Cases: Inborn Errors of Metabolism

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Case 1:

- 3 day old male brought to the ED for progressive poor feeding, lethargy – admission requested for "rule out sepsis"
- On your assessment, HR 180, RR 90, SaO2 97% RA, BP 80/50, T 36.5. Lethargic and hypotonic

Case 1:

- CBC, lytes, liver enzymes normal
- Cultures all pending
- U/A normal, no ketones
- Gas 7.5/28/24
- Ammonia 400
- BUN 0.8, creatinine 90

Hyperammonemia

- IEM
  - Urea cycle defects
  - Organic acidemias
  - FAODs
  - Galactosemia
  - Hereditary fructose intolerance
  - Hyperornithinemia, hyperammonemia, homocitrullinemia syndrome
  - Pyruvate carboxylase deficiency
  - Hyperammonemia/Hyper insulinemia syndrome
  - Hereditary fructose intolerance
- Liver
  - Liver failure (any cause)
  - Sepsis
  - Perinatal depression/hypoxia
- Iatrogenic
  - VPA
  - TPN
- Other
  - Transient hyperammonemia of the newborn
  - Transient neonatal hyperammonemia

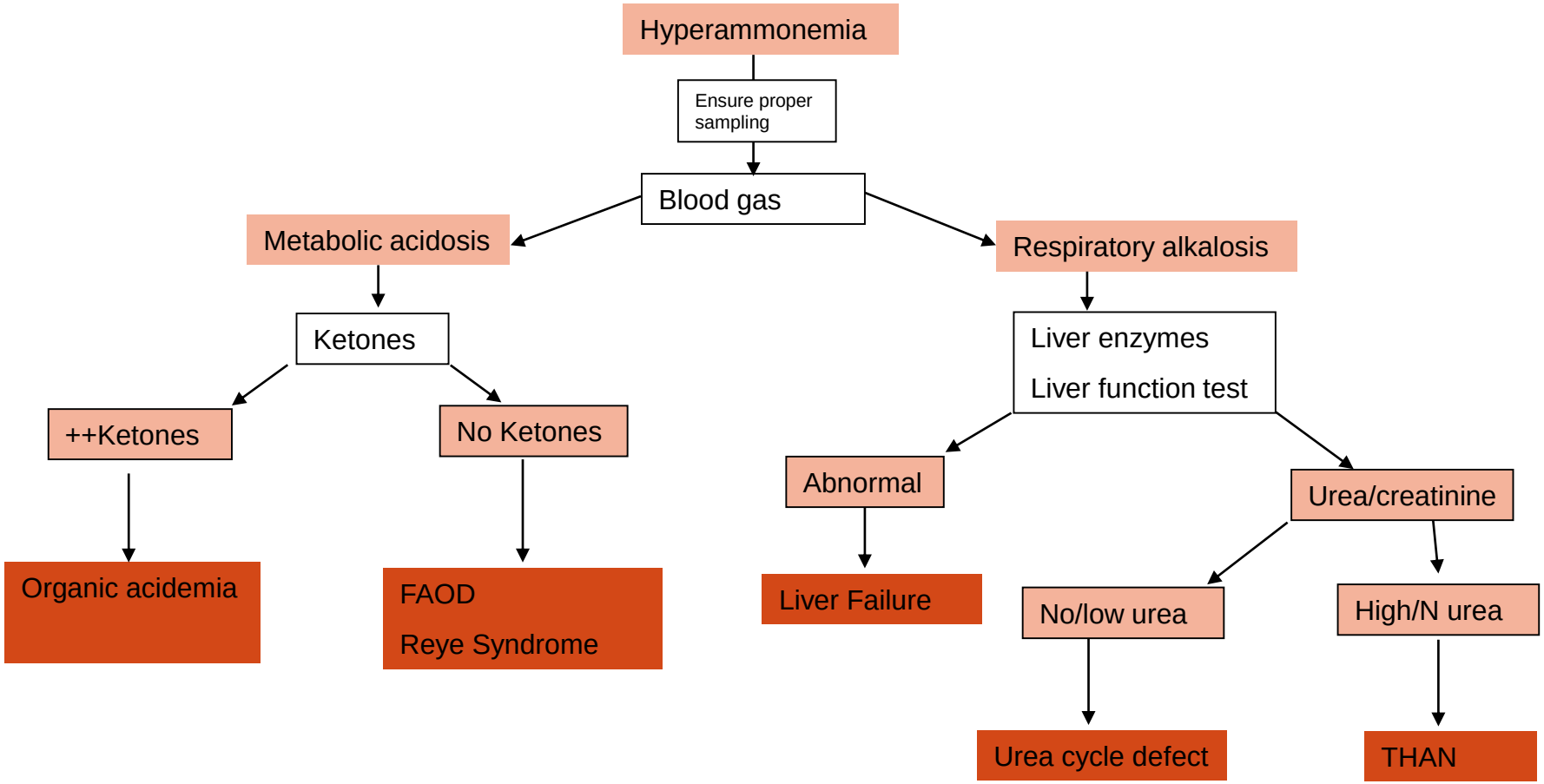
Work up

- Plasma ammonia level
- Liver function and liver enzymes
- Plasma amino acid
- Urine organic acid
- Lactate levels
- Blood gas
- BUN level

Case 1:

- CBC, lytes, liver enzymes normal
- Cultures all pending
- U/A normal, + ketones
- Gas 7.2/20/10
- Ammonia 400
- BUN 10, creatinine 90

Approach to Hyperammonemia



Plasma amino acids

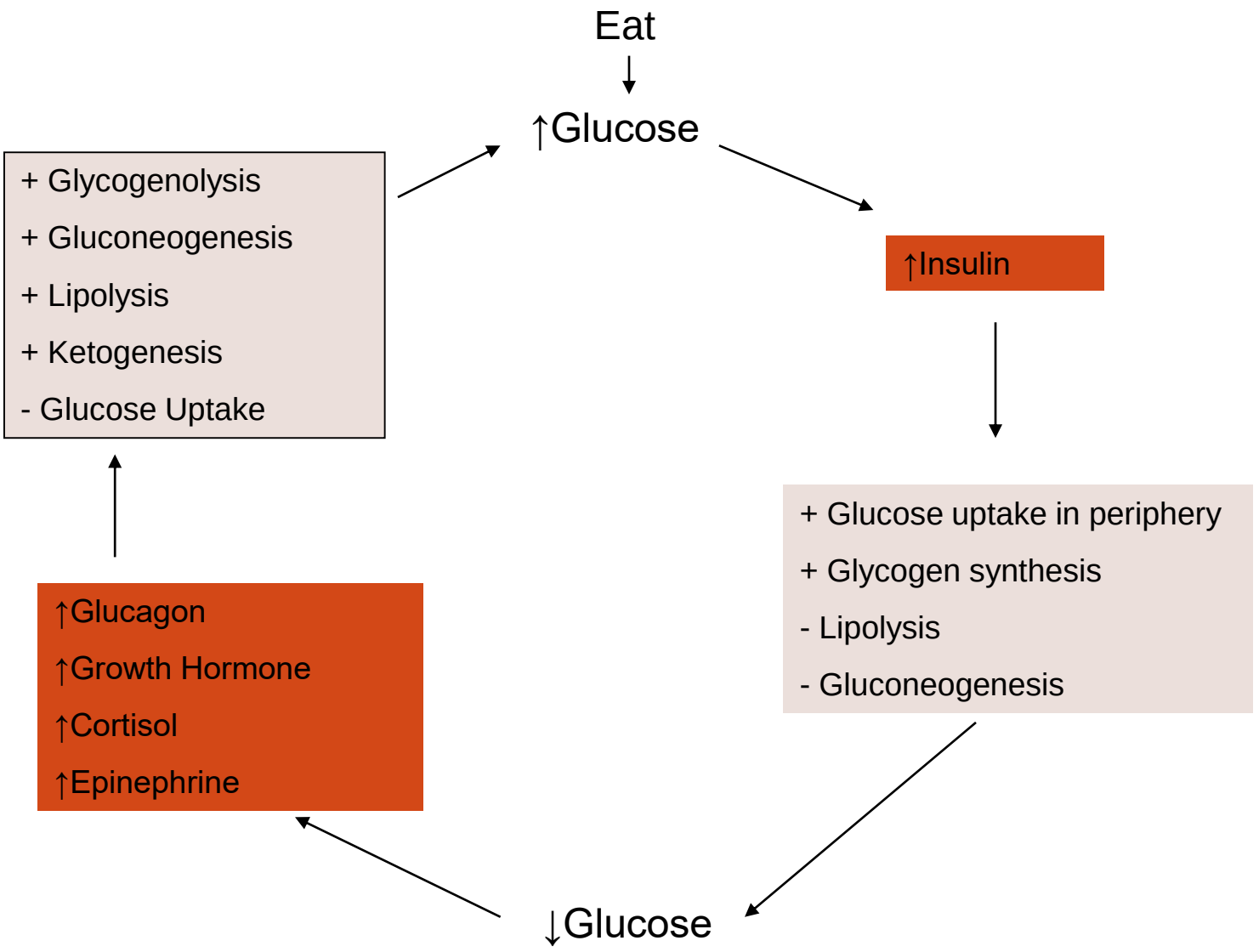
Plasma organic acids

Urine amino acids

Case 2

- 3 month male with progressively poor feeding, lethargy, hypoglycemic seizure – admission requested for "rule out sepsis"
- On your assessment, HR 150, RR 48, SaO2 99% RA, BP 80/50, T 36.5.
- Admitted for Abx, but ongoing hypoglycemic every time you try to wean fluids

Glucose Regulation



Hypoglycemia

Liver Failure

↓ Substrate

- Prolonged fast
- Prematurity
- SGA
- Ketotic Hypoglycemia

Endocrine

Hyperinsulinism

- IDM
- Birth Asphyxia
- Persistent Hyperinsulinemia Hypoglycemia of infancy
- Insulin adenoma
- Beckwidth Weidman

Decreased Counterregulation

- Panhypopituitarism
- GH deficiency
- ACTH deficiency
- Hypothyroid
- Adrenal insufficiency

Metabolic

Carbohydrate

- Glycogen Storage Diseases (some types)
- Inability to metabolize substrate (fructosemia, galactosemia)
- Gluconeogenesis problem
- Pyruvate metabolism problem

Lipids

- FAOD
- Carnitine Deficiency

Proteins/Amino acids

- Organic Acidemia (PA, MMA, IVA)
- Urea Cycle Defects
- Aminoacidopathy (MSUD)

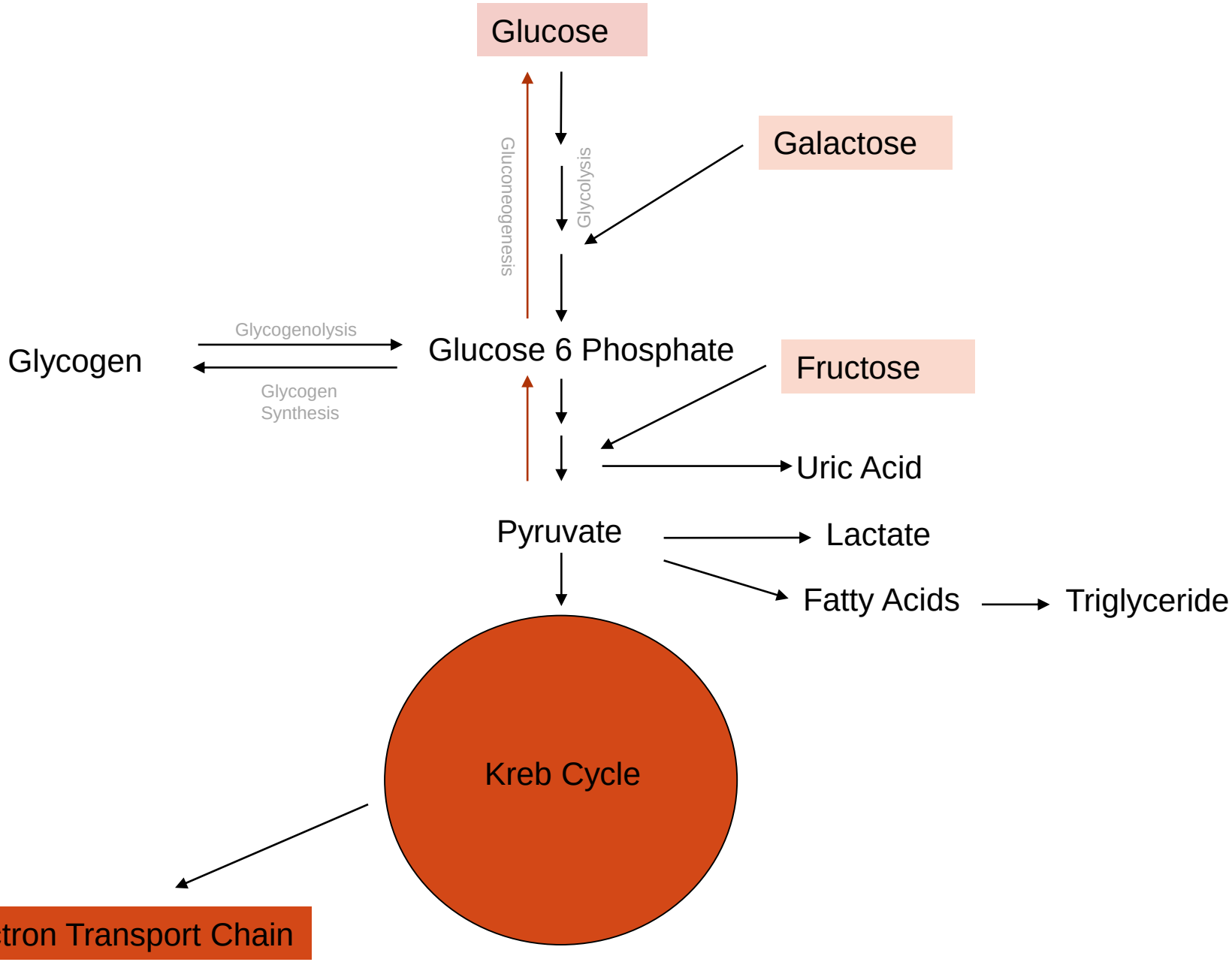
↑ Demand

Systemic Disorders

- Sepsis
- CHF
- Renal
- Malnutrition
- Shock
- LGA infants?

Drugs

- Insulin
- Sulfonylurea drugs


Glucose
Galactose
Gluconeogenesis
Glycolysis
Glycogenolysis
Glycogen
Glycogen Synthesis
Glucose 6 Phosphate
Fructose
Uric Acid
Pyruvate
Lactate
Fatty Acids
Triglyceride
Kreb Cycle
Electron Transport Chain

Investigations

The Critical Sample

- Glucose ↓
- Insulin ↓
- Growth Hormone ↑
- Epinephrine ↑
- IGF-1 ↑
- Lactate N
- Pyruvate N
- Blood Gas 7.35/45/24

- Ketones – Urine, serum βhydoxybutyrate ↑
- Free Fatty acids ↑
- Free Carnitine N
- Acyl Carnitine profile N
- Ammonia N
- Urine organic acids P
- Urine amino acids P
- Plasma amino acids P

Investigations

The Critical Sample

- Glucose ↓
- Insulin ↓
- Growth Hormone ↑
- Epinephrine ↑
- IGF-1 ↑
- Lactate ↑
- Pyrutate ↑
- Blood Gas 7.20/30/60/15

- Ketones – Urine, serum βhydoxybutyrate ↑
- Free Fatty acids ↑
- Free Carnitine N
- Acyl Carnitine profile N
- Ammonia N
- Urine organic acids P
- Urine amino acids P
- Plasma amino acids P

Investigations

The Critical Sample

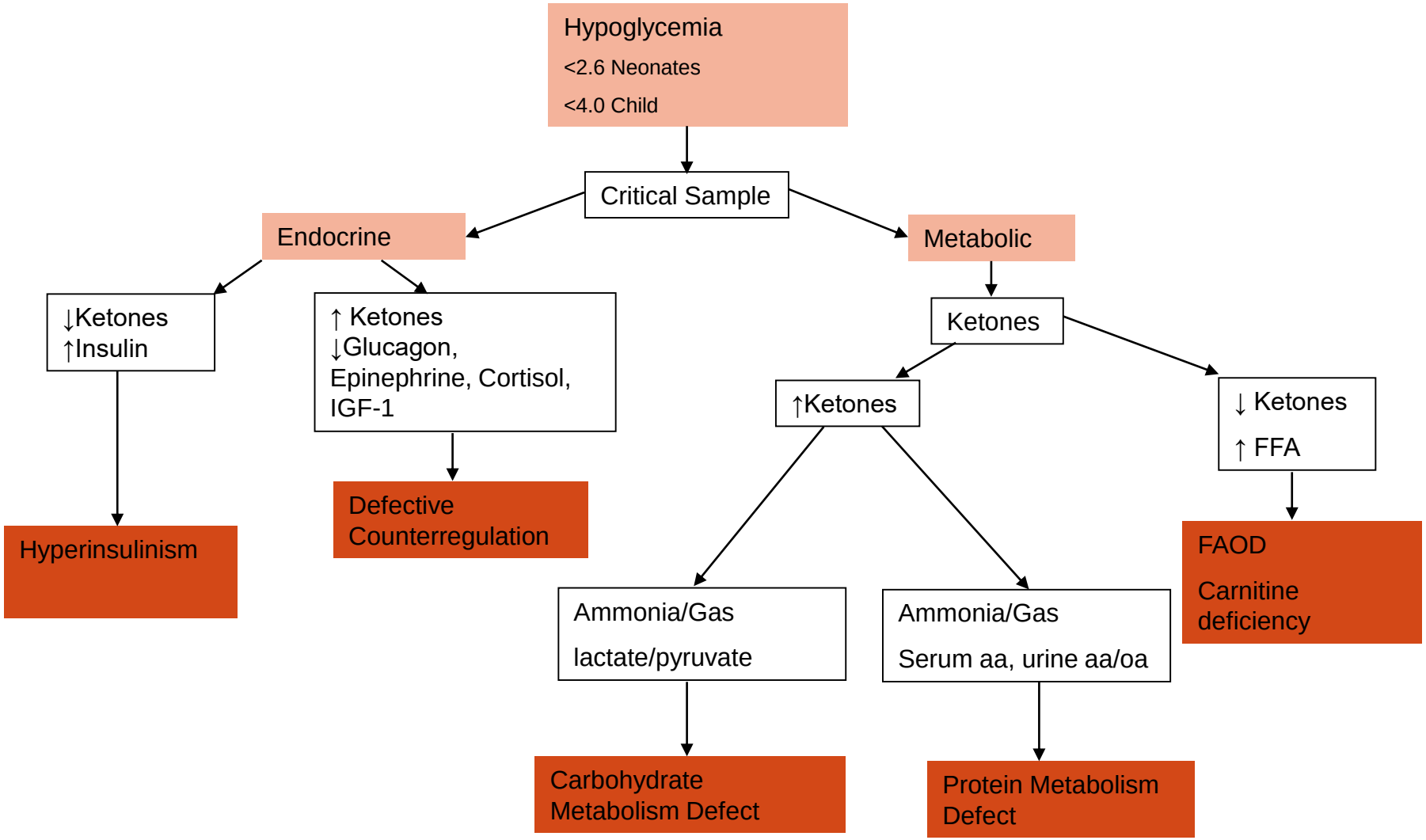
- Glucose ↓
- Insulin ↑
- Growth Hormone ↑
- Epinephrine ↑
- IGF-1 ↑
- Lactate N
- Pyrutate N
- Blood Gas 7.35/45/24
- Ketones – Urine, serum βhydoxybutyrate Negative
- Free Fatty acids ↓
- Free Carnitine N
- Acyl Carnitine profile P
- Ammonia P
- Urine organic acids P
- Urine amino acids P
- Plasma amino acids P

Investigations

The Critical Sample

- Glucose ↓
- Insulin ↓
- Growth Hormone ↑
- Epinephrine ↑
- IGF-1 ↑
- Lactate N
- Pyrutate N
- Blood Gas 7.35/45/24
- Ketones – Urine, serum βhydoxybutyrate Negative
- Free Fatty acids ↑
- Free Carnitine N
- Acyl Carnitine profile P
- Ammonia 200
- Urine organic acids P
- Urine amino acids P
- Plasma amino acids P

Interpretation of The Critical Sample



Resources

- **Paul A. Levy. Inborn Errors of Metabolism. Pediatrics in Review. April 2009, VOLUME 30 / ISSUE 4**

- Gregory M. Rice, Robert D. Steiner. Inborn Errors of Metabolism (Metabolic Disorders). Pediatrics in Review. January 2016, VOLUME 37 / ISSUE 1

- https://newenglandconsortium.org/

- **Gene reviews**

Questions

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