

CYSTINOSIS – AN INBORN
ERROR OF METABOLISM
AND ASSOCIATED SEQUALAE

PATIENT CARE REPORT
AN UNUSUAL DIAGNOSIS

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Clinical Practicum 2022

- T.K. is a 26-year-old male with a genetic inborn error of metabolism – cystinosis
- Admitted 4/11 to CPRMC. Transferred to SWC 4/12 for neurosurgical consult due to SAH
- Presented w/ **AMS, metabolic acidosis**, acute on chronic renal failure and SAH
- GCS score 9 = moderate brain injury



PATIENT
PROFILE

- PMH: **cystinosis, Fanconi syndrome, CKD stage IV**, chronic anemia, schizophrenia, polysubstance abuse
- Past surgical Hx: **Lithotripsy**
- Social Hx: Current smoker > 10 cigarettes/day, alcohol use - 5-6 drinks/day
- Family Hx: mother with bipolar disorder
- Code Status: Full code



PATIENT
PROFILE



PHYSICAL FINDINGS

Upon presentation:

- tachypneic w/ clear breath sounds
- +3 pitting BLE edema
- multiple small wounds over left forearm and right leg, multiple wounds at various stages of healing
- Vomit in beard
- Only oriented to himself



MEDICAL FINDINGS

Upon presentation:

- Neuro: AMS, SAH of the left parieto-occipital junction w/ possible cortical ischemic infarction
- CV: acute pericardial effusion, elevated BNP, elevated troponin
- Resp: tachypnea, pneumonia
- Heme/Onc: anemia of chronic disease
- GU/Renal: AKI superimposed on CKD stage IV
- Infectious Disease: sepsis - MSSA
- Fluids/Electrolytes: hypocalcemia, hypokalemia, hypomagnesemia, metabolic acidosis

ANTHROPOMETRICS

Ht: 66 inches (167.64 cm)

Admit Wt: 62.2 kg (136.84 lb)

Previous Wt: 53.9 – 64.0 kg in past year

IBW: 142 lb (64.5 kg)

%IBW: 96.4%

BMI at admit: 22.1 kg/m²

Dosing Wt: 62.2 kg

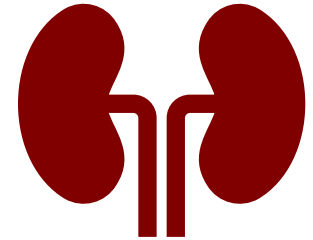
ENERGY REQUIREMENTS

PROTEIN REQUIREMENTS

Energy 25 – 35 Kcal/kg per day per KDOQI

27 kcal/kg x 62.2 kg = 1679 kcal

30 kcal/kg x 62.2 kg = 1866 kcal



Protein 1.0 – 1.3 g/kg per day **pending renal Fx** due to sepsis, pneumonia, tachypnea and general stress of hospitalization

0.8 g pro/kg x 62.2 kg = 50 g pro

1.3 g pro/kg x 62.2 kg = 81 g pro

DIET ORDERS AND ENTERAL NUTRITION: TIMELINE

SLP 4/11 – admit to SWC, NPO per SLP – failed bedside swallow test, AMS

4/12 - 4/25 requires MBSS, not appropriate

RD 4/12 - Initial assessment. NPO per SLP. DHT ordered

P: Inadequate oral food/beverage intake

E: Confusion and/or mental status changes

S: NPO

M/E 1. Food and beverage intake: goal is to restart diet in 24-48 hrs.

2. Digestive system: goal for a BM q 1-3 days.

3. Anthropometrics: goal is to maintain lean body weight.

4. Skin: goal for wound healing and prevention of breakdown.

Surg 4/12 - pericardiocentesis - positive for gram +ve cocci (MSSA). DHT placed

RD 4/12 - Basal EE = 1,575 Kcal/day (MSJ) – use 1.2 stress factor

Est. EE = 1900 = 29 kcal/kg

Est. Pro = 0.8 - 1.3 g/kg = 52 – 85 g Pro pending renal fxn

Start TF s/p pericardiocentesis. Nepro @ goal 45 ml/hr (1080 ml formula, 1944 kcal, 87 g Pro, 848 ml free water)

DIET ORDERS AND ENTERAL NUTRITION: TIMELINE

RD 4/20 – TF on hold. TEE and pericardiocentesis

Surg 4/20 – TEE, intubated, sedated. pericardiocentesis

RD 4/21 – Reassessment. NPO per SLP. Intubated, vented AC/VC

Est. EE = 1,922 Kcal/day (Penn State T_{max} 38.2, V_e 9.08) = 32 kcal/kg

Est. Pro = 0.8 - 1.3 g/kg = 49 – 79 g Pro pending renal fxn

Due to pressor support restart Nepro @ 20 ml/hr (480 ml formula, 864 kcal, 39 g Pro, 349 ml free water)

Resume Nepro @ 40 ml/hr (960mL formula, 1728 kcals, 78g pro, 698mL free water) after withdrawal of pressor support

P: Inadequate protein-energy intake

E: Current enteral/parenteral support

S: Nutrition support not meeting estimated needs

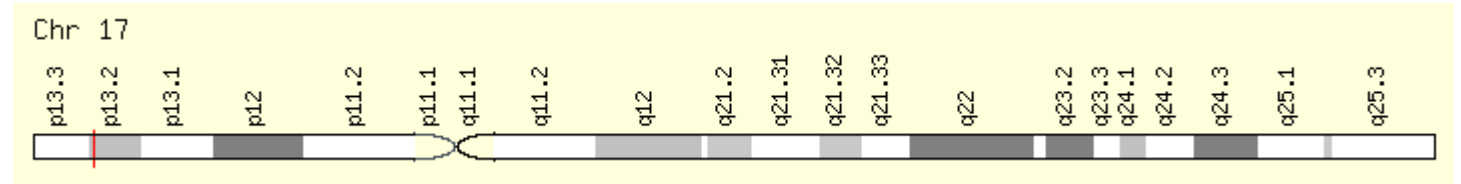
- M/E
1. Food and Beverage Intake: Goal for pt to meet 80-100% of their estimated energy and protein needs via EN in next 48 hr
 2. Digestive system: Goal for a BM q 1-3 days
 3. Skin/Musculoskeletal Function: Goal for maintenance of skin integrity during LOS
 4. Electrolyte/Renal Profile: Goal for LFTs, BUN and Cr to trend WNL
 5. Endocrine Profile: Goal to maintain BG between 80-180 mg/dl

CYSTINOSIS: THE GENETICS

- The *CTNS* gene causes cystinosis - encodes the lysosomal transmembrane **cystine-proton co-transporter** cystinosin
- **Autosomal recessive**
- Over 140 pathogenic *CTNS* mutations
- There are three major phenotypes of cystinosis:
 - **Infantile – vast majority of mutations**
 - Juvenile – 15 mutations
 - Ocular – 4 mutations

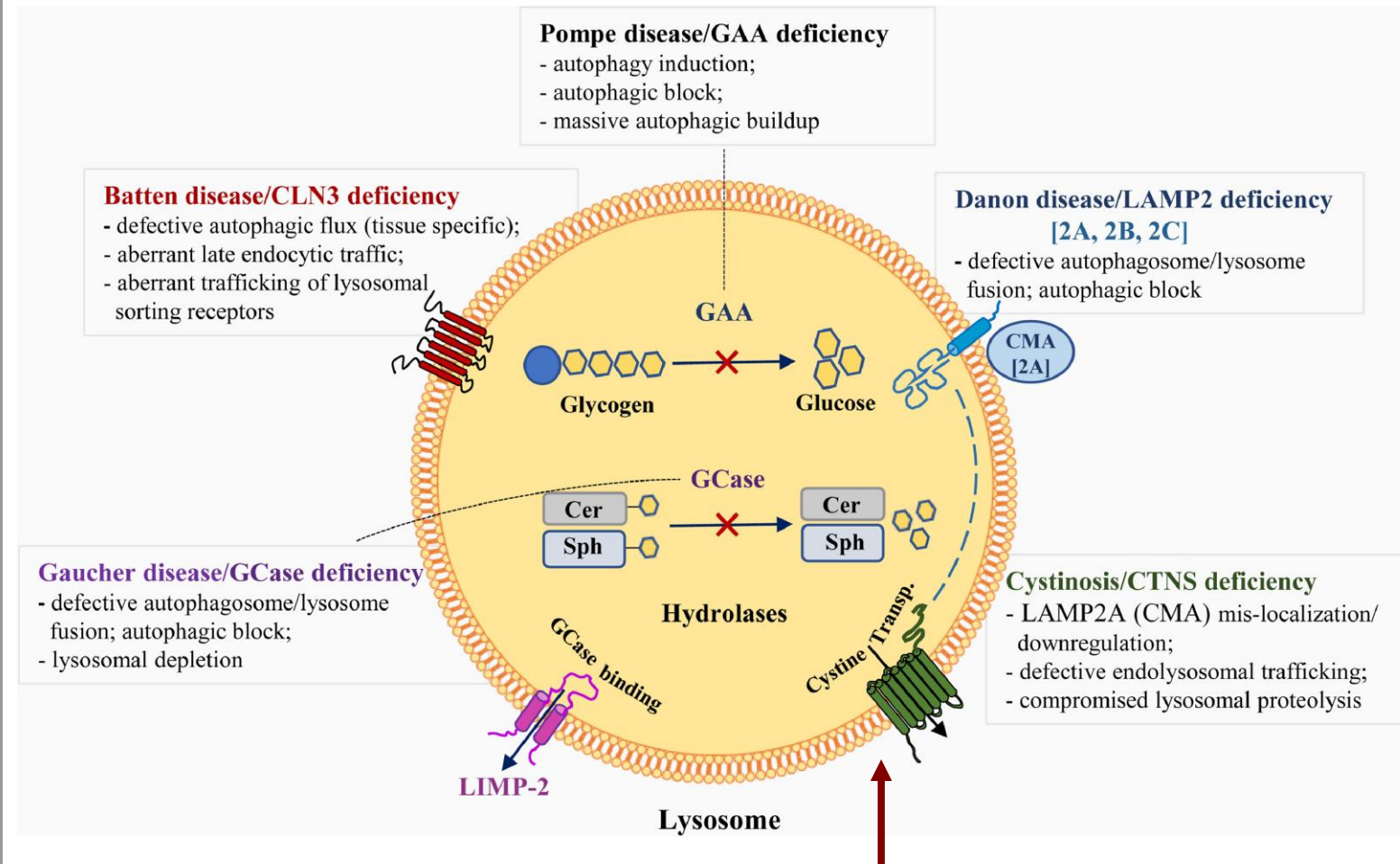
CYSTINOSIS: GENETIC MUTATIONS OF THE *CTNS* GENE

CTNS gene



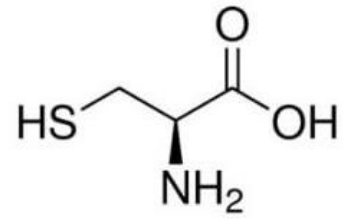
- 367 amino acids, molecular mass: 41738 Da, 17p13.2
- Lysosomal storage disease
- Infantile nephropathic cystinosis affects ~95% of patients
- Causes glomerular dysfunction
- If untreated results in ESRD around 10 years old - fatal

CYSTINOSIS ACCUMULATION OF CYSTINE IN THE LYSOSOME

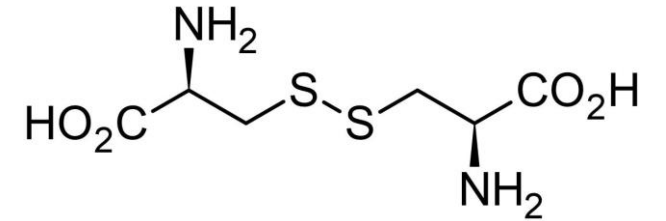


- Cystinosis - **rare** genetic condition
- Affects an estimated **500** patients in the U.S. and about **3,000** patients worldwide

CYSTEINE VS CYSTINE

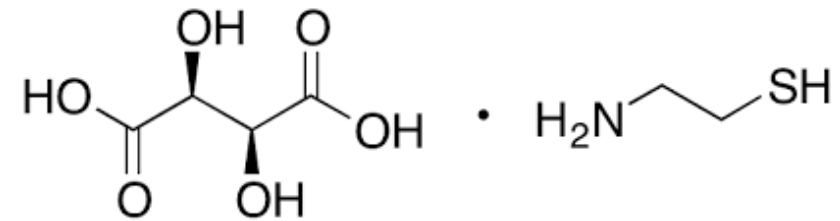


Cysteine



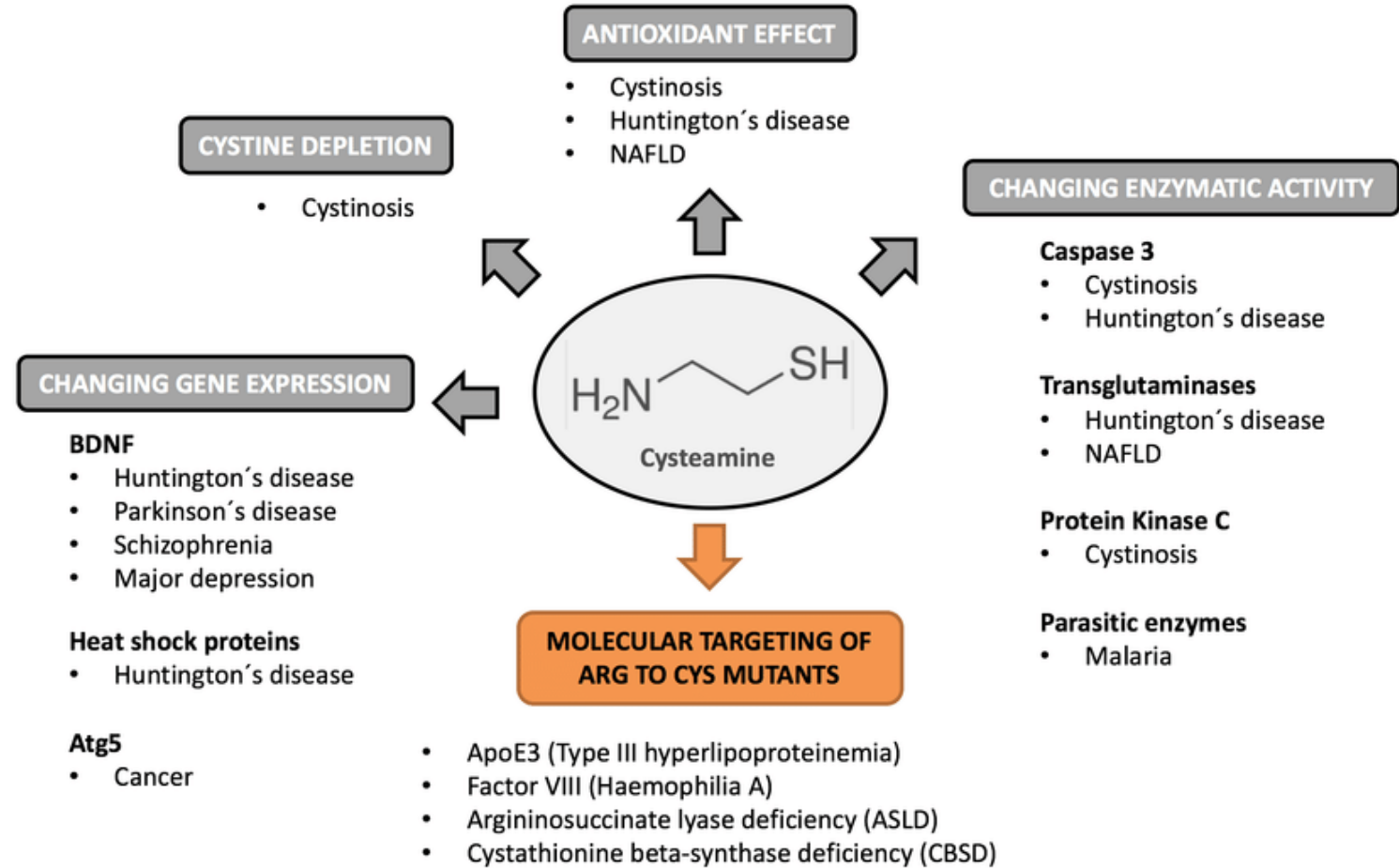
Cystine – a dimer of cysteine

THE TREATMENT



Cysteamine bitartrate

THE TREATMENT



THE TREATMENT

Cystagon immediate-release

Dosage 60 - 90 mg/kg/day or 1.35–1.90 g/m² BSA/day q6h continuous

FDA approved in 1994



Procysbi delayed-release capsule

patients ages 6 years and older

Dosage for cysteamine-naïve patients is 0.2- 0.3 g/m² divided into 2 doses q12h

Not to exceed 1.95 grams/m² per day

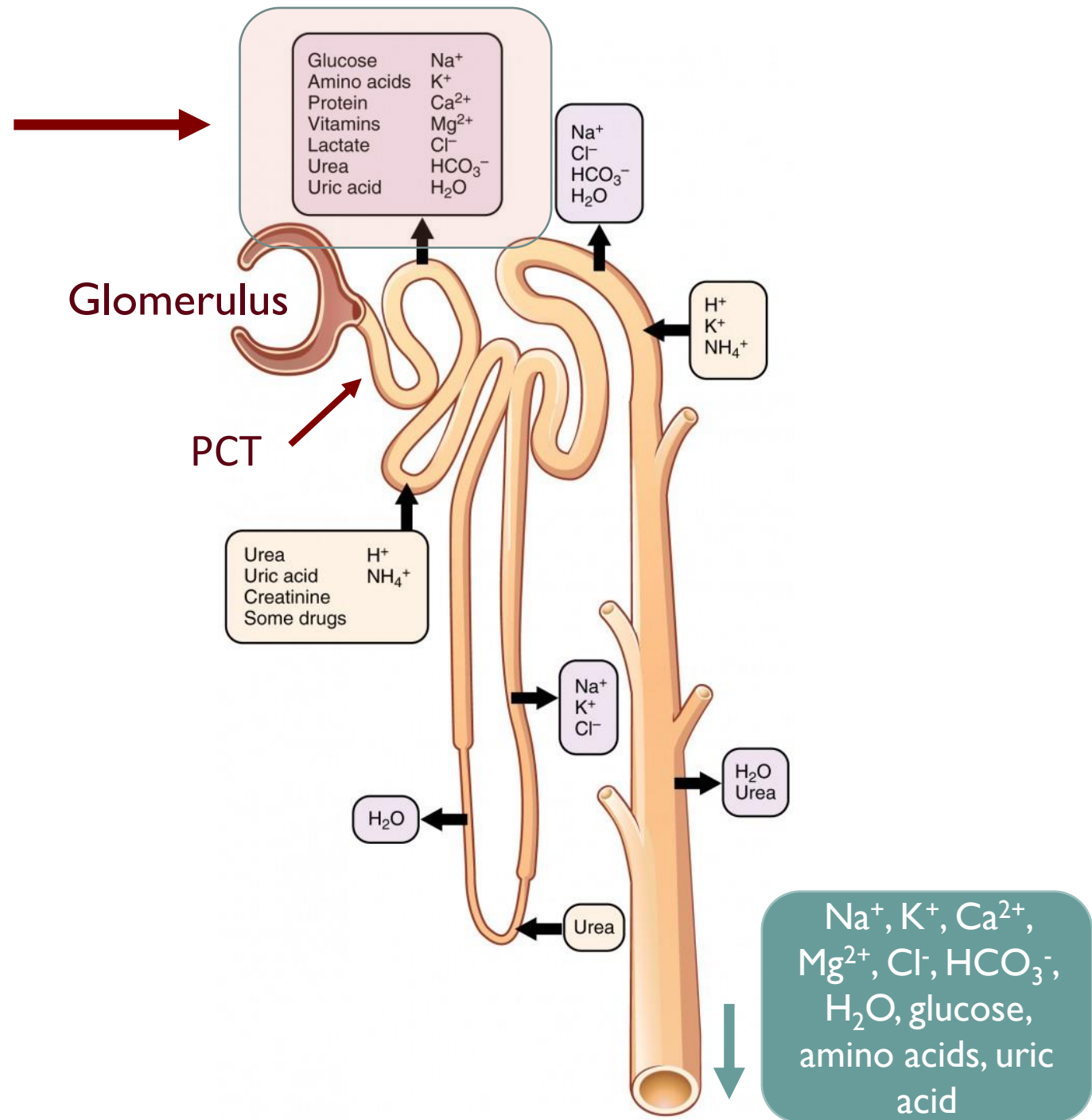
FDA approved 2013



FANCONI
SYNDROME:
MOST COMMONLY
CAUSED BY
CYSTINOSIS

- Defect of the proximal tubule of the nephron
- Prevents absorption of electrolytes, amino acids, bicarbonate, glucose, phosphate, proteins, and uric acid
- Treatment usually targets the etiology and deficiencies in volume status, nutrition and electrolytes
- Symptoms - excessive urinary excretion of amino acids, calcium, bicarbonate, glucose, phosphate, and uric acid, dehydration, electrolyte imbalances, rickets, osteomalacia, and growth failure
- Bicarbonate deficiency can lead to acidosis

FANCONI
SYNDROME:
REABSORPTION IN
THE PROXIMAL
CONVOLUTED
TUBULE



CYSTINOSIS: SEQUELAE

- Deposition cystine in the bone marrow, liver, kidney, pancreas and CNS
- Hx of cystine stone formation
- Inherited forms associated with multiple organ dysfunction and failure

Pertinent Laboratory Values

	Na⁺ 135-145 mmol/L	K⁺ 3.5-5.2 mmol/L	Ca²⁺ 8.6-10.3 mg/dL	Mg²⁺ 1.2-3.1 mEq/L	Phos 2.8-4.5 mg/dL	AGAP 3-10 mEq/L	BUN 6-24 mg/dL	Creatine 0.6-1.3 mmol/L	GFR Stage IV 15-29 ml/min
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4/15	153	3.8	7.8			15	108 - 113	5.6 – 5.7	12
4/14	153	3.7	7.9			15	114 - 122	5.7 – 5.9	12
4/13	150	3.6	7.7			20	118	5.9 – 6.2	12

Now in range

Pertinent Laboratory Values

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Potassium not fully controlled

Recent Laboratory Values

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Not depleted considering albumin correction
 Values

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Pertinent **Now stabilized** Labs

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Pertinent Laboratory

Uncontrolled

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Pertinent Laboratory Values

Due to Cl^- and HCO_3^- depletion

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Consistently elevated

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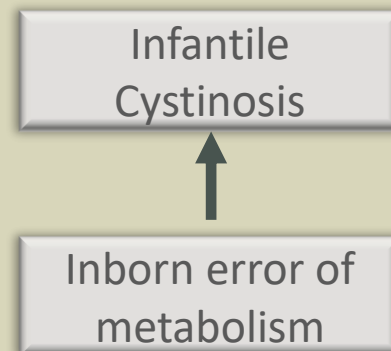
Stage V?

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4/24	142	3.4 - 3.6	6.4	2.0		17 - 20	50 - 52	5.1 – 5.3	13 - 14
4/23	142	3.4 - 3.7	6.2	1.6 - 2.1	5.2	16 - 19	55 - 58	5.1 – 5.2	13 - 14
4/22	144	3.4 - 3.7	6.1		7.2	17 - 20	59 - 64	5.0 – 5.3	13 - 14
4/21	144	3.1 - 3.7	5.8 - 6.3			20 - 23	68 - 76	5.3 – 5.5	13
4/20	141	3.8 - 5.9	6.5 - 7.9	2.6	7.3	17	75 - 77	5.4	13
4/19	138	3.1 - 4.2	7.6	1.8 - 4.8		15	75	5.1	14
4/18	151	3.9	7.6			14	91	5.4	13 - 14
4/17	157	3.6	7.6			15	107	6.0	11
4/16	155	4.0	7.9			13	111	5.9 – 6.0	11 - 12
4/15	153	3.8	7.8			15	108 - 113	5.6 – 5.7	12
4/14	153	3.7	7.9			15	114 - 122	5.7 – 5.9	12
4/13	150	3.6	7.7			20	118	5.9 – 6.2	12

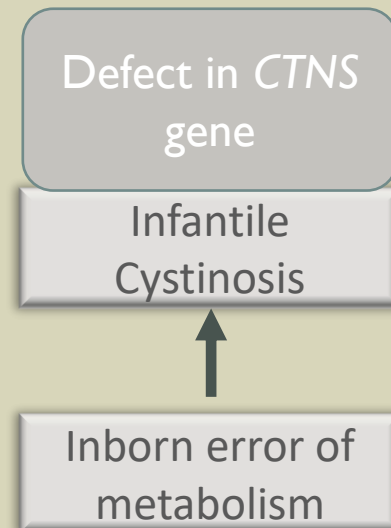
Concept Map

Inborn error of
metabolism

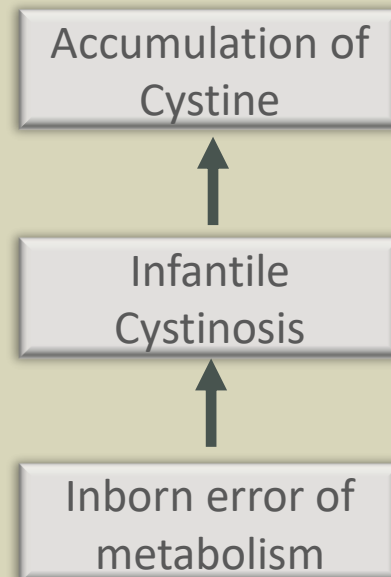
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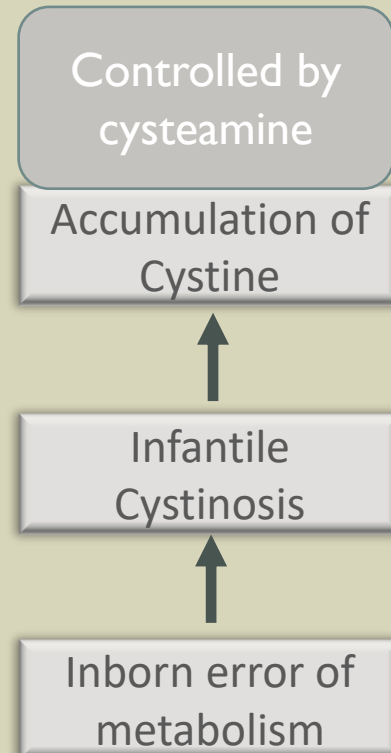
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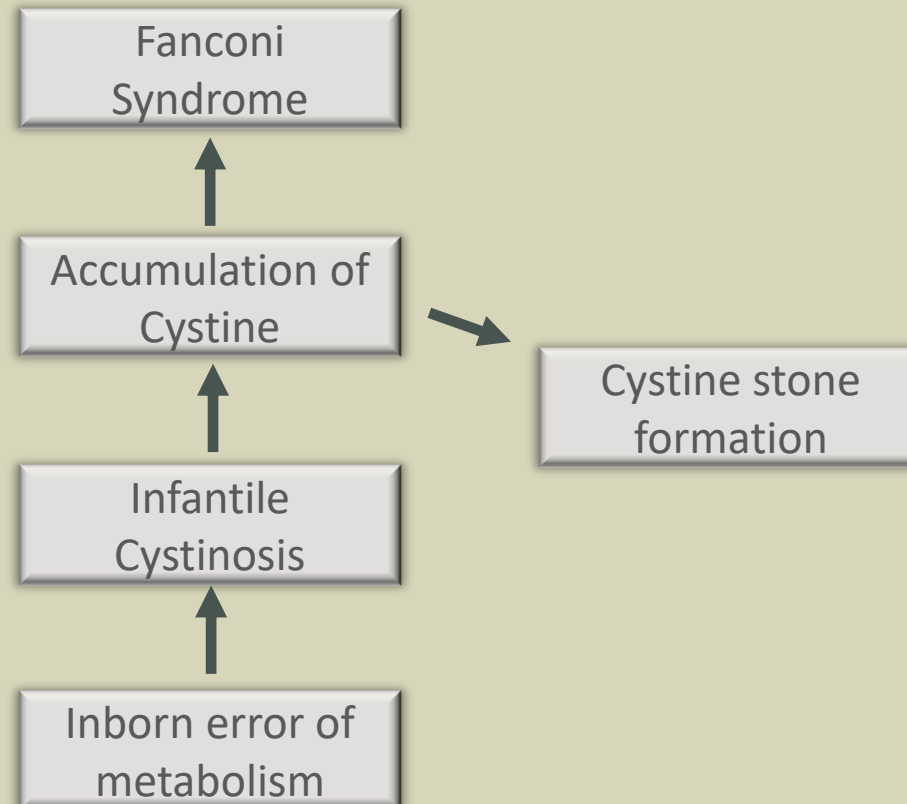
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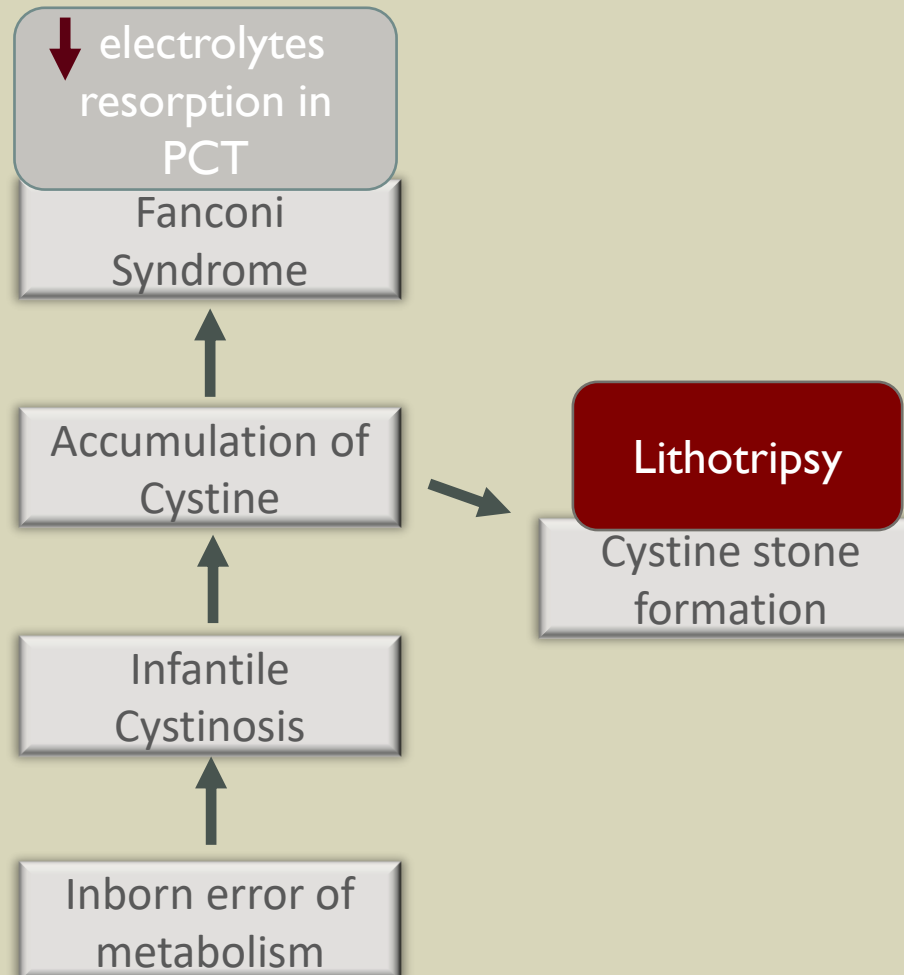
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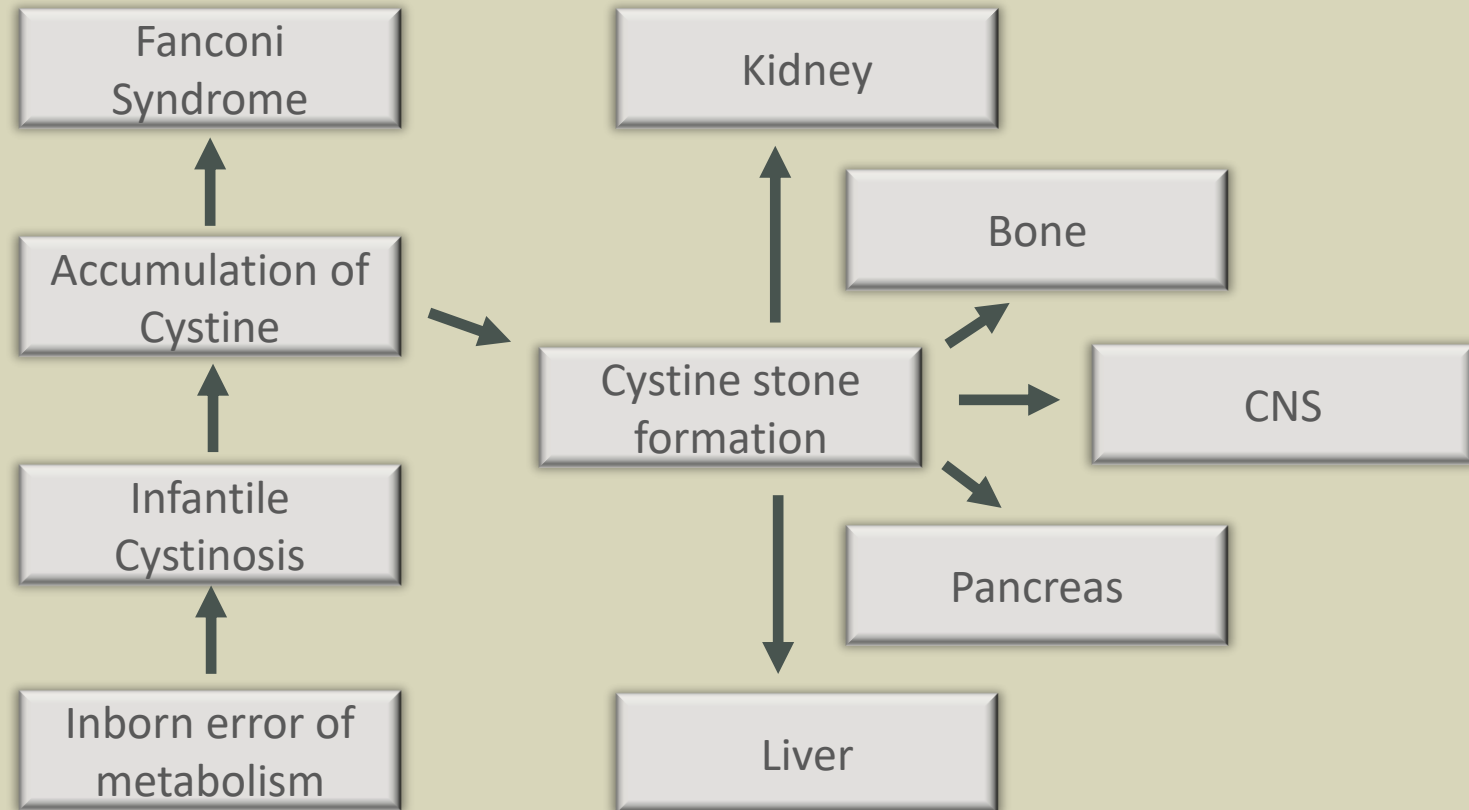
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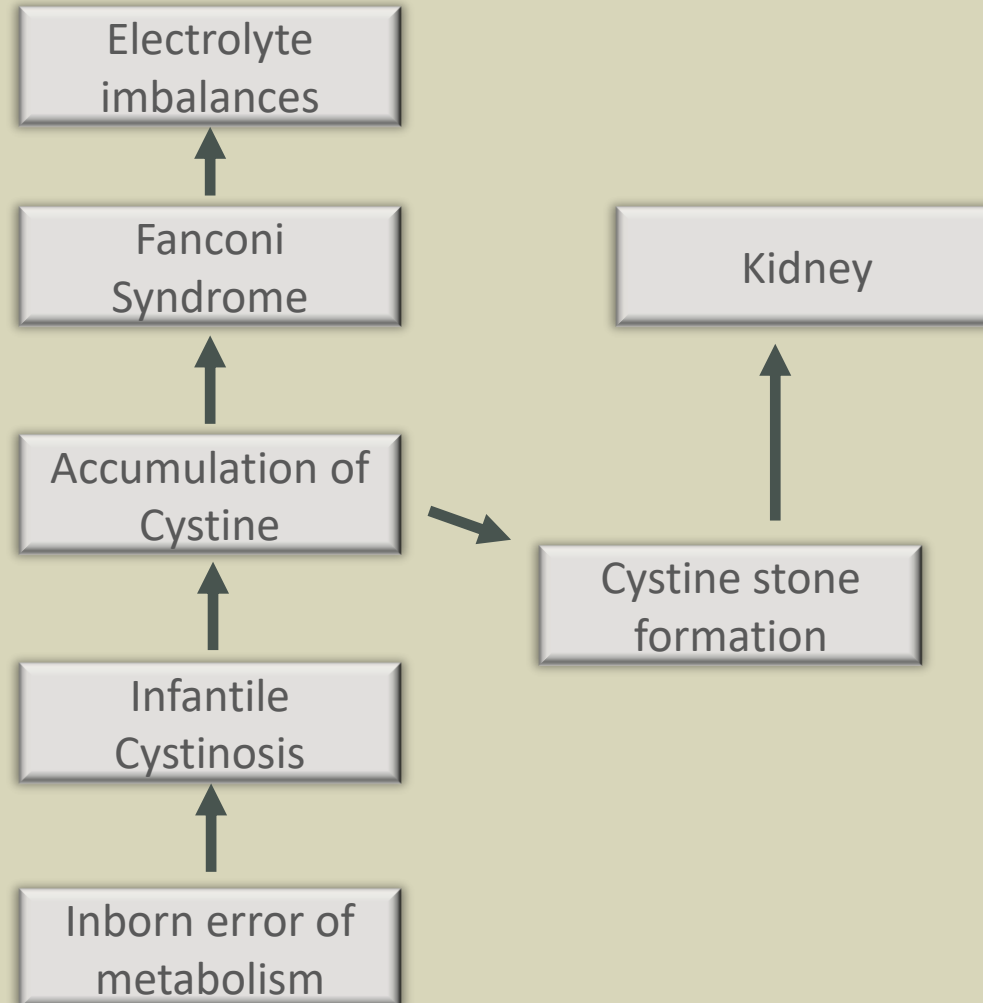
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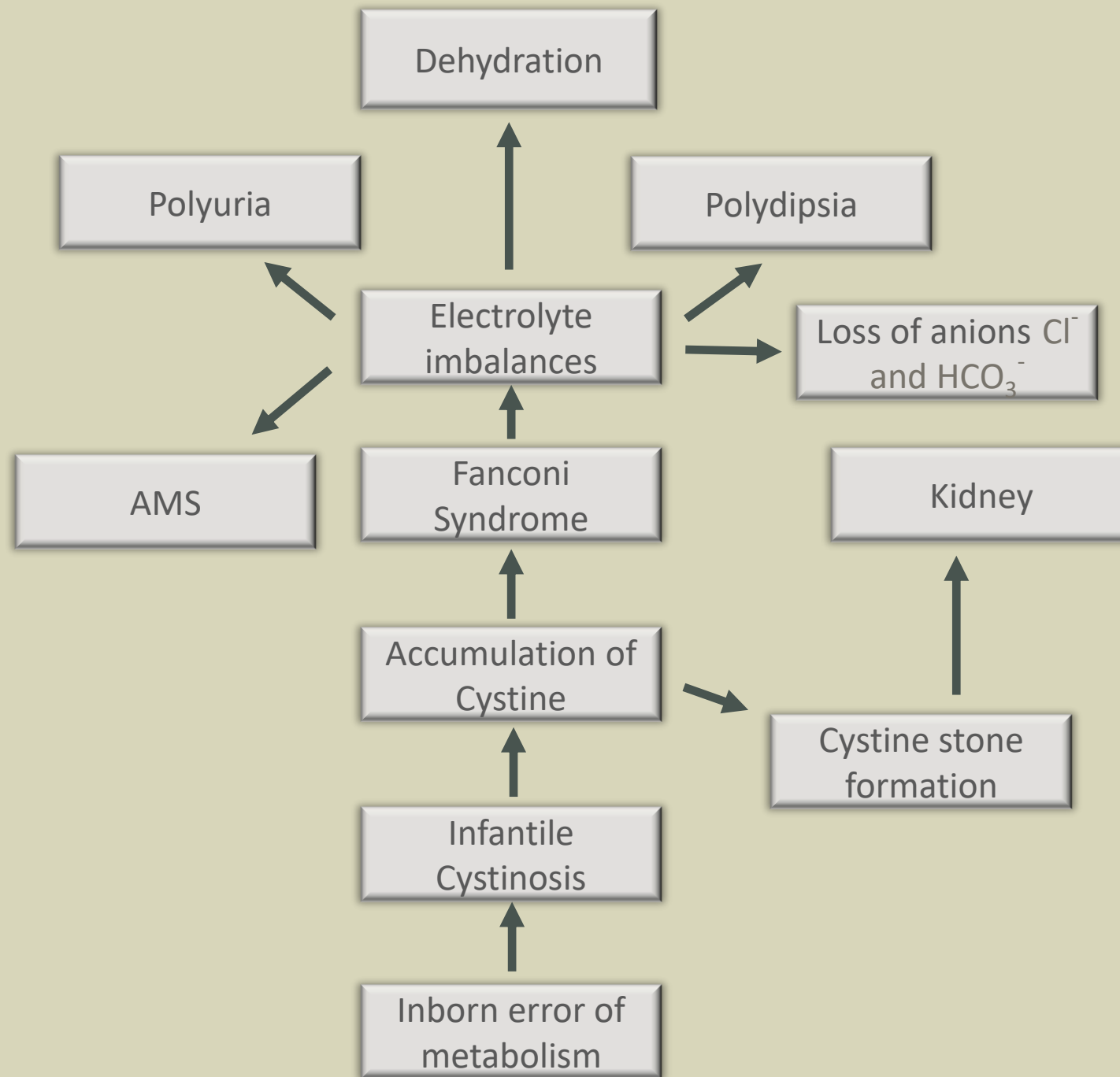
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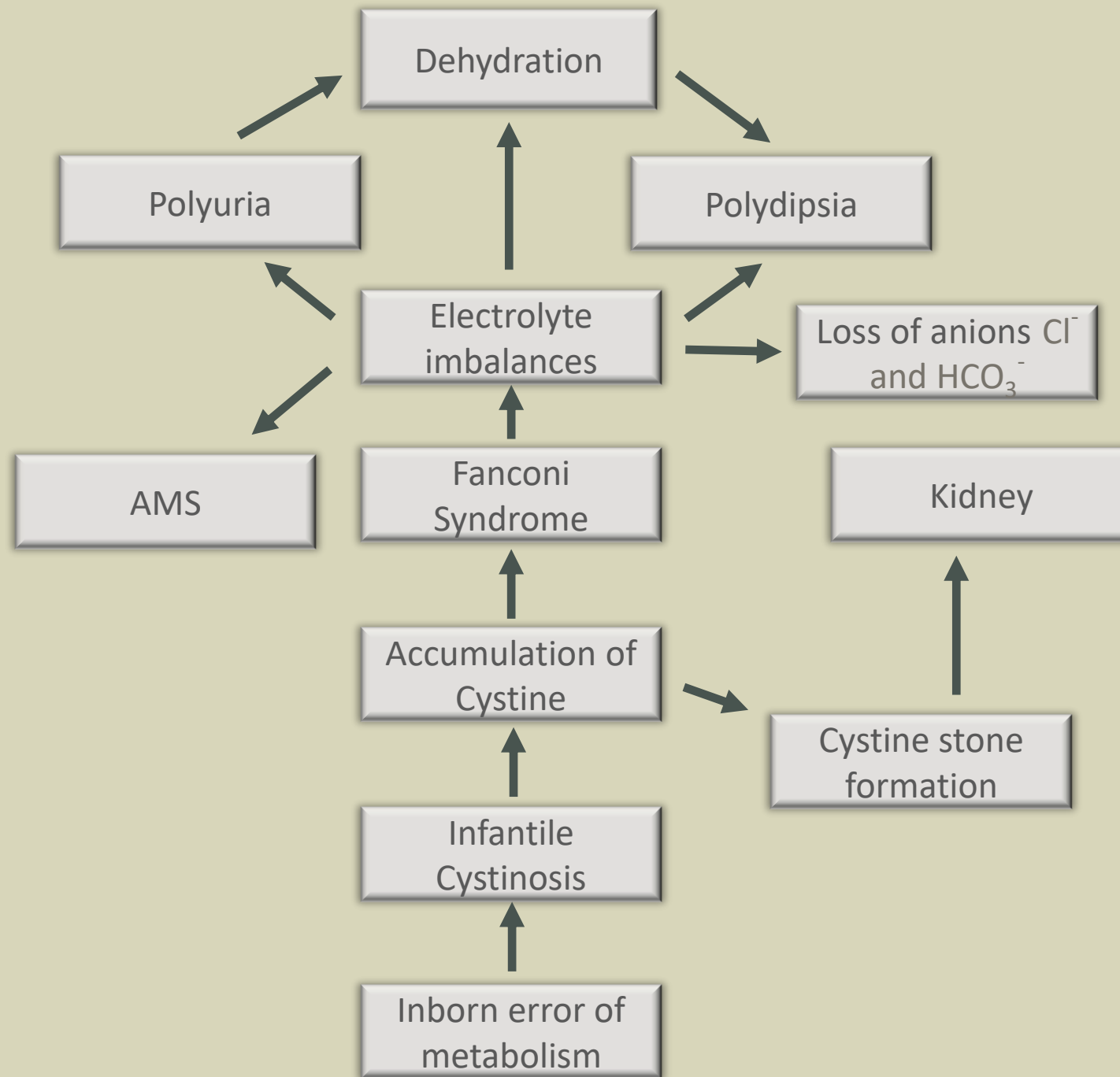
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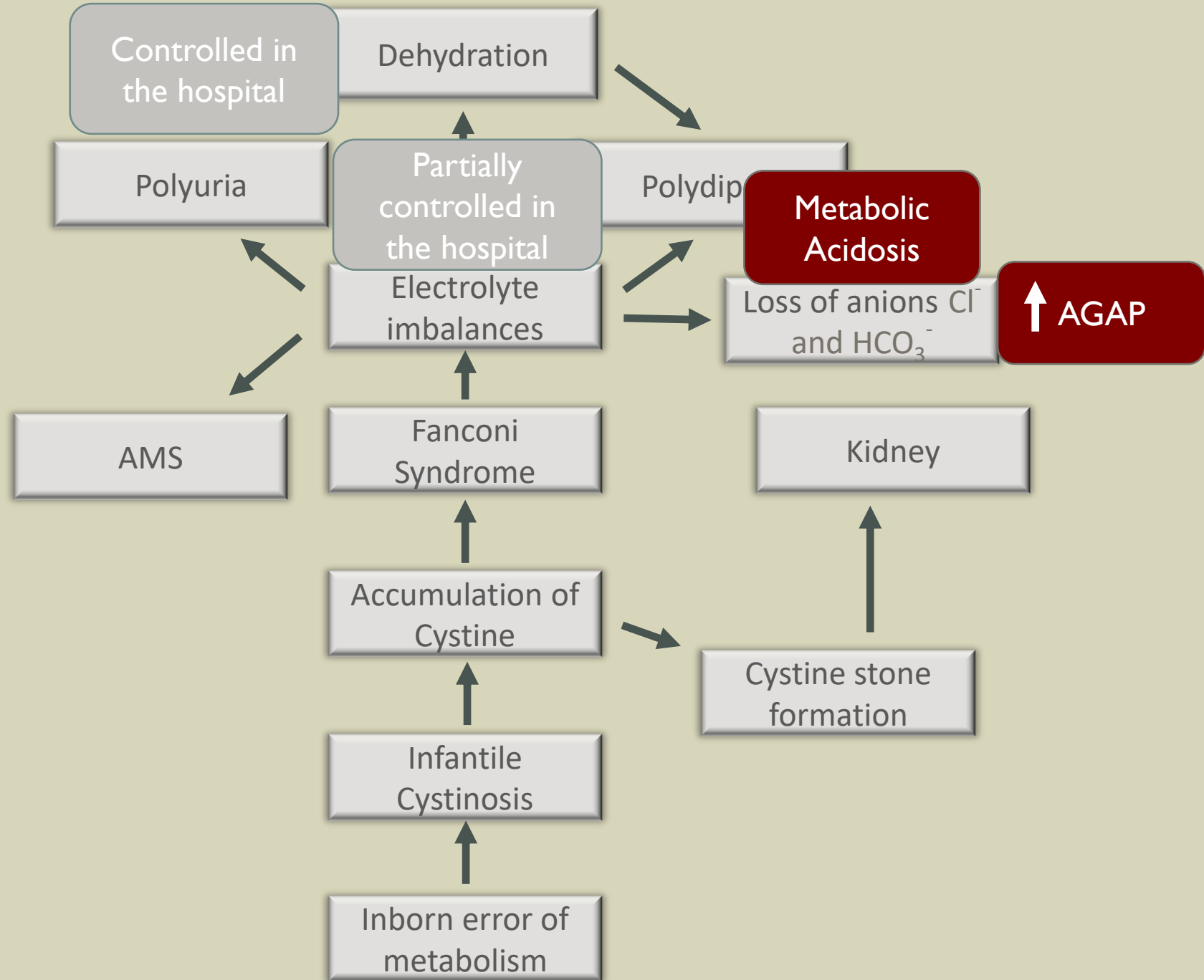
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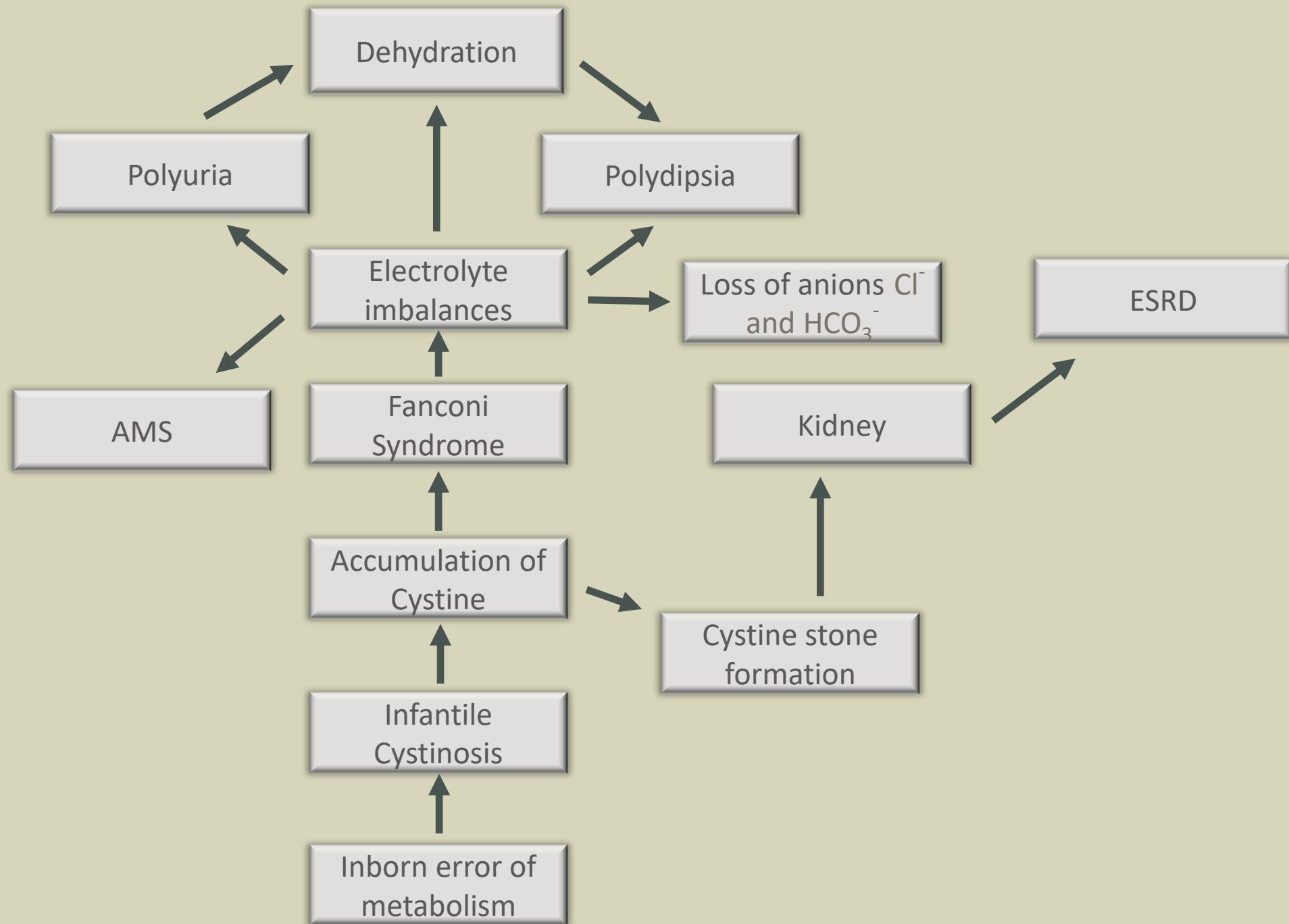
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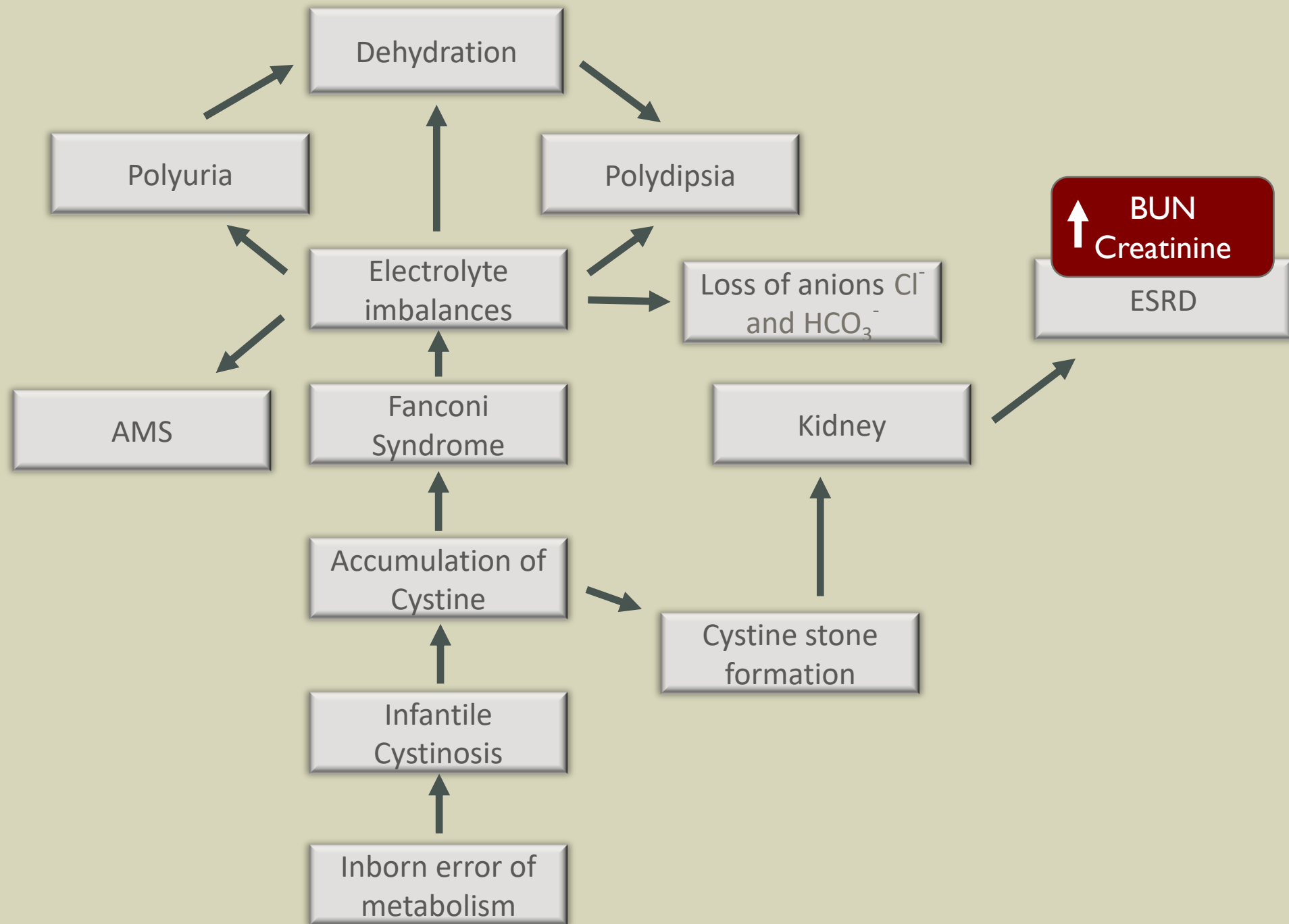
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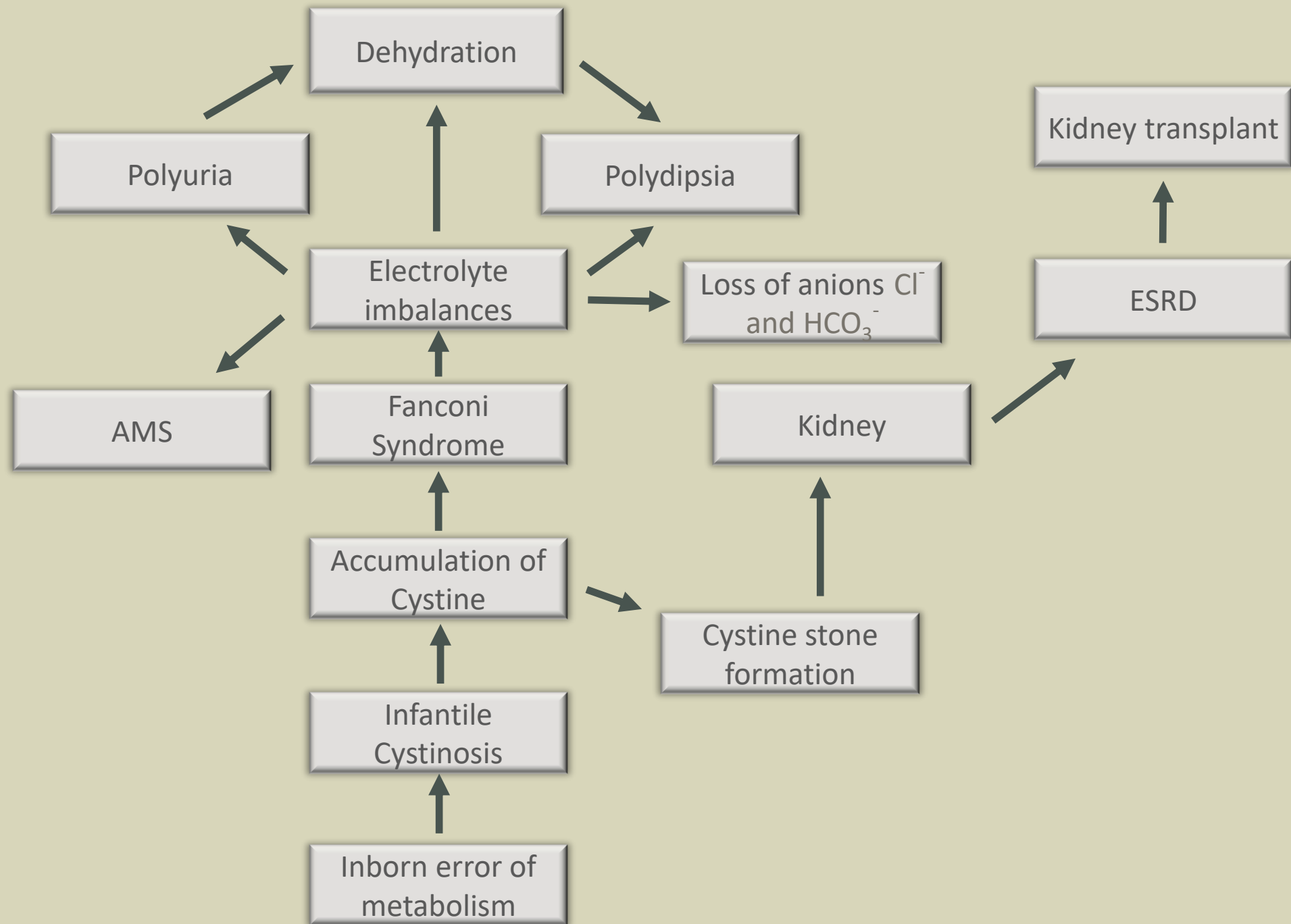
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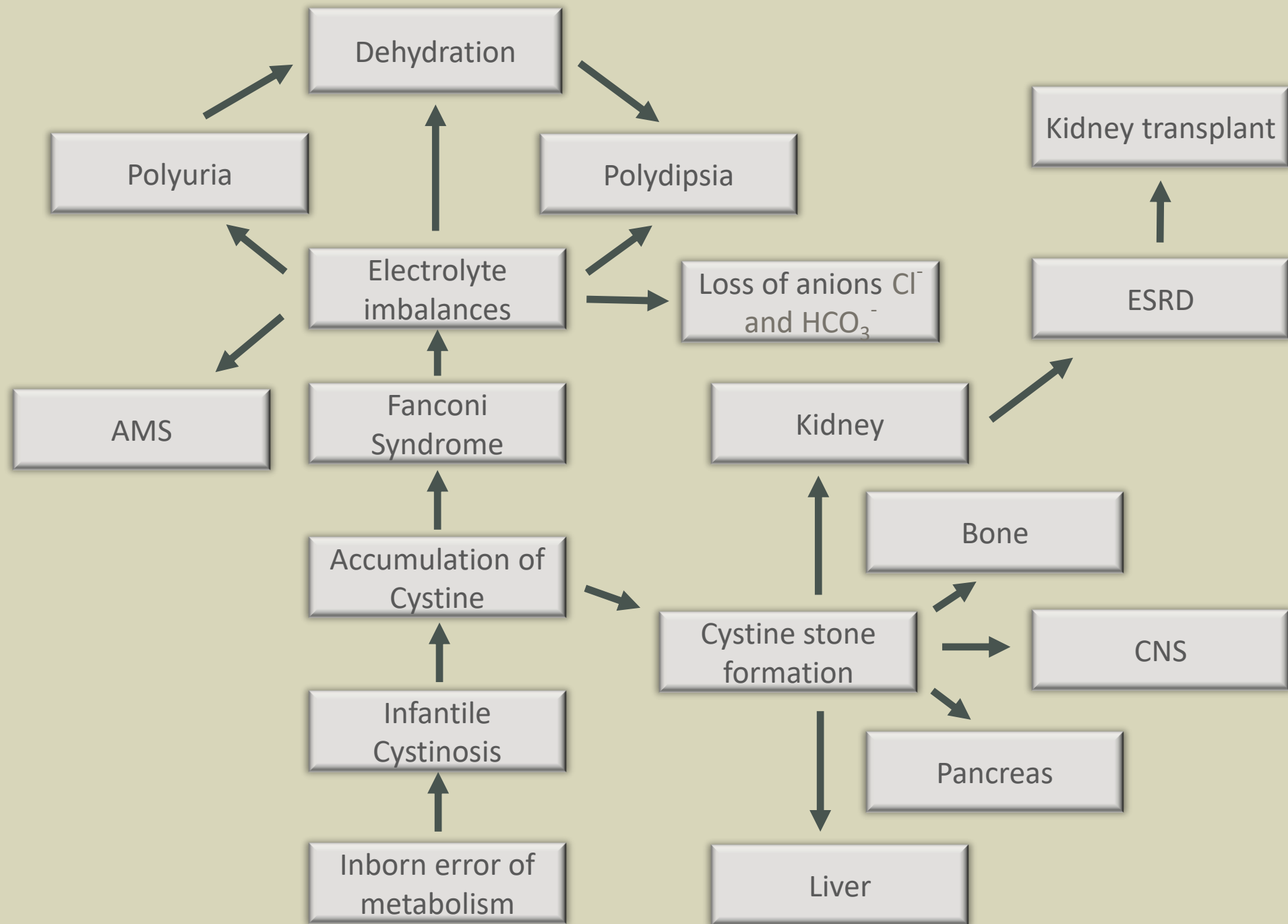
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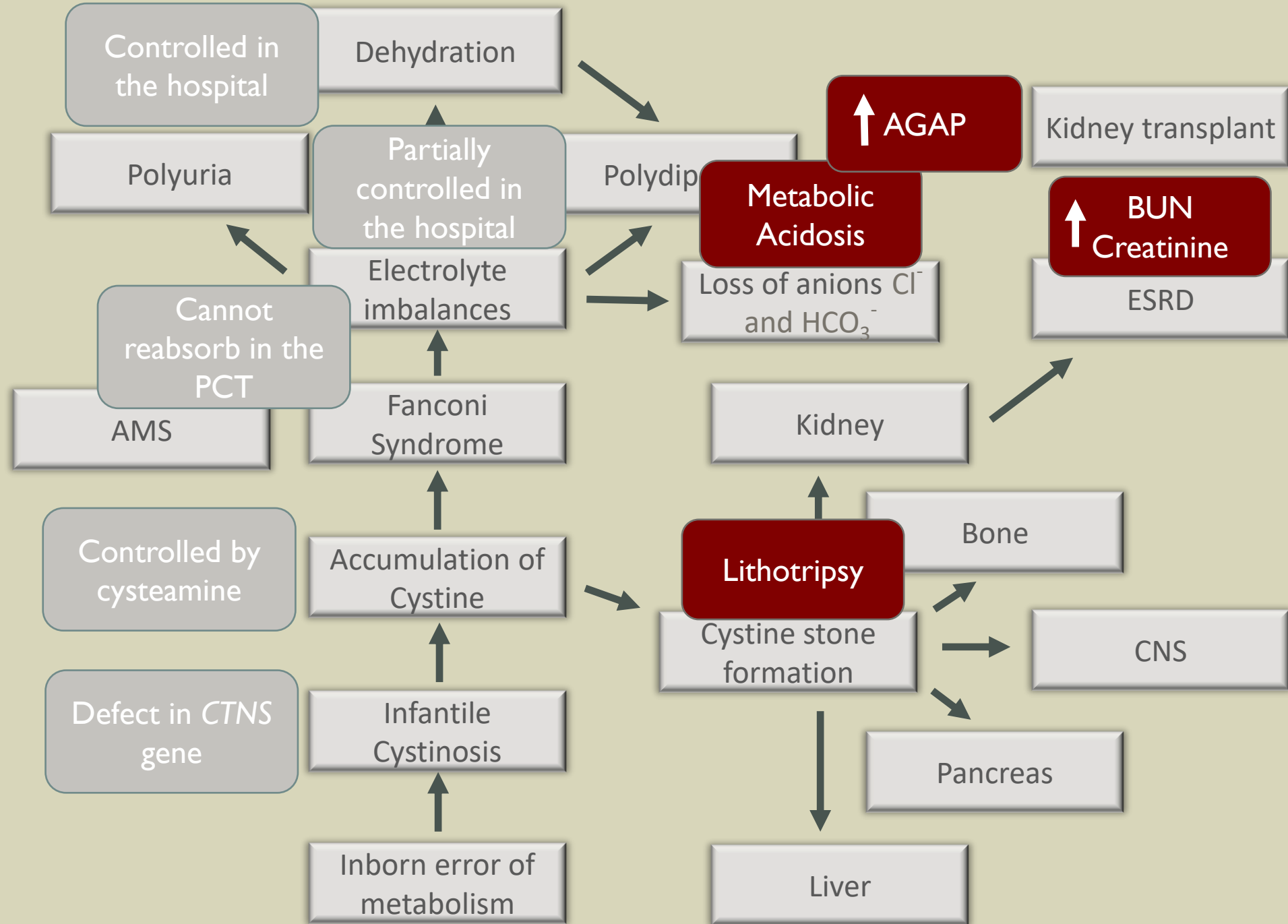
Concept Map



Concept Map



Concept Map



Thank You!