Acute hypotonia:
Metabolic causes

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Pediatrics
Inherited Metabolic disorders

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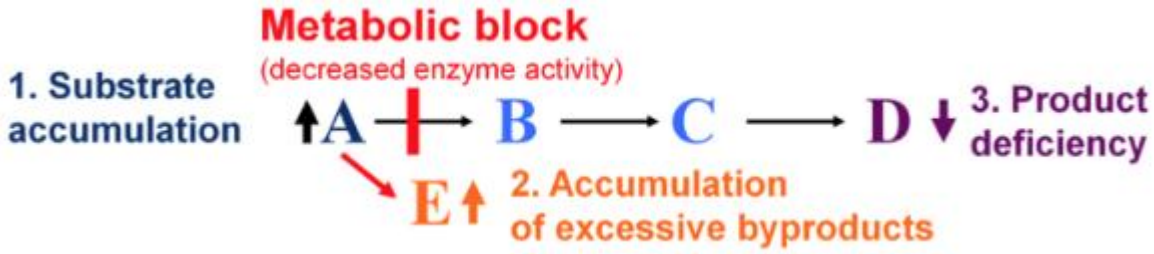
Inborn errors of metabolism

- Rare inherited disorders
- Resulting from
  - Enzyme defect in metabolic pathways which affects proteins, fats, carbohydrates metabolism
  - Impaired organelle function

Common metabolic disorder concerns in primary care practice : Marisha Agana, Julia Frueh, Manmohan Kamboj, Dilip R. Patel, and Shibani Kanungo ʾ Ann Transl Med. 2018 Dec; 6(24): 469., doi: 10.21037/atm.2018.12.34

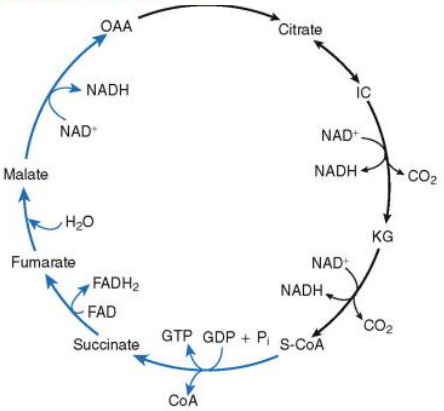
IEM: Three Categories

Intoxication



Energy metabolism disorders

- Deficiency in energy met
- Hypoglycemia

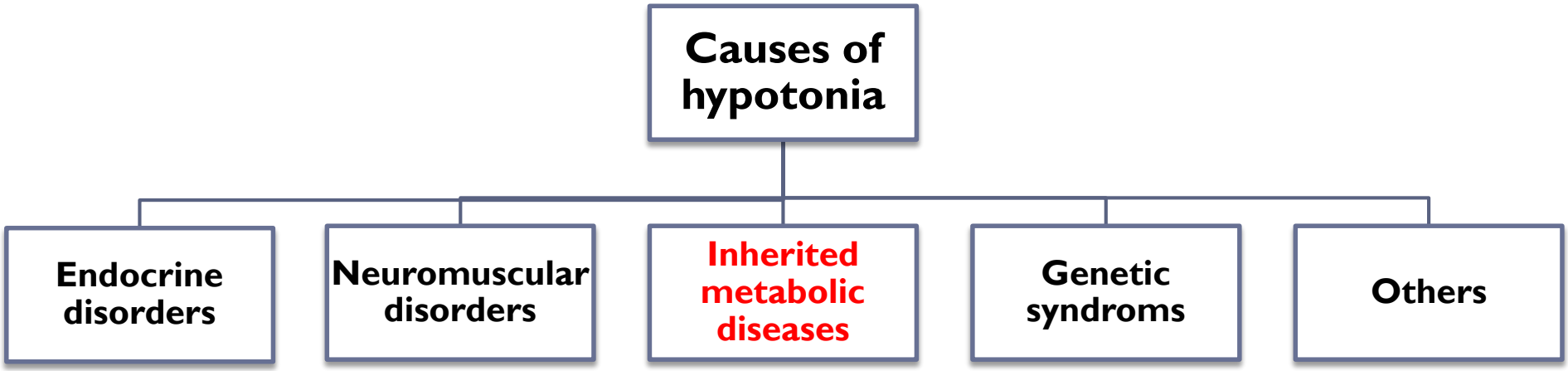


Complex molecules disorders

- Affects the synthesis or the catabolism of complex molecules
- CGD, LSD, Peroxysomal…

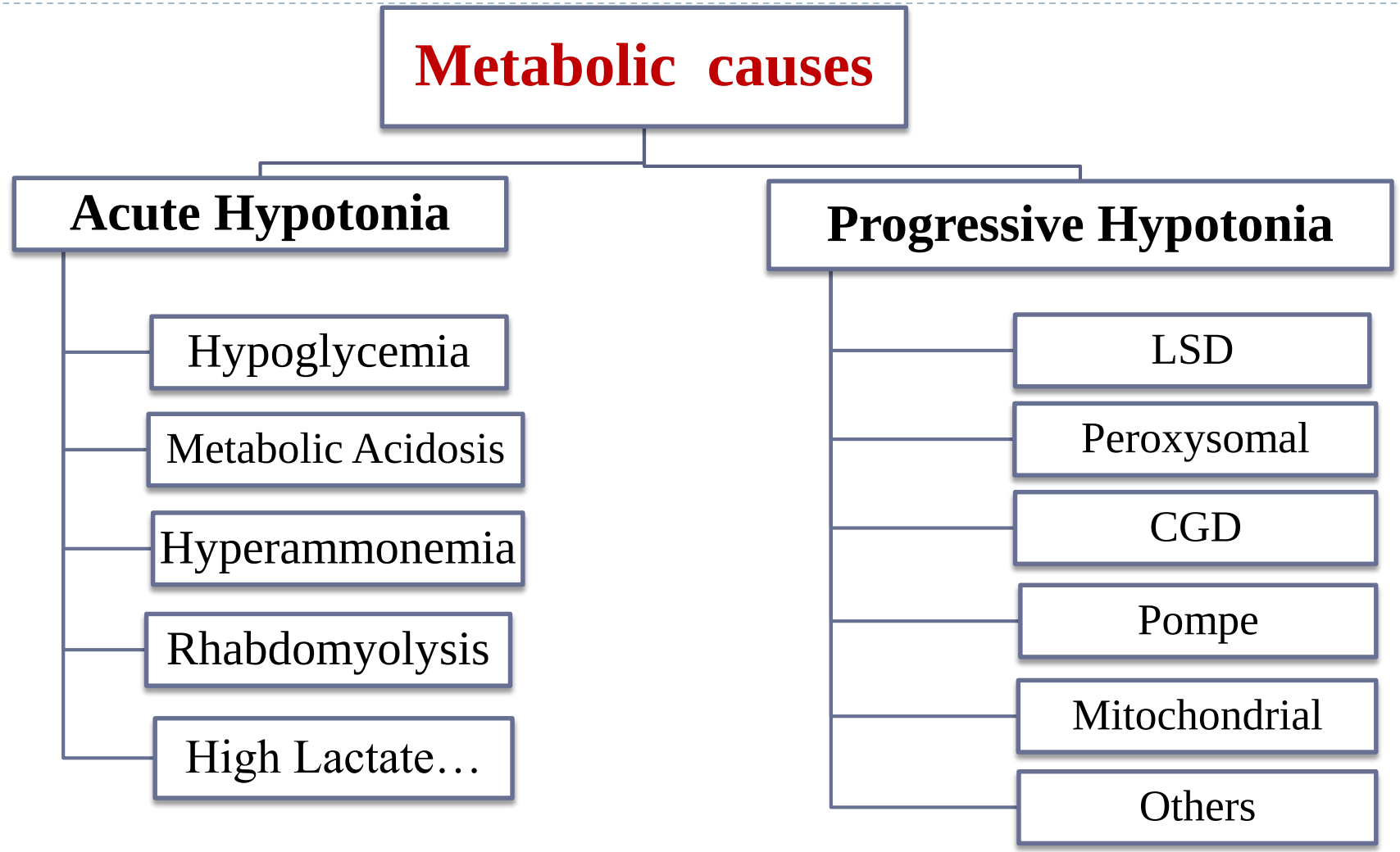
Clinical approach to inherited metabolic disorders in neonates: an overview J. M. Saudubray, M. C. Nassogne, P. de Lonlay and G. Touati. Semin Neonatol 2002; 7: 3–15 doi:10.1053/siny.2001.0083

Hypotonia



The Floppy Infant, Dawn E. Peredo, Mark C. Hannibal, Pediatrics in Review, September 2009, VOLUME 30 / ISSUE 9

Hypotonia


Metabolic causes
Acute Hypotonia
Hypoglycemia
Metabolic Acidosis
Hyperammonemia
Rhabdomyolysis
High Lactate…
Progressive Hypotonia
LSD
Peroxysomal
CGD
Pompe
Mitochondrial
Others

Case 1

- 1rst child of a non consanguineous parents
- Normal delivery 37 W
- W 2660g, Ht 47 cm, HC 33 cm, APGAR 10/10

- DOL 2
  - Intermittent Moaning/Refuse feeding
  - Sepsis work up: negative
  - ATB started
- DOL 3
  - Neurologic deterioration
    - Acute axial hypotonia ⟹ severe hypotonia
      ⟹ Respiratory distress

Case 1

- **TTT**
  - Intubation
  - Quadritherapy

- **Labs**
  - ABGs, CBC, CRP, PCT, Ionogram, urea, creat
  - UA
  - LP
  - Ammonia, lactate

Case 1

- Sepsis work up: normal
- ABGs
  - pH = 7,24, bicarbonate = 17, pCO2 = 40
  - Lactate = 12 mmol/L
- Ammonia : 1500 µmol/L (N<150)

Causes of Hyperammonemia

INHERITED		ACQUIRED
PRIMARY	**SECONDARY**	
Urea Cycle Defect	Organic aciduria	Transient hyperammoniemia of the newborn
Intermediate transport defect of UCD	Fatty acid beta oxydation disorders	Hepatocellular insufficiency - Hepatitis - Reye syndrom - Portocave shunt - Intoxication
	Galactosemia, tyrosinemia..	Medications - Valproate, Asparaginase
NH3 ↑↑↑	NH3 ↑	Urease positive bacteria

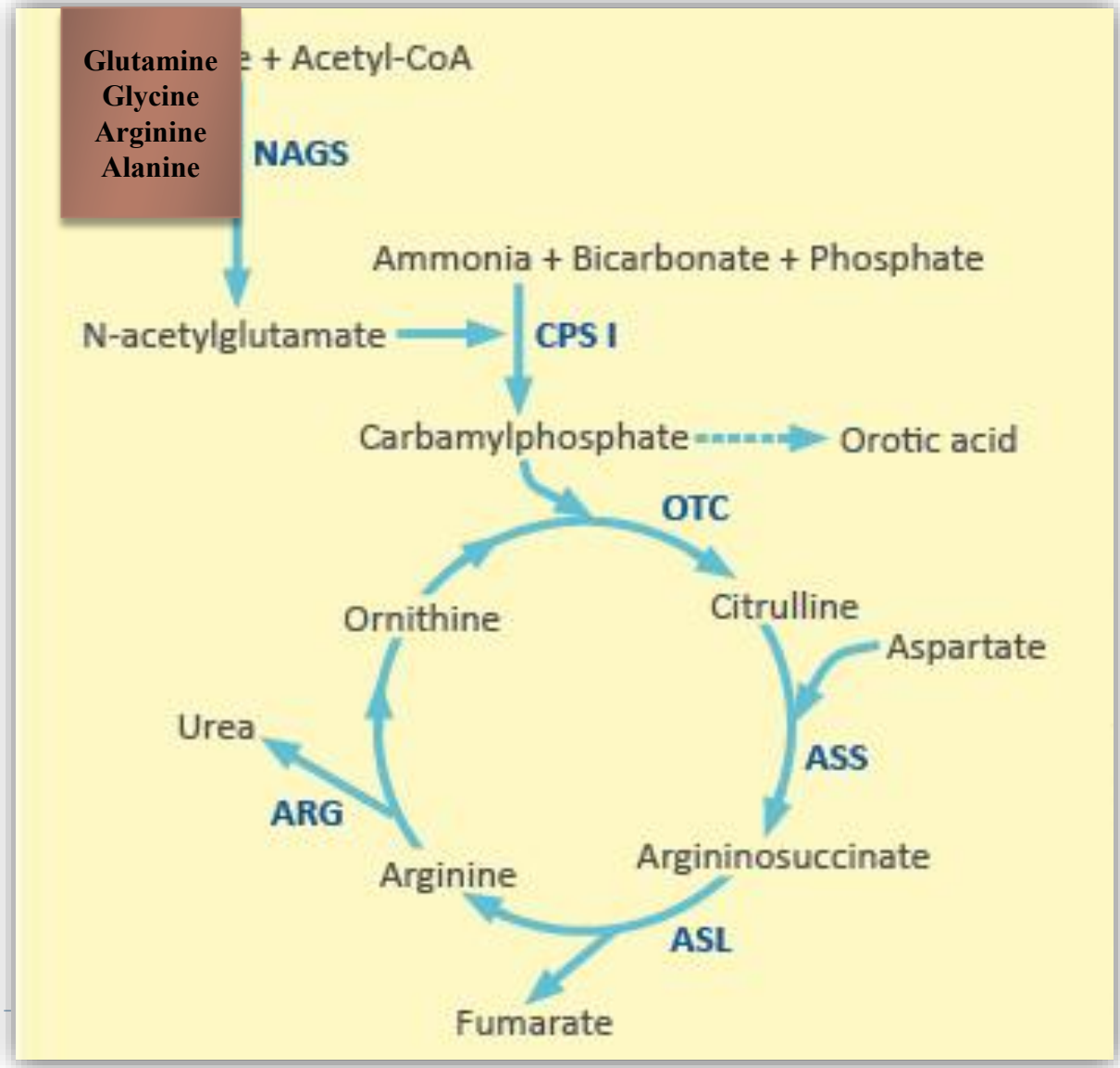
Prise en charge médicale et diététique des maladies héréditaires du métabolisme, P. de Lonlay et al, Springer-Verlag France 2013

Case 1

- Sepsis work up negative
- ABGs:
  - pH 7,24, bicarbonate 17, pCO2 40
  - Lactate 12 mmol/L
- Ammonemia :
  - 1500 µmol/L (N<150)
  - 3000 µmol/L

Case 1

- **PAAC :**
  - Glutamin 2139 µmol/l
  - Glycin 402 µmol/l
  - Arginin 26 µmol/L
  - Citrullin 2 µmol/l
- **Orotic acid :**
  - 834 mmol/molcreat



Case 2

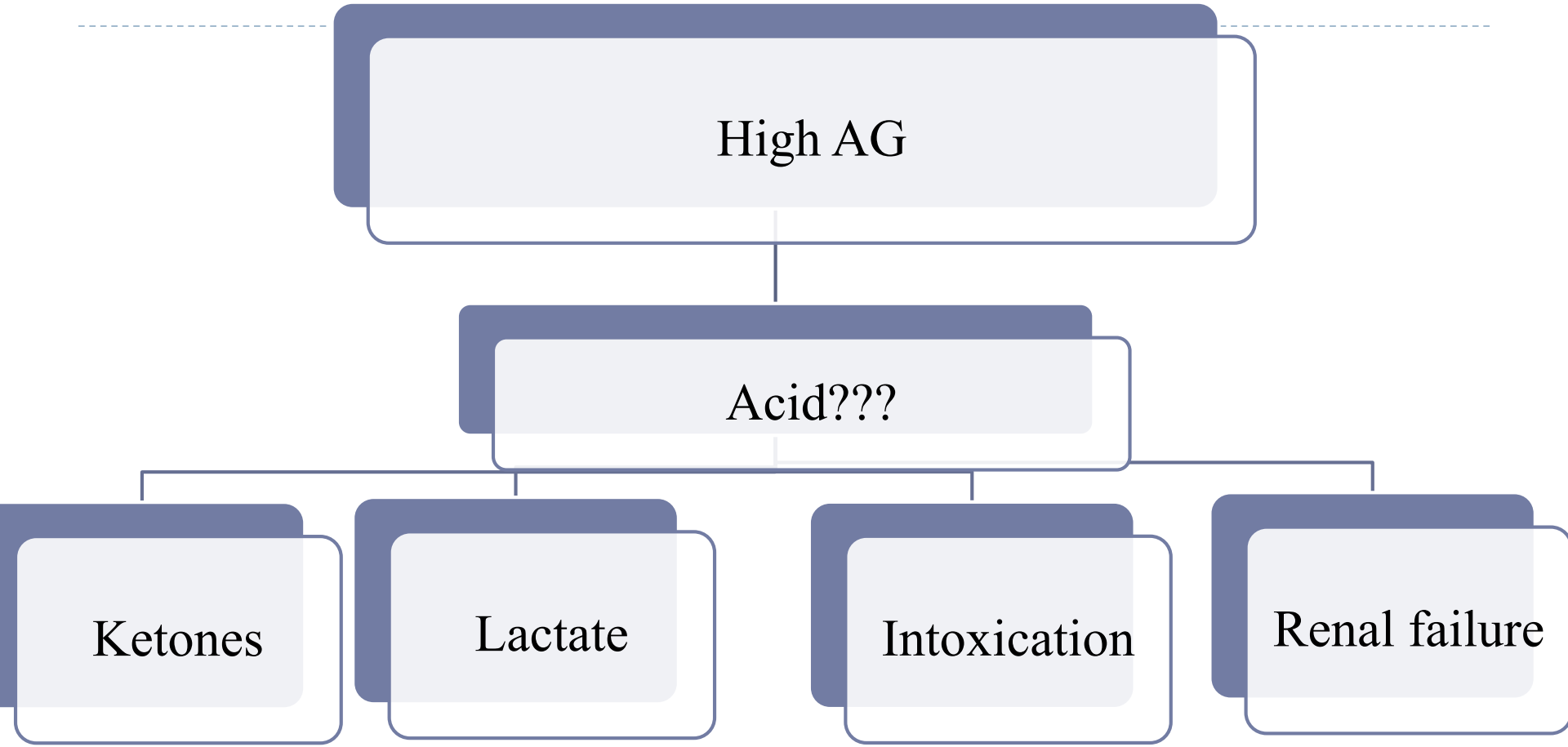
Case 2

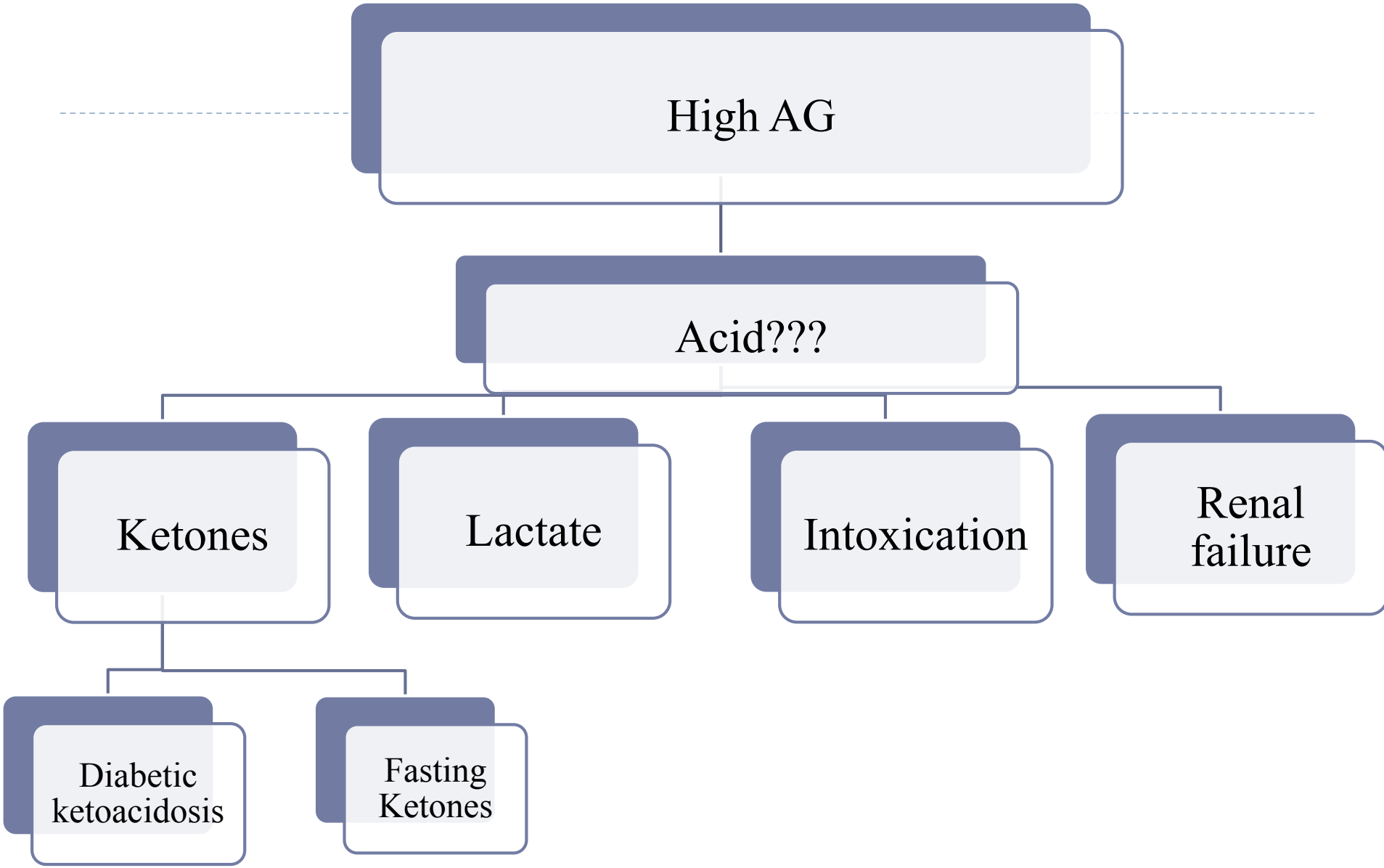
- 2nd child, non consanguineous parents
- 41 Weeker
- PN: 3kg, T: 48cm, PC: 32cm, Apgar:10/10
- Smooth pregnancy and delivery

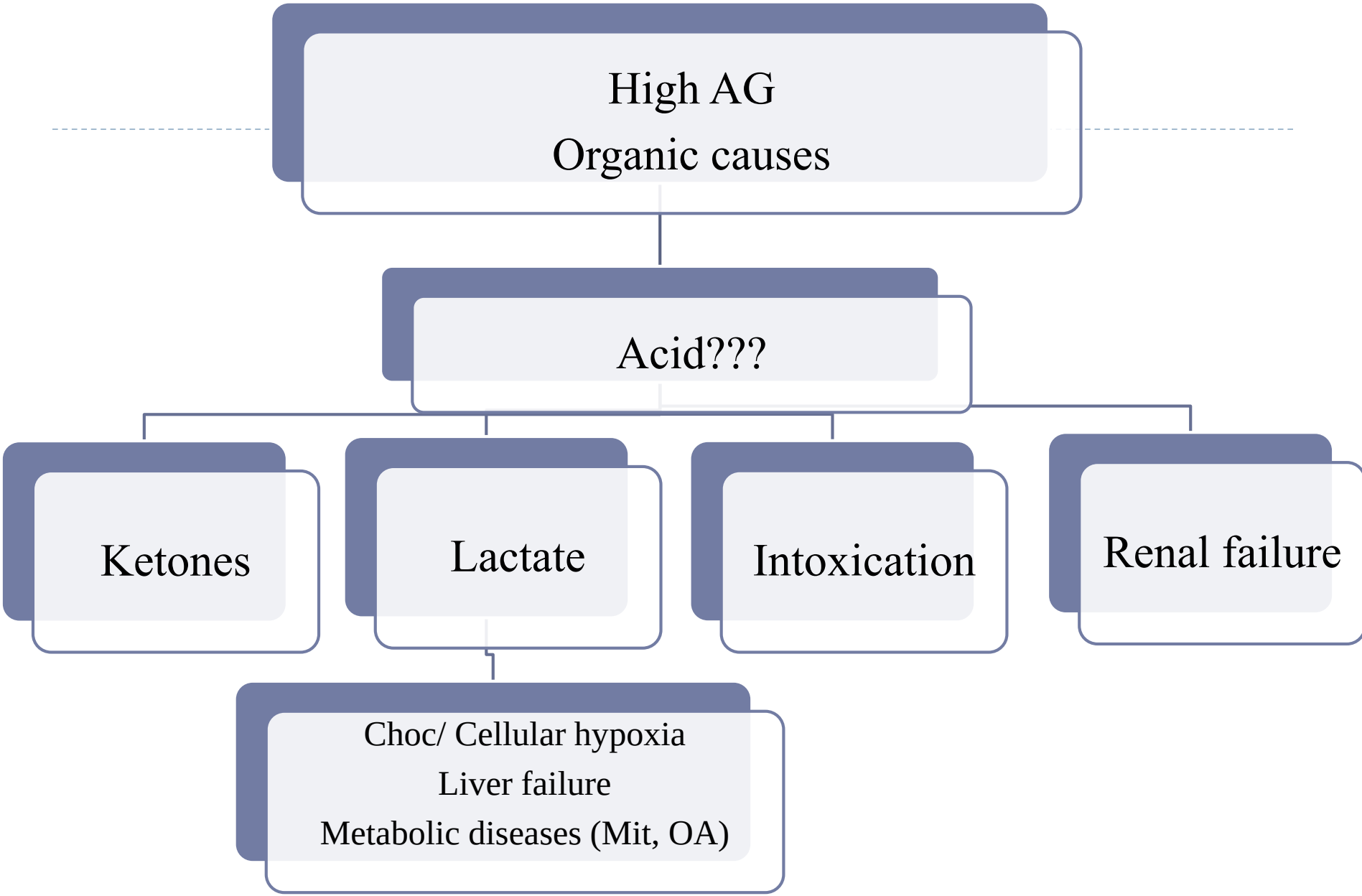
- DOL 3:
  - Decrease appetite
  - Hypotonia
  - Polypnea
  - Loss of weight (450g)

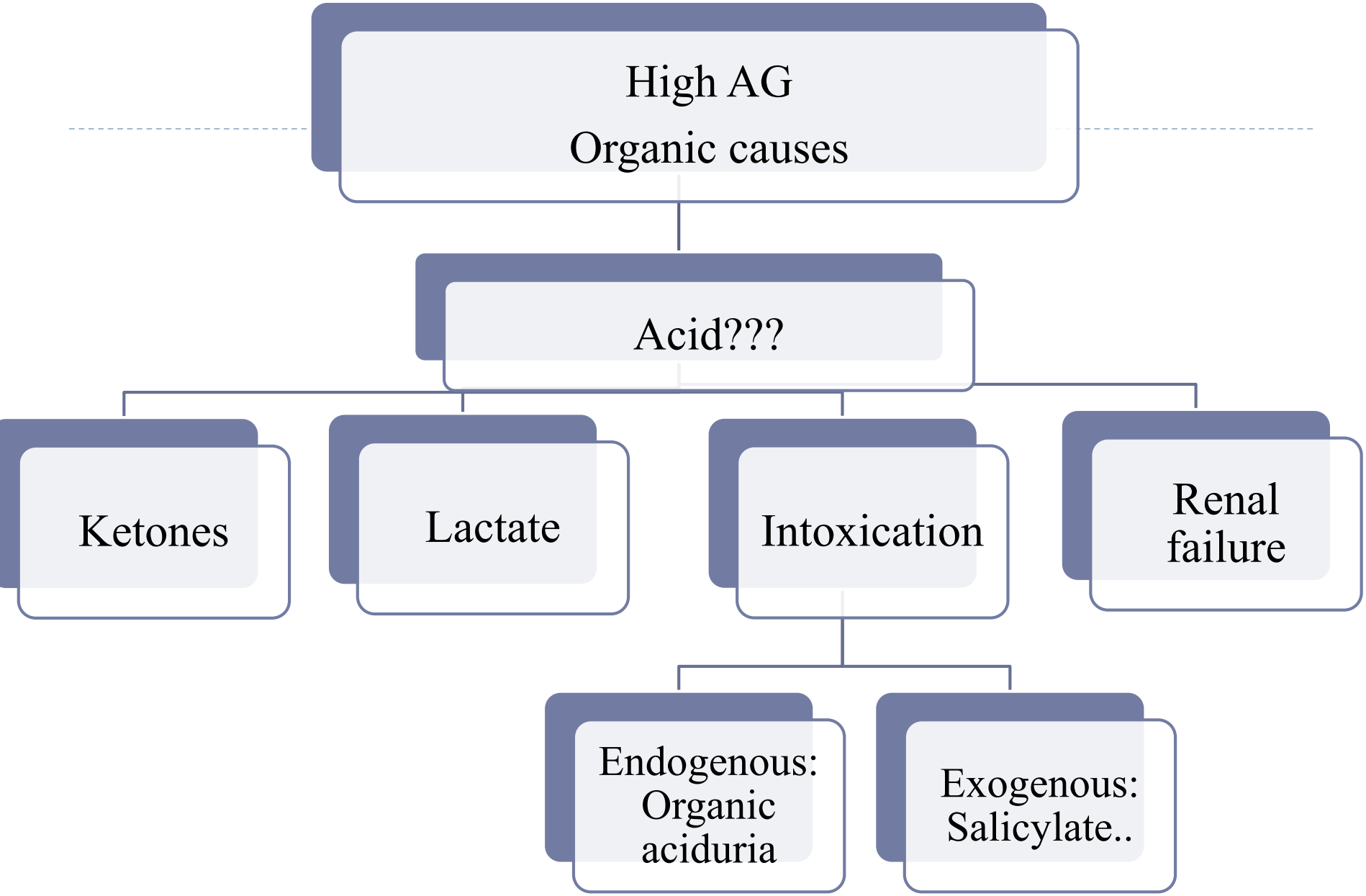
Case 2

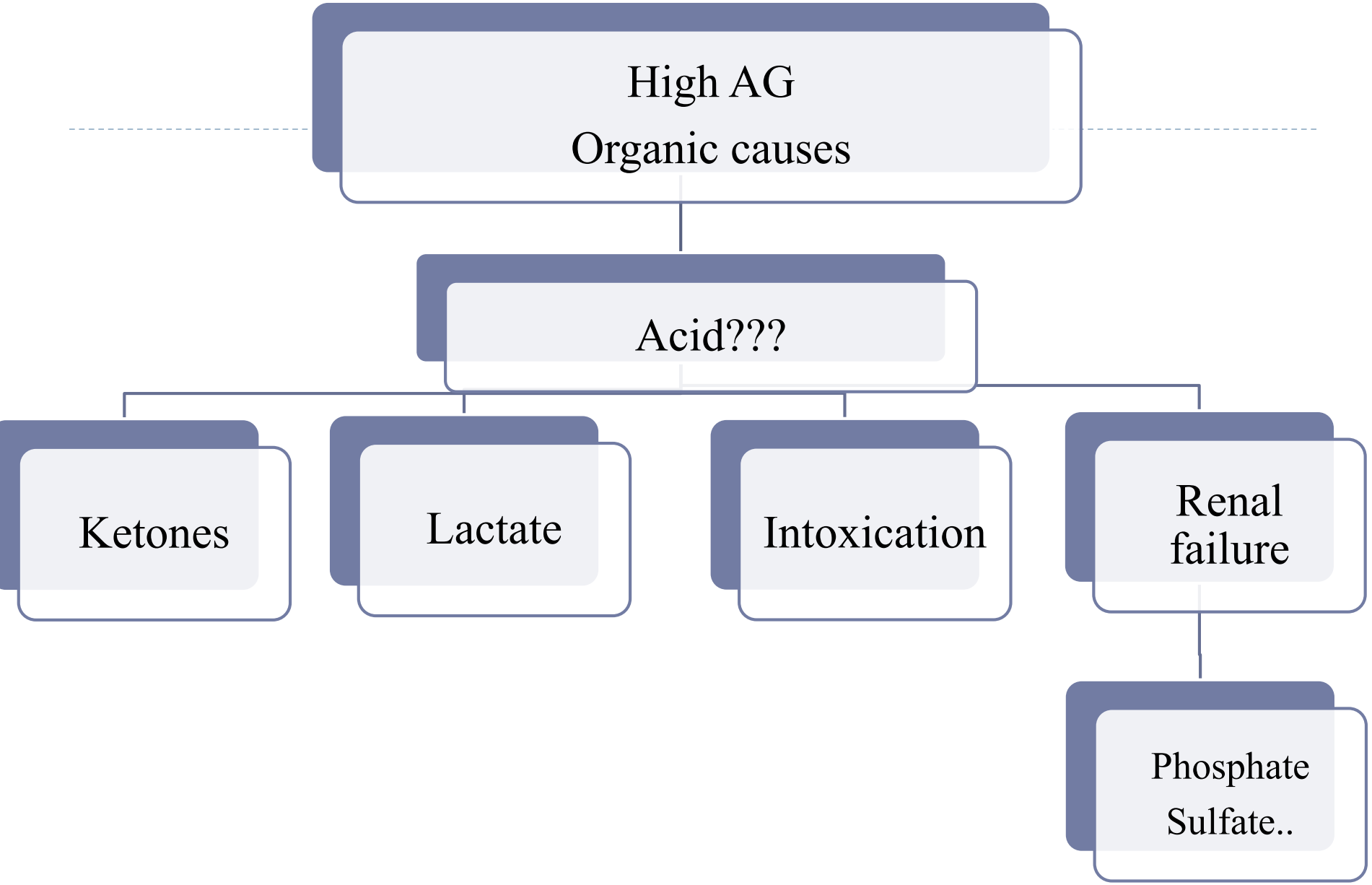
- Lab
  - Sepsis work up : Negative
  - ABGs : ph 7.08 PCO2 14, Bicar 4
  - LFT : Normal
  - Iono : Na 135, K: 4, Cl 100
  - Ammonia : 350µmol/l (N<150)
  - AG : 31


High AG
Acid???
Ketones
Lactate
Intoxication
Renal failure


High AG
Acid???
Ketones
Lactate
Intoxication
Renal failure
Diabetic ketoacidosis
Fasting Ketones


High AG
Organic causes
Acid???
Ketones
Lactate
Intoxication
Renal failure
Choc/ Cellular hypoxia
Liver failure
Metabolic diseases (Mit, OA)


High AG
Organic causes
Acid???
Ketones
Lactate
Intoxication
Renal failure
Endogenous: Organic aciduria
Exogenous: Salicylate..


High AG
Organic causes
Acid???
Ketones
Lactate
Intoxication
Renal failure
Phosphate
Sulfate..

Case 2

- Labs :
  - AG : 31
    - Ketones : ++++
    - Lactate: 1.3 mmol/l
    - Ur. Org. Ac Chromatography
    - Acylcarnitine profile

Case 2

- Ur. Org. Ac. Chromatography
  - Methylmalonic acid 

Case 3

Case 3

- 2nd second of non consanguineous parents
- Pregnancy and delivery normal
- Ht, W, HC normal, APGAR:10/10

- DOL 9:
  - Refuse feeding
  - Somnolence, Hypotonia
  - Abnormal mouvements of the extremities

Case 3

Labs

- pH: 7.36 pCO2: 27mmHg, Bicar 23
- Glycemia: 0.55g/l, Ca: 112 urea, creat normal
- Ammonia: 19micromol/l
- Lactate: 1.4mmol/l
- CBC: normal, coag: normal

UA: Ketones ++

Case 3

- PAAC

  - Leucine : 3587 µmol/l
  - Valine : 789 µmol/l
  - Isoleucine : 336 µmol/l
  - Alloisoleucine : 218 µmol/l

MSUD

Case 4

- 7 month-old-girl
- 3 days of febrile gastroenteritis
- ER: Acute Hypotonia with somnolence
- Hgt: Lo
- PE: Hepatomegaly

Hypoglycemia

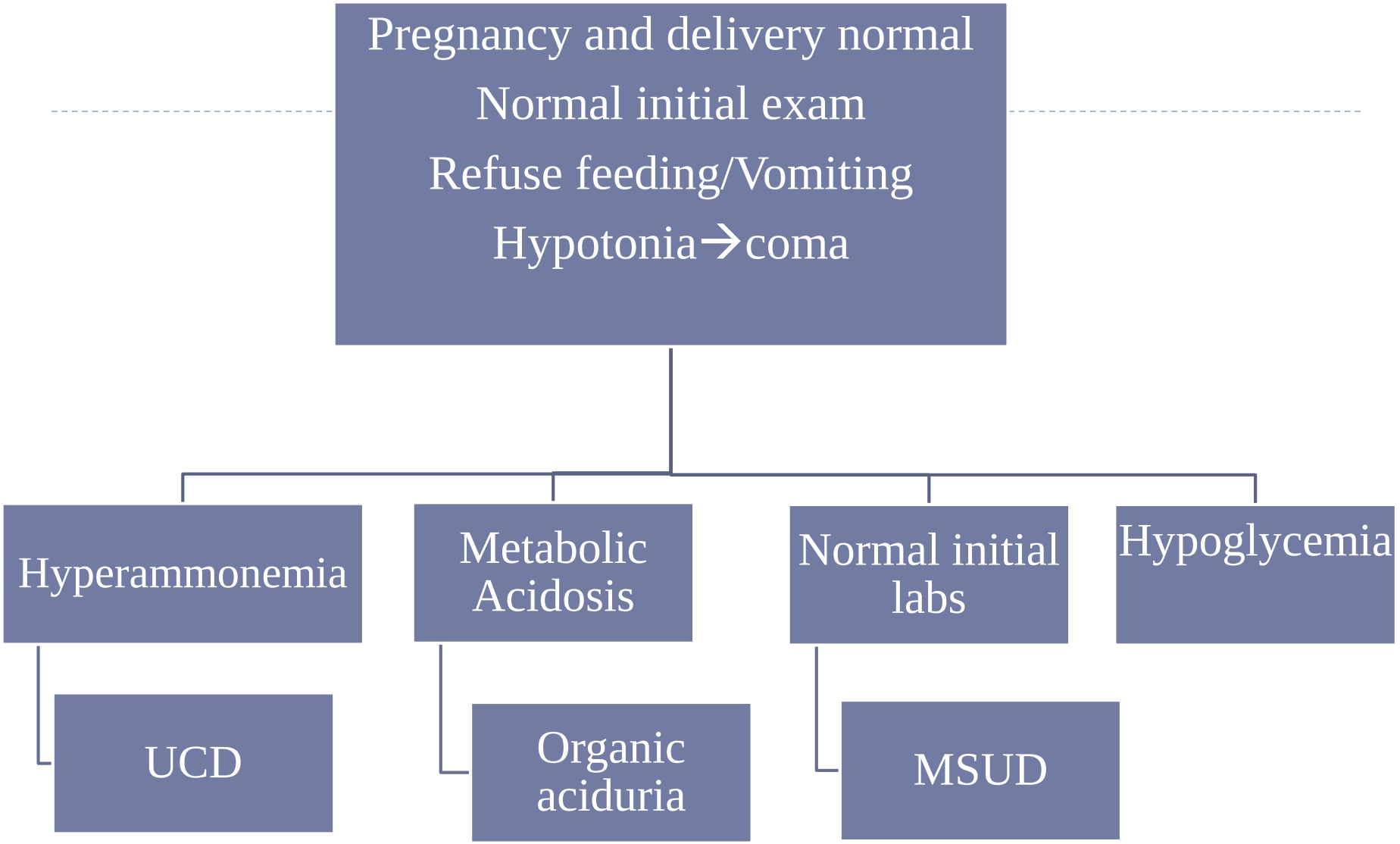
Fasting <2-4 hours	4-8 hrs	>8 hours
Hyperinsulinism	Glycogenosis	FAO
Fructosemia	Neoglucogenesis	Ketogenesis
Galactosemia	GH	Ketolysis
		Cortisol

Case 4

- Hypoglycemia with absence of ketosis
- pH 7,33, bicarbonate 20mmol/l
- CPK, LFTs, lactate, ammonia normal
- Insulin, C-peptide and the cortisol normal

Case 4

- UOA: Urinary dicarboxylic acids
- Acylcarnitines profile : Increased concentration of C2, C14: 1 and C18: 1
- Fatty acid oxidation study in vitro on lymphocytes: normal
- Genetic testing for Mitochondrial HMG CoA synthase: positive


Pregnancy and delivery normal
Normal initial exam
Refuse feeding/Vomiting
Hypotonia→coma
Hyperammonemia
Metabolic Acidosis
Normal initial labs
Hypoglycemia
UCD
Organic aciduria
MSUD

Thank you