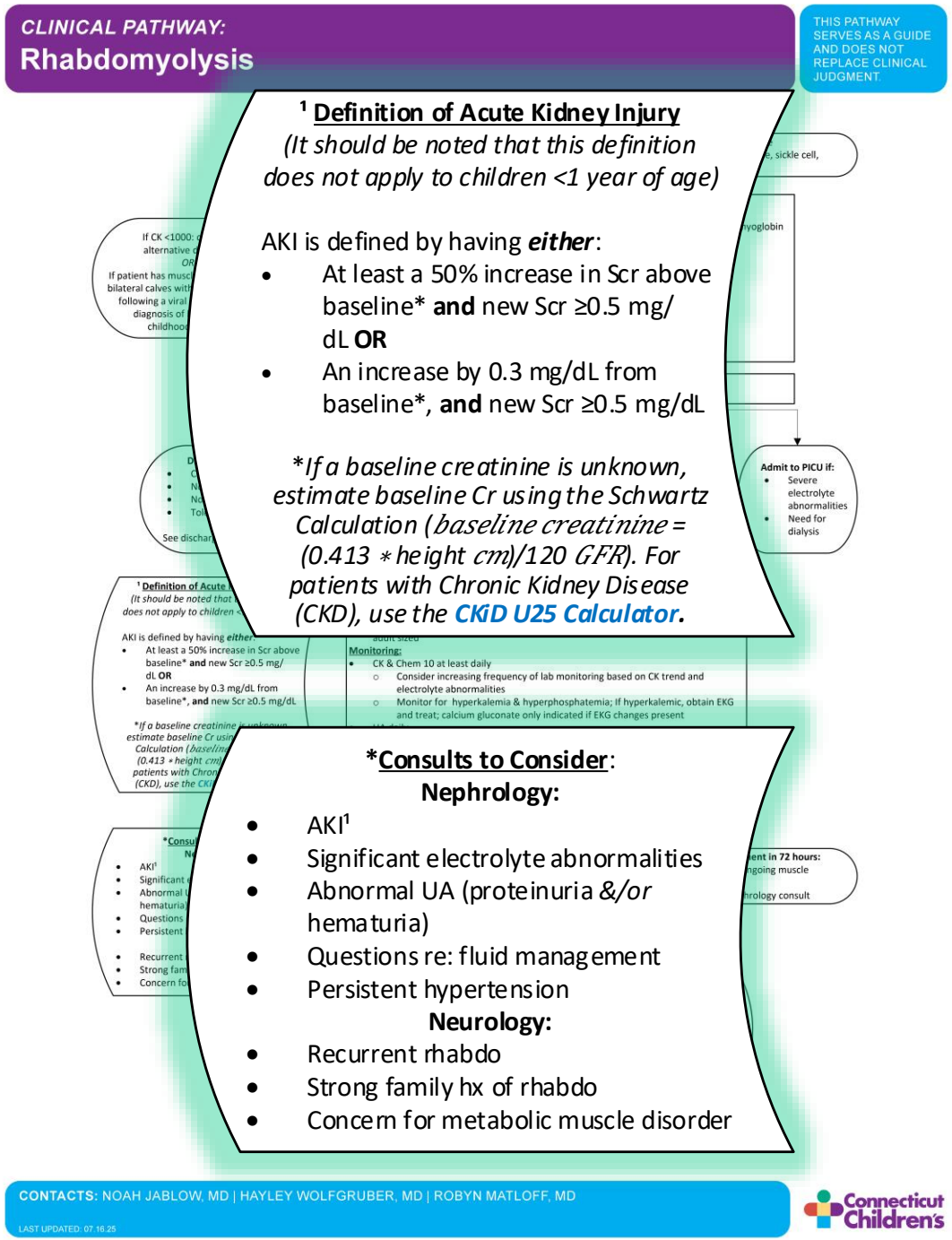
Consults:

- Consider placing a Nephrology consult if:
  - AKI is present, or there is concern for AKI developing
  - Electrolyte abnormalities
  - Lack of improvement in 72hrs

- Consider placing a Neurology consult if:
  - History is concerning for underlying neurologic condition.

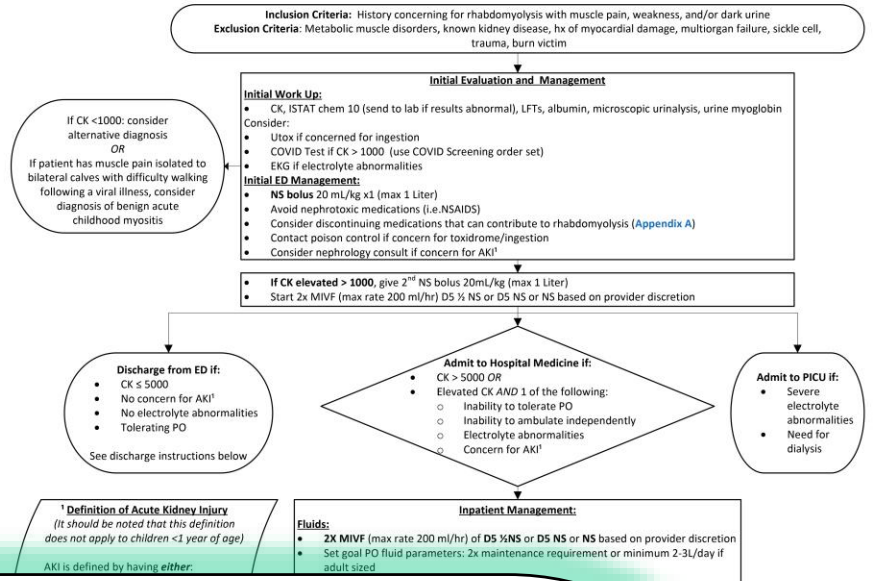
Consults may be placed in the ED, upon admission, or at any time during hospitalization



Discharge:

- Discharge should be considered when CK is less than 8000 and patient is otherwise clinically well
- PCP follow up should be in place
- Patients should have slow return to activities
  - This can help identify patients with underlying myopathies and reduce the risk of recurrence

Discharge instructions are available in EPIC using the smartphrase .rhabdodc



Discharge Criteria:

- CK <8000 with consistent downtrend AND all of the following:
  - Normal renal function and electrolytes
  - Udip heme negative
  - Ability to maintain UOP at 1- 2mL/kg/hr
  - Ability to meet PO fluid parameters
  - Able to ambulate independently
- PCP follow up in place
- Follow up with Elite Sports Medicine for return to play guidance for sports-related rhabdomyolysis

Discharge Instructions:

- Avoid physical activity, encourage PO hydration, avoid nephrotoxic medications, close follow up until symptoms resolved and CK <500
- Repeat CK, chem 10, UA 2-3 days post-discharge
- Weekly CK until serum CK<500
  - If CK remains elevated for 4-6 weeks, recommend outpatient neurology referral

Review of Key Points

- IV fluids are the main treatment for rhabdomyolysis
- Acute kidney injury is a known complication of rhabdomyolysis and renal function should be closely monitored
- PMD follow up after discharge is recommended to trend labs and to counsel on graduated return to activity in order to prevent recurrence and identify patients with underlying myopathies

Quality Metrics

- Percentage of patients with pathway order set usage
- Percentage of patients receiving 2 normal saline boluses
- Percentage of patients with appropriate continuous IV fluid administration per pathway recommendation
- Percentage of patients with rising serum creatinine levels
- Percentage of patients with acute renal failure secondary to rhabdomyolysis
- Average length of stay ED (minutes)
- Average length of stay Inpatient (days)
- Returns to ED within 30 days
- Readmissions to hospital within 30 days

Pathway Contacts

- Noah Jablow, MD
  - Pediatric Emergency Medicine
- Hayley Wolfgruber, MD
  - Pediatric Hospital Medicine
- Robyn Matloff, MD
  - Pediatric Nephrology

References

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Thank You!

About Connecticut Children's Pathways Program

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings. These pathways serve as a guide for providers and do not replace clinical judgment.