
1

## Disclosures:

I have no relevant relationships with ineligible companies to disclose within the past 24 months.

2

## Objectives

| | | | |
|---|---|---|---|
| Na | Cl | BUN | Glucose |
| K | HCO3 | CR | |

- Recognize that hypernatremia and hyponatremia are water problems
- Implement the medical management of hyperkalemia
- Describe which labs to order to evaluate the cause of anion-gap metabolic acidosis. Recognize how to treat lactic acidosis
- Recognize when to suspect a renal tubular acidosis (RTA)
- Learn the criteria to diagnose acute kidney injury and describe the management of acute tubular necrosis, one of the most common causes of AKI

3

## Question:

- Ale has a favorite uncle, Taco, who unfortunately had a heart attack. Taco underwent a Coronary Artery Bypass Grafting (CABG) in the hospital.
- When Ale went to visit his uncle, Taco appeared uncomfortable and mentioned he was thirsty. Taco's nurse mentioned that since Taco has been confused, he was not allowed to drink water due the risk of aspiration.
- What do you expect to see on his labs?

A) Hyponatremia
B) Hypernatremia
C) Metabolic acidosis

4

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B) Hypernatremia
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## Hypernatremia

- Hypernatremia is a water problem
- Most common cause is decreased/not enough free water intake
    1) Restricted access to water (altered mentation, intubated patients, infants, older adults)
- Increased free water loss
    1) Hypotonic fluid loss (GI or cutaneous losses)
    2) Pure water loss (central diabetes insipidus or nephrogenic diabetes insipidus)
- Rarely sodium gain (iatrogenic)

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## Question:

- You decide to give the patient intravenous water (D5W) rather than oral due to the concern for aspiration.
- However, the PA student on the team pointed out that Ale's uncle is already on oxygen and she was concerned that it would lead to volume overload.

- What would you do?

A) Give the D5W because it shouldn't make the volume worse and it is safe

B) Hold the D5W due to volume overload because intubation is worse than having the patient feel thirsty

C) I am not sure

7

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8

## Hypernatremia treatment

- Volume and water are two different things:

Fluid Compartments

| Intracellular space | Extracellular space |
|---|---|
| 2/3 of total body water is intracellular | 1/3 of the total body water is extracellular<br>-of this:<br>20% in blood plasma<br>80% in the interstial space |

Volume: Isolated to the extracellular space

Water: Both intracellular and extracellular space

***When you replete with water, most of it goes intracellular without significantly worsening hypervolemia

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## Question:

- Ale's uncle, Taco, recovered and left the hospital. Taco inspired Ale to live a healthy lifestyle and he decided to run a marathon. But he did not train for it. He started feeling severe muscle pain and started urinating coca cola colored urine. His labs were notable for a CK of 20,000. His serum Cr went from 1 to 5.

- Does Ale have an Acute Kidney Injury?

A) Yes

B) No

C) Need more information

10

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## Acute Kidney Injury

- Sudden impairment of kidney function resulting in retention of nitrogenous and other waste products normally cleared by the kidneys

Definition of AKI according to The Kidney Disease: Improving Global Outcomes (KDIGO) 2012

- A rise in serum Cr concentration of equal or greater than 0.3mg/dl within 48hrs

OR

- A rise in serum Cr concentration of equal or greater than 50% within 7 days

OR

- Urine output less than 0.5 mL/kg/h for 6 hours (ie. 70kg male, 35ml/hr)

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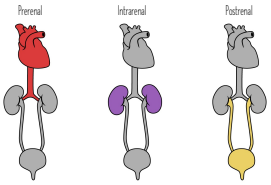
## Acute Kidney Injury- etiology

- When thinking about the etiology of AKI, it is helpful to think about them in 3 major categories.

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## What is the difference between prerenal and ATN?

- Both with decrease in glomerular filtration due to renal hypoperfusion
- Prerenal
  - -Integrity of the renal parenchyma is not disrupted. Without glomeruli or tubular injury

- ATN (Part of intrinsic/intrarenal) AKI.
  - -WITH direct tubular injury

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## Prerenal vs Intrarenal: Response to fluid repletion

- Gold standard for distinction between pre-renal disease secondary to volume depletion and intrarenal cause is response to fluid repletion

- Return of serum Cr to previous baseline within 24-72 hrs is considered to represent correction of prerenal.

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# Question:

- No improvement with intravenous fluid challenge
- What is the most likely cause of Ale's acute kidney injury?

A)Prerenal

B)Acute Tubular Necrosis

C) Glomerulonephritis

D) AIN

E) Post-renal

Serum Creatinine:
1 to 5mg/dL

Creatinine Kinase:
20,000

Fractional Excretion of sodium:
FENa= 50%

| UA, MACROSCOPIC | |
|---|---|
| Specimen | CLEAN CATCH |
| Color | Yellow |
| Clarity | Hazy ! |
| Specific Gravity | 1.027 |
| Glucose | Negative |
| Ketone | Negative |
| Blood | 1+ ! |
| pH | 5.0 |
| Protein | Negative |
| Nitrite | Negative |
| Leuk esterase | Negative |
| **UA, MICROSCOPIC** | |
| RBC, urine | 0-3 |
| WBC, urine | 0-2 |
| Squamous cells | |
| Mucous threads | Rare |
| Bacteria | No significant ... |
| Urine comment | Automated urine... |

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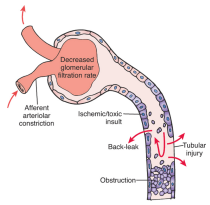
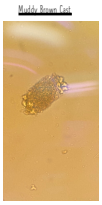
# Acute Tubular Necrosis (ATN)

- Sudden decline in kidney function resulting from ischemic or toxic-related damage to the renal tubular epithelium

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## Nephrotoxic ATN: Endogenous Toxins

Rhabdomyolysis- clinical syndrome associated with muscle necrosis and release of intracellular contents into the extracellular space

- Physical Injury- trauma, crush injuries, immobilization
- Muscle-Fiber Exhaustion- Excessive exercise, Seizures, Heat Stroke
- Medications/Drugs- SSRIs, Statins, Fibrates, Amphetamines, Cocaine, Alcohol

- Toxin: Myoglobin (direct tubular toxin)
- Blood tests: Elevated creatine kinase (CK).

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## Nephrotoxic ATN: Endogenous Toxins

Rhabdo causes:

Pigment nephropathy

DX: UA with significant positivity for heme/myoglobin protein with few or no RBCs seen on microscopy.

| UA, MACROSCOPIC | |
|---|---|
| Specimen | CLEAN CATCH |
| Color | Yellow |
| Clarity | Hazy ! |
| Specific Gravity | 1.027 |
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| RBC, urine | 0-3 |
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| Squamous cells | |
| Mucous threads | Rare |
| Bacteria | No significant... |
| Urine comment | Automated urine... |

Treatment for rhabdomyolysis:

- Early aggressive fluid repletion is the most important factor.

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## Question:

- Does Ale need dialysis? He still makes a few liters of urine a day but these are his labs:

A) Yes

B) No

| | |
|---|---|
| Sodium, Ser/Plas | 134 |
| Potassium, Ser/Plas | 6.2 * c[2] |
| Chloride, Ser/Plas | 105 |
| CO2, Ser/Plas | 17 |
| Urea Nitrogen,Ser/... | 132 |
| Creatinine, Ser/Plas | 5.79 * |
| eGFR | 9 * |
| eGFR (African Amer... | 10 * |
| Fasting | See Comment * |
| Glucose, Ser/Plas | 195 * |
| Anion Gap | 12 |
| Calcium, Ser/Plas | 7.8 |

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# ATN Treatment

- Supportive care

Indications for dialysis: AEIOU

- Acidosis
- Electrolyte Disturbances
- Intoxication
- Overload
- Uremia

| | |
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| Sodium, Ser/Plas | 134 |
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# Question:

- You decide to pursue medical management of hyperkalemia for AIe.
- Which of the following is a *definitive* measure of excreting potassium after you give them IV Calcium to stabilize their cardiac membrane?

A) Dextrose/Insulin

B) Sodium bicarbonate

C) Furosemide

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| Anion Gap | 12 |
| Calcium, Ser/Plas | 7.8 |

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## Hyperkalemia Treatment

- For hyperkalemia to persist, urinary K+ excretion capacity must be reduced.

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## Question:

- Ale received intravenous fluids and furosemide, his myoglobin started clearing (CK 20K to 1K) and his renal function started improving.
- Unfortunately, he started developing a fever and cough the next day. His blood pressure dropped from 120/80 to 70/50. He was transferred to the ICU and started on vasoactive medications. His blood gas on ABG showed:
- His anion gap was ELEVATED at 20.
- What are the 4 labs to order when evaluating anion gap metabolic acidosis?

A) Lactate, urine ketone, serum creatinine, serum osmolarity

B) 24hr urine, lactate, serum potassium, glucose

C) Lactate, serum creatinine, LDH, uric acid

| | |
|---|---|
| PH (a), ISTAT | 7.27 |
| pCO2 (a), ISTAT | 32.2 |
| PO2 (a), ISTAT | 150 |
| HCO3 (a), ISTAT | 14.7 |

Normal Values:
pH: 7.35- 7.45

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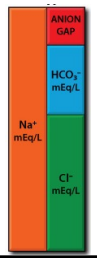
27

## Anion Gap- to distinguish the cause of metabolic acidosis (Bicarb<22mEq/L)




- Positive charges = Negative Charges
- Cations= Anions
- Anion gap= [Na+] - ([Cl-] +[HCO3-])= ~12

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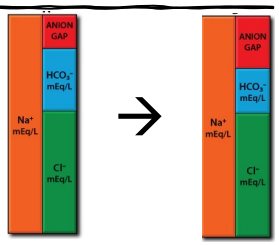
## Anion-Gap Metabolic acidosis (AGMA)

- Adding acid to the system

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## Anion-Gap Metabolic acidosis differential

- Lactic Acidosis → Lactate
- Ketoacidosis → Urine Ketone
- Renal Failure → Serum Creatinine
- Ingestions → Serum Osmolarity

30

# Question:

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- His anion gap was elevated at 20.
- Assuming that his renal function is *now normal* what is the most likely cause of his anion gap metabolic acidosis?

A) Acute kidney Injury

B) Lactic acidosis

C) Ketoacidosis

D) Ingestions

31

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# Lactic Acidosis

- Definition: When plasma lactate level exceeds 4 mEq/L

How it happens:

1) Increased lactate production
   - Impaired tissue oxygenation/Anaerobic metabolism
2) Diminished lactate utilization

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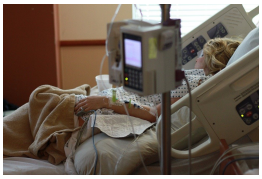
## Lactic Acidosis

- Systemic Hypoperfusion
  - Sepsis
  - Hypovolemia
  - Cardiac Failure/Arrest
- Increased metabolic rate
  - Grand mal seizure
  - Severe exercise
- Drugs
  - Drug-induced mitochondrial dysfunction



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## Question:

- Ale's lactate returned:

| Lactate, Whole Bld | 15.0 |
|---|---|

How would you treat his lactic acidosis?

A) Bicarb drip or pushes

B) Antibiotics or treatment of infection

C) Dialysis

D) I am not sure

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|---|---|

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## Lactic Acidosis Treatment

Diagnosis: Elevated serum lactate

Treatment:

- Correction of the underlying disorder (ie. Shock, sepsis), otherwise transient
- Role of sodium bicarbonate– controversial. Expert opinion pH<7.1

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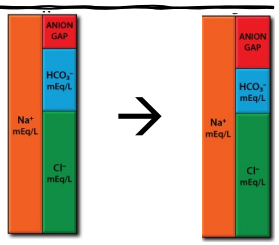
## Summary: Anion-Gap Metabolic acidosis (AGMA)

- Adding acid to the system

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## Summary: Anion-Gap Metabolic acidosis differential

- Lactic Acidosis → Lactate
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- Ingestions → Serum Osmolarity

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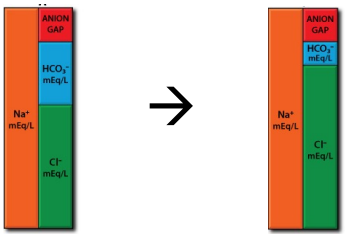
## Non-Anion Gap Metabolic Acidosis

Gastrointestinal

- Loss of bicarbonate

Renal

- Loss of bicarbonate
- Impaired hydrogen excretion

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## Evaluation of Non-Anion Gap Metabolic acidosis

Make sure no diarrhea!

Consider...

Renal Tubular Acidosis (RTA)- *despite well preserved renal function,* metabolic acidosis develops

- Has to do with... inability of renal tubules to perform the normal function to maintain acid-base balance.

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- Ale's infection was treated and when he left the hospital, he decided to train for a marathon the proper way.

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## Question:

- Unfortunately, he fell on a rock while running and fractured his tibia.
- He arrived in the hospital in severe pain.
- On labs, he was noted to be profoundly hyponatremic to 125mEq/L. It was normal at 140mEq/L when he left the hospital 1 week ago.
- When we think of hyponatremia, is it a salt problem or a water problem?

A) Salt problem

B) Water problem

43

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## Hyponatremia evaluation

- Hyponatremia is a water problem
- Excess water compared to sodium– regardless of volume status.

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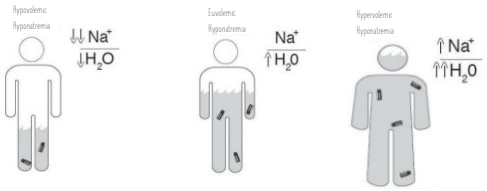
## Hyponatremia is a water problem

Hyponatremia is a WATER problem

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## Normal response to hyponatremia

- Ability to excrete water is so great that water retention resulting in hyponatremia usually doesn't happen
- When your body senses that you have too much water... this happens:

- BUT it doesn't happen in patients with hyponatremia... WHY?

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## ADH= ANTI-diuretic hormone, helps retain water

- This hormone is WHY patients develop hyponatremia


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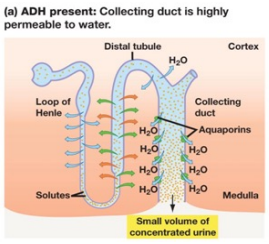
## ADH= ANTI-diuretic hormone, helps retain water

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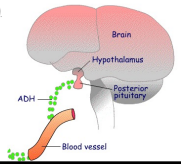
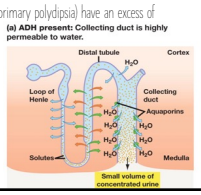
## Physiology of Hyponatremia

- Remember hyponatremia is a WATER PROBLEM.
- One becomes hyponatremic when there is a problem with EXCRETION of free water
- Virtually all hyponatremic patients (exception of those with renal failure and primary polydipsia) have an excess of Anti-diuretic hormone (ADH).

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## There are 2 triggers for ADH

(1) High serum Osmolality (not enough water aka **hypernatremia**).

- ---Not relevant in hyponatremia

(2) Extreme Volume Depletion

- Extreme Hypovolemia/Decrease in effective blood volume. During times of hypovolemia (ie. Shock), ADH kicks in

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## In hyponatremia, is ADH on appropriate?

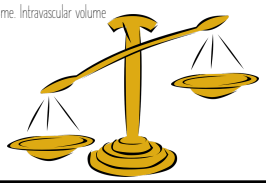
Appropriate

Extreme Hypovolemia- ie) Shock

Decrease in effective blood volume. Intravascular volume depleted states- CHF/Cirrhosis

Inappropriate

Syndrome of inappropriate antidiuretic hormone (SIADH)



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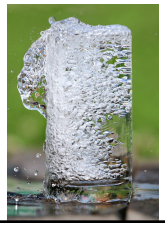
## SIADH- Syndrome of inappropriate Anti-diuretic Hormone

- Characterized by **nonphysiologic release of ADH** (ie. Not due to usual stimuli such as hypernatremia or intravascular volume depletion)



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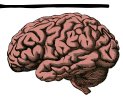
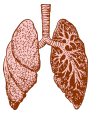
## SIADH-Syndrome of inappropriate Anti-diuretic Hormone

- **Increased hypothalamic production of ADH**
  - **Neuropsychiatric disorders/CNS**
    - Infections- meningitis, encephalitis, abscess, herpes zoster
    - Vascular: thrombosis, subarachnoid or subdural hemorrhage
    - Neoplasm: primary or secondary
    - Psychosis
  - **Pulmonary disease**
    - Pneumonia: viral, bacteria, or fungal
    - TB
    - Acute respiratory failure
    - Other: Asthma, atelectasis, pneumothorax





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## SIADH


- **Postoperative patient**—inappropriate ADH secretion is common and persists for 2-5 days. Appears to be mediated by **pain afferents**
- **Severe nausea**
- **Drugs:** SSRIs, thiazides

• **Ectopic (nonhypothalamic production of ADH)**
- **Carcinoma**: small cell of lung

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## We care about hypoosmolar hyponatremia

• Cerebral edema!


Under normal conditions, osmolality (solutes diluted in water) are equal


When there is hyposomolar "true" hyponatremia, water goes from the extracellular space into the intracellular space

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## Symptoms of hyponatremia

Serum sodium levels:

- Under 135 mEq/L – Hyponatremia
- Below 125 mEq/L --- Nausea and malaise
- Between 115 and 120 mEq/L --- headache, lethargy and obtundatation
- Less than 115mEq/L-- More severe changes of seizures, coma and respiratory arrest

Depends on chronicity:

- Chronic– few symptoms.
- Acute–more symptoms (esp acute <48hrs)


Under normal conditions, osmolality (solutes diluted in water) are equal


When there is hyposomolar "true" hyponatremia, water goes from the extracellular space into the intracellular space

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## SIADH Treatment- Symptomatic

- Acute Hyponatremia/symptomatic:
  - Cerebral edema
  - Hypertonic 3% saline until symptoms resolve
  - Increase of 4-6 mEq/L usually sufficient to reduce symptoms
  - Should NOT exceed 8mEq/L in first 24hrs
  - Loop diuretics may be used if concurrent volume overload


Under normal conditions, osmolality (solutes diluted in water) are equal


When there is hyposomolar "true" hyponatremia, water goes from the extracellular space into the intracellular space

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## SIADH Treatment- Asymptomatic

For our patient, Ale, with SIADH, he is asymptomatic.

Given that he is asymptomatic, what would be the appropriate management?

A. Treat the underlying problem (pain)
B. Fluid (free water) restriction to 0.8L
C. Start furosemide
D. Give salt tablets
E. Provide a high protein diet

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## SIADH Treatment- Asymptomatic

- Stop the trigger: Treat the underlying problem
- Prevent the sodium from getting worse: Water restrict
- Help with excretion of free water: Furosemide, High protein diet, Sodium Chloride tablets
- Monitor for overcorrection- no more than 6-8 mEq/L correction per day

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## Takeaways

- Hyponatremia and hypernatremia are water problems. Water is not the same thing as volume
- Hyperkalemia, urinary and bowel excretion are the definitive ways to excrete potassium from the body
- The Anion-gap helps you determine the cause of the metabolic acidosis
- Treatment of lactic acidosis is the underlying problem, bicarbonate is just a patch
- Suspect RTAs with non-anion gap metabolic acidosis when it is not diarrhea
- With acute kidney injury, there is no benefit to starting dialysis earlier than necessary
- You are awesome, thank you for listening

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## Thank you!

Questions: Adleywong@stanfordhealthcare.org

Special Thanks

- Dr. Pedram Fatehi
- Dr. Tara Chang
- Shira Simpson PA-C

Great Reference

- National Kidney Foundation's Primer on Kidney Disease

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