Amino acid Metabolism

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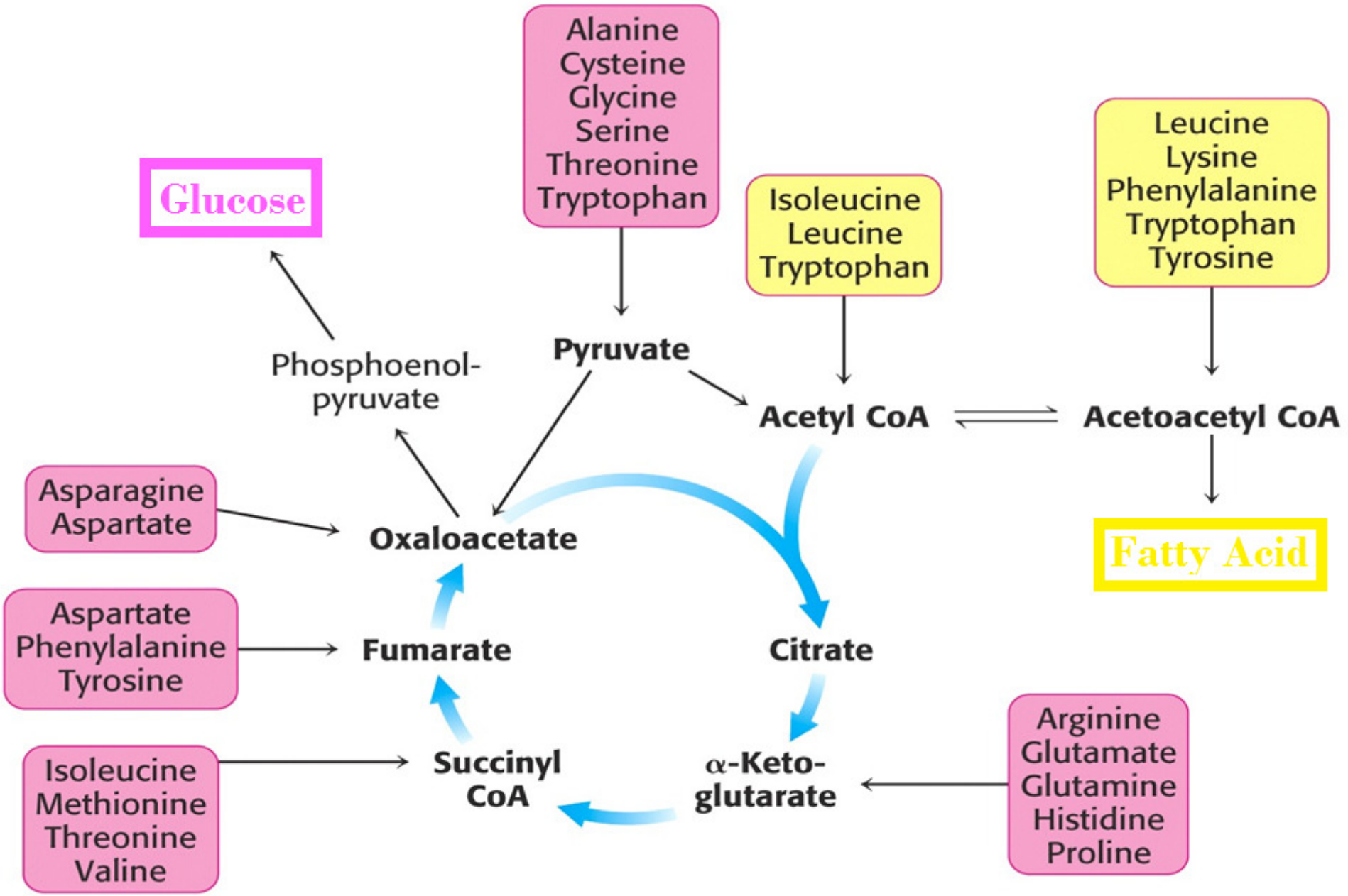
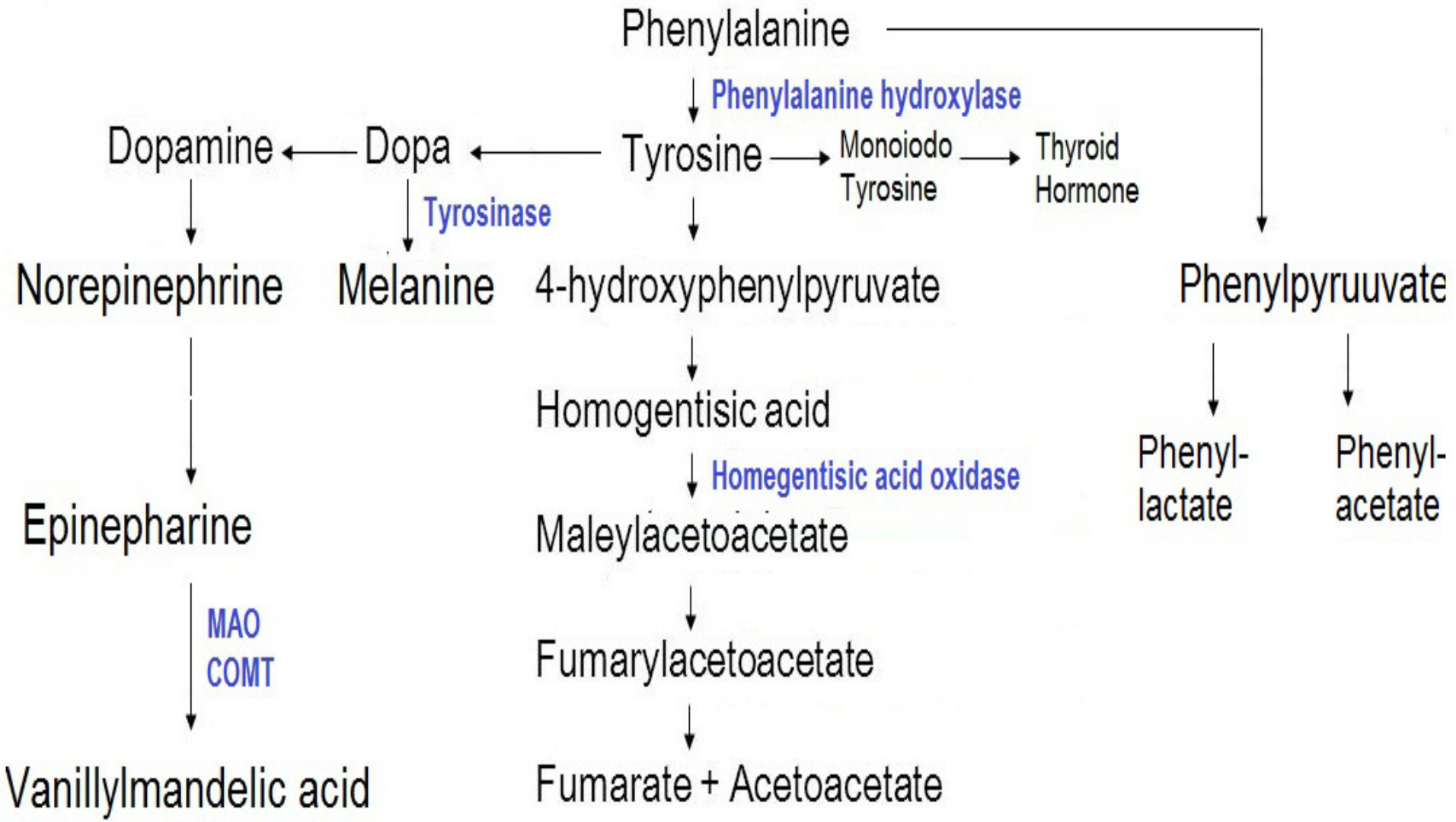
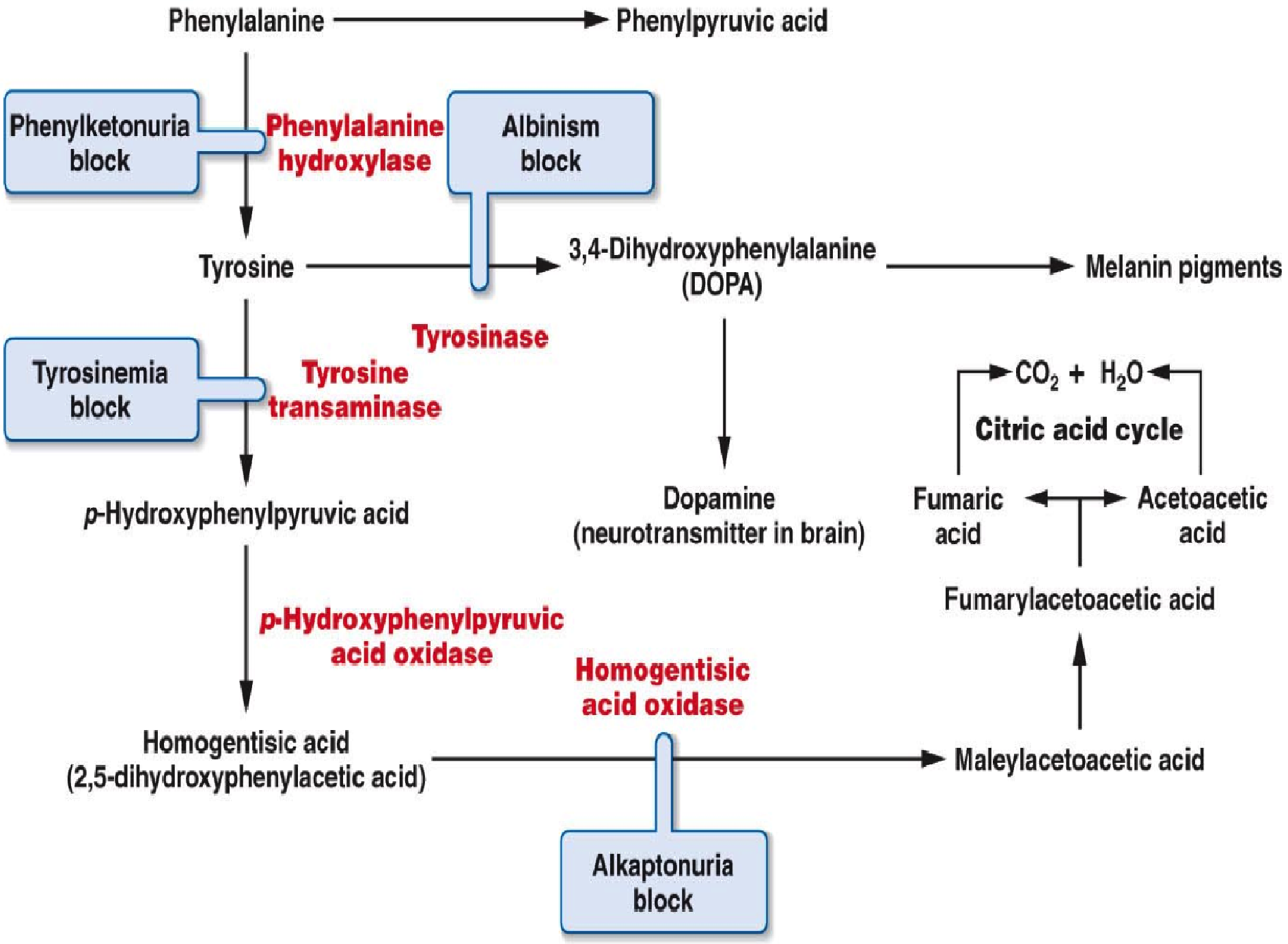
Surat

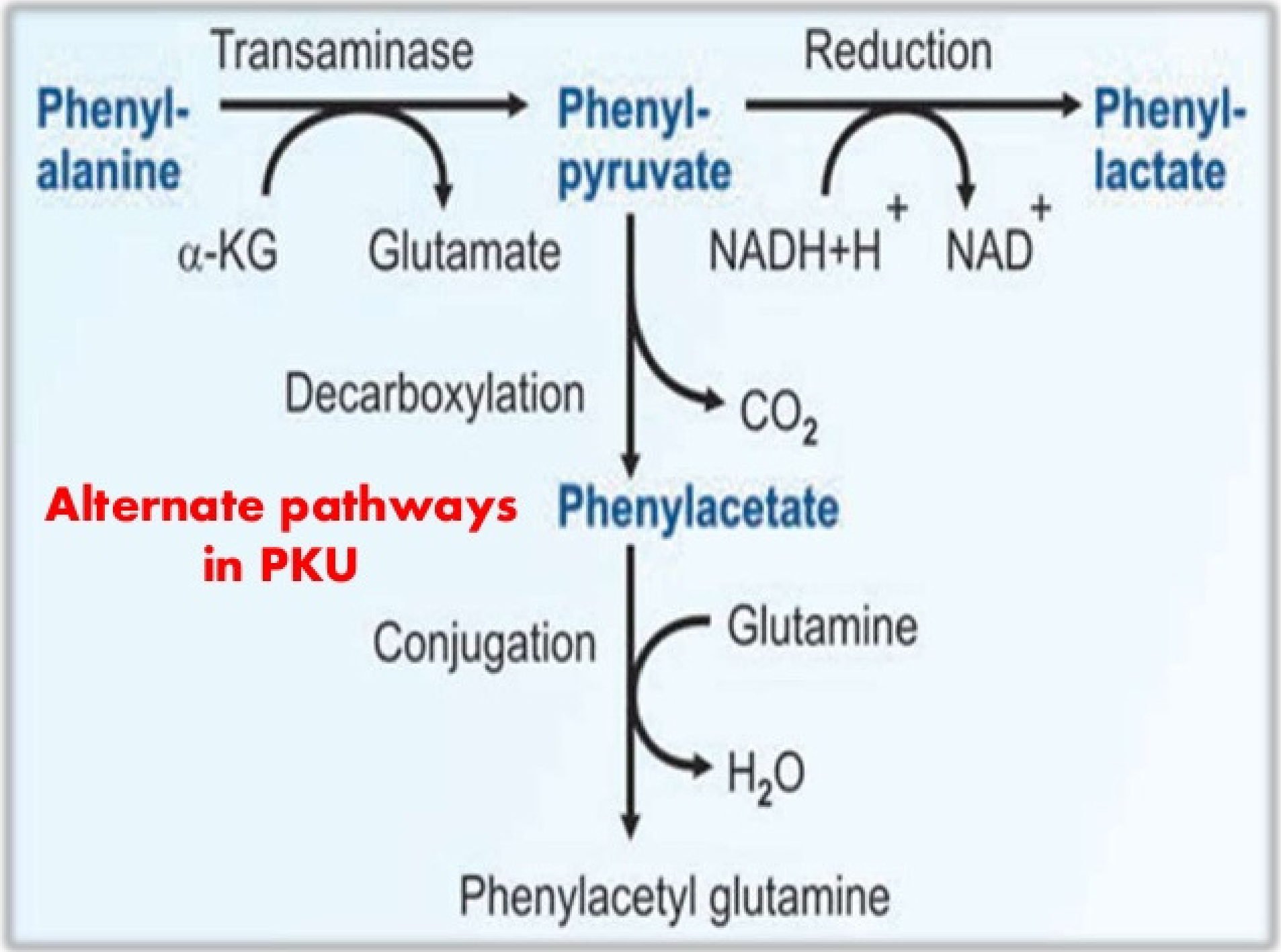
Fates of carbon skeleton of amino acid



Overview of Phenylalanine & Tyrosine Metabolism




Phenylalanine
Phenylpyruvic acid
Phenylketonuria block
Phenylalanine hydroxylase
Albinism block
Tyrosine
3,4-Dihydroxyphenylalanine (DOPA)
Melanin pigments
Tyrosinase
Tyrosinemia block
Tyrosine transaminase
$CO_2 + H_2O$
Citric acid cycle
p-Hydroxyphenylpyruvic acid
Dopamine (neurotransmitter in brain)
Fumaric acid
Acetoacetic acid
Fumarylacetoacetic acid
p-Hydroxyphenylpyruvic acid oxidase
Homogentisic acid oxidase
Homogentisic acid (2,5-dihydroxyphenylacetic acid)
Maleylacetoacetic acid
Alkaptonuria block


Transaminase
Reduction
Phenyl-alanine
Phenyl-pyruvate
Phenyl-lactate
α-KG
Glutamate
NADH+H+
NAD+
Decarboxylation
CO2
Alternate pathways in PKU
Phenylacetate
Conjugation
Glutamine
H2O
Phenylacetyl glutamine

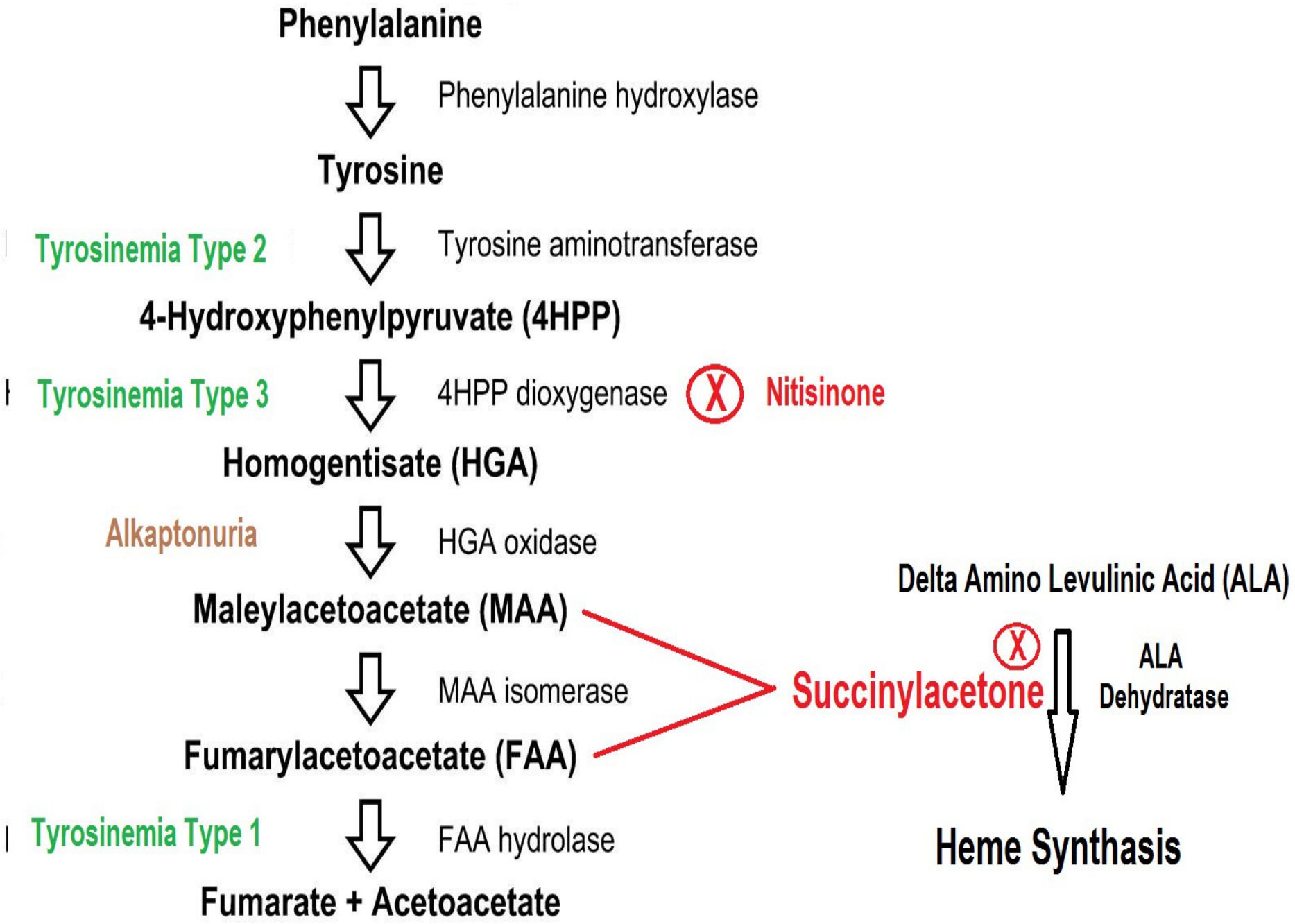
Alkaptonuria

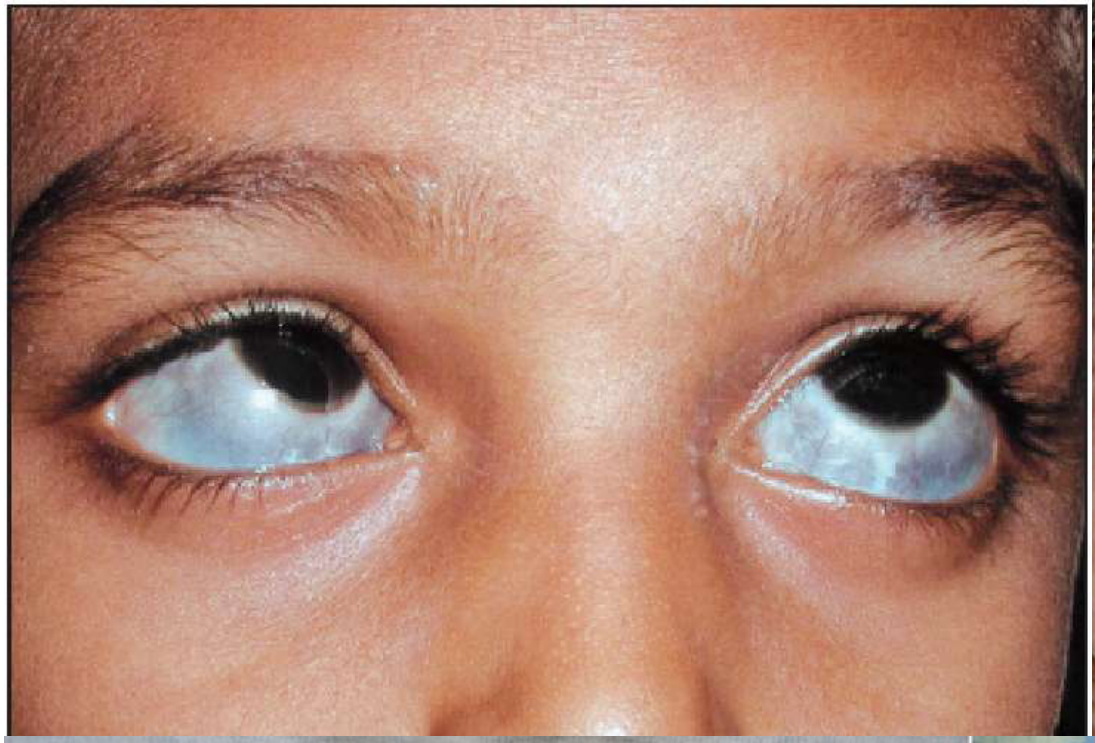
- Inherited disorder of the Tyrosine metabolism
- Absence of Homogentisate oxidase.

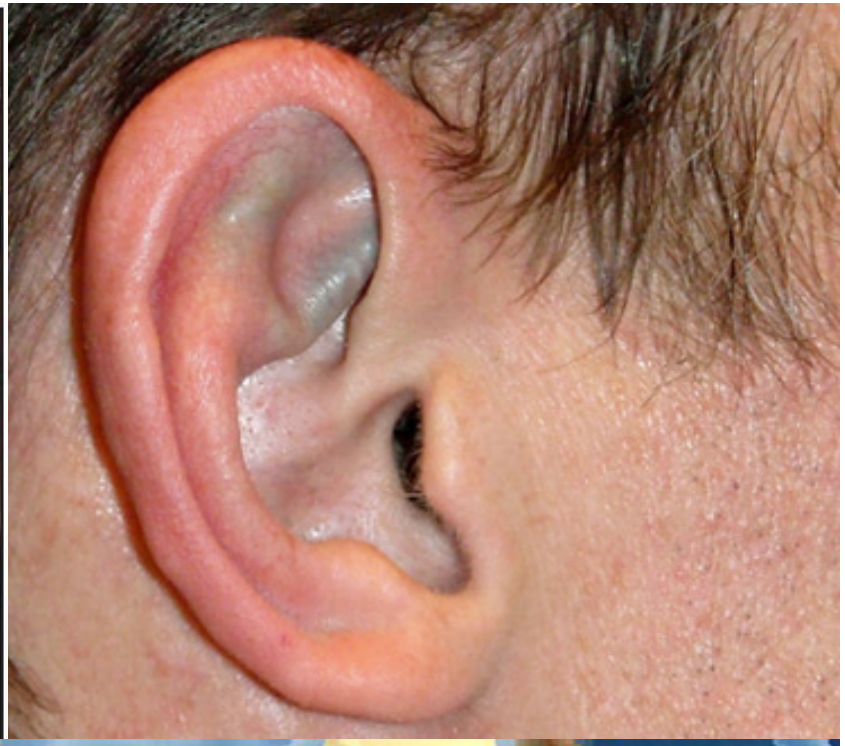
- Homogentisic acid is accumulated
- Excreted in the urine
- Turns black (Benzoqinone Acetate) on exposure to air

Clinical Features

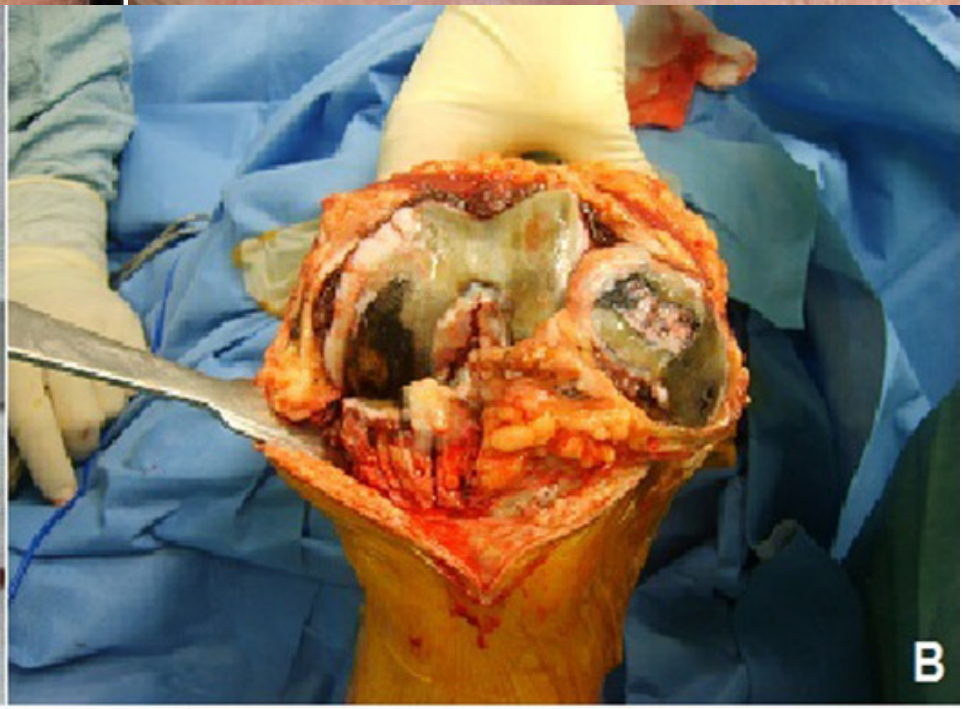
- In children:
  - Urine in diaper = Black Stain
- In adults:
  - Connnective tissue Pigmentation (Ochronosis)
  - Darkening of the Ear
  - Dark spots on the on the sclera and cornea

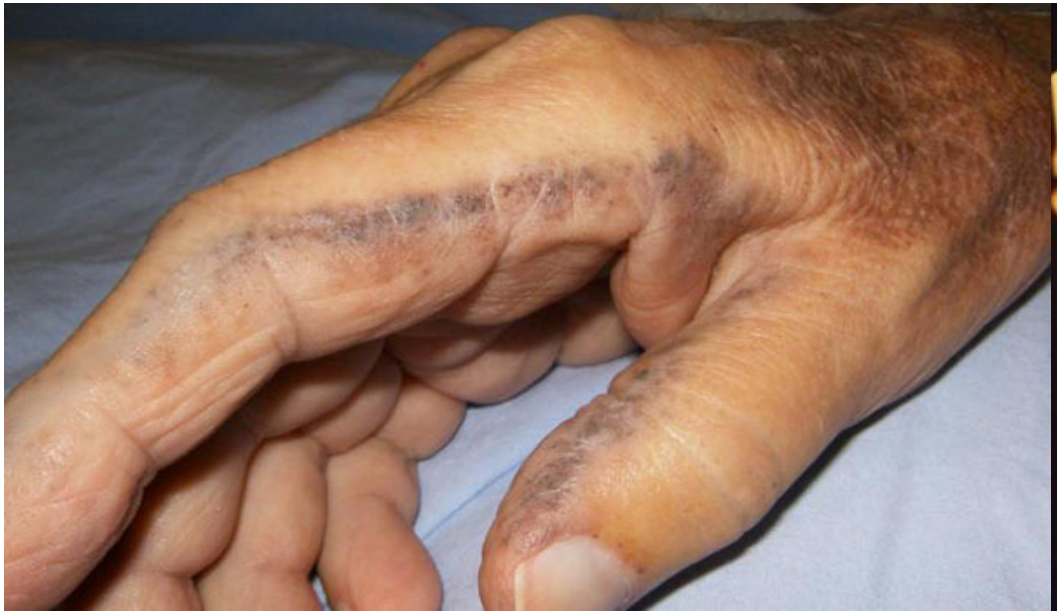

Phenylalanine
Phenylalanine hydroxylase
Tyrosine
Tyrosinemia Type 2
Tyrosine aminotransferase
4-Hydroxyphenylpyruvate (4HPP)
Tyrosinemia Type 3
4HPP dioxygenase
X
Nitisinone
Homogentisate (HGA)
Alkaptonuria
HGA oxidase
Maleylacetoacetate (MAA)
MAA isomerase
Fumarylacetoacetate (FAA)
Tyrosinemia Type 1
FAA hydrolase
Fumarate + Acetoacetate
Delta Amino Levulinic Acid (ALA)
X
Succinylacetone
ALA
Dehydratase
Heme Synthasis



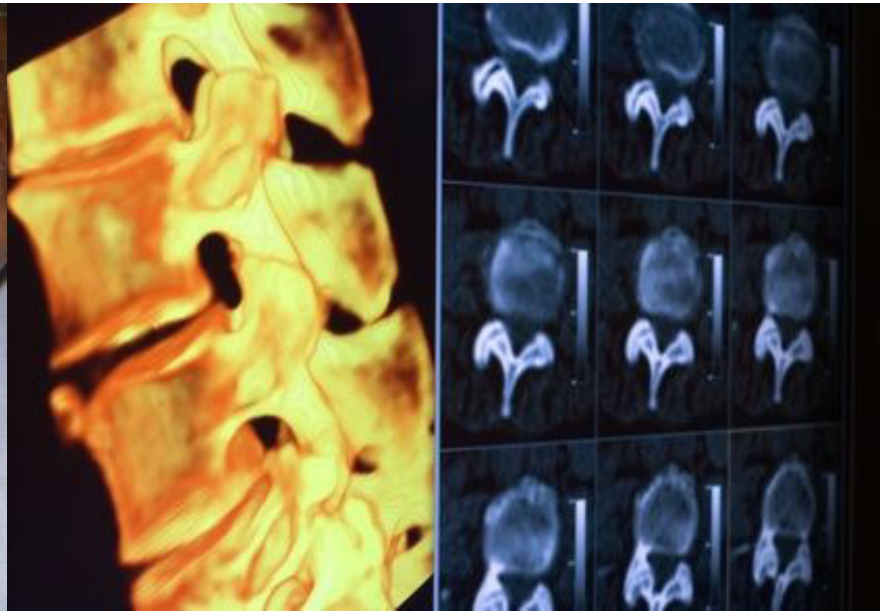



A

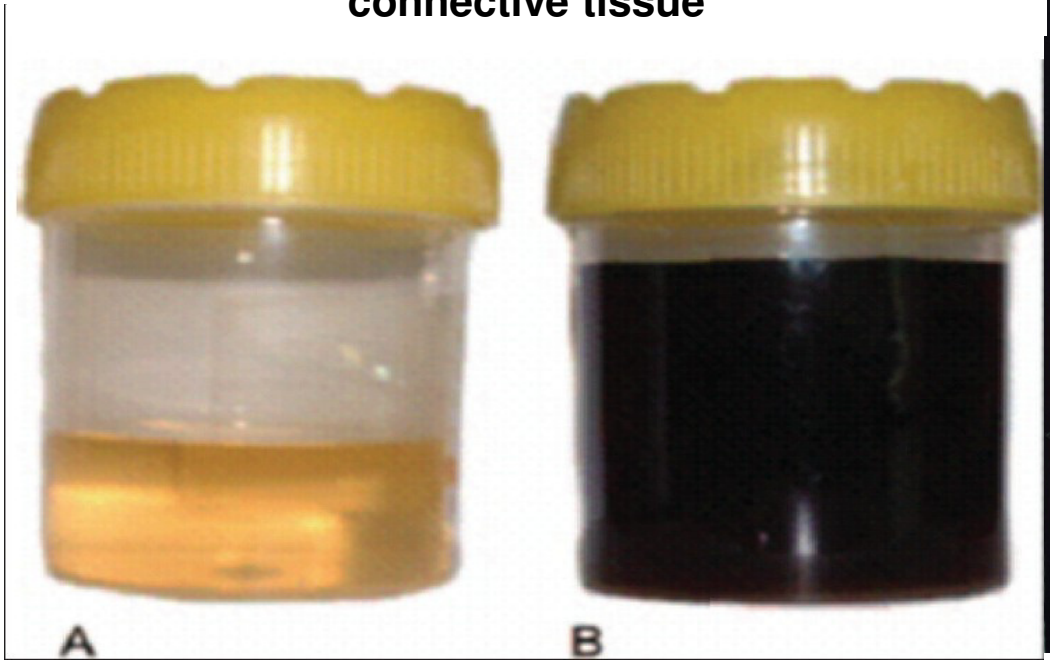

B



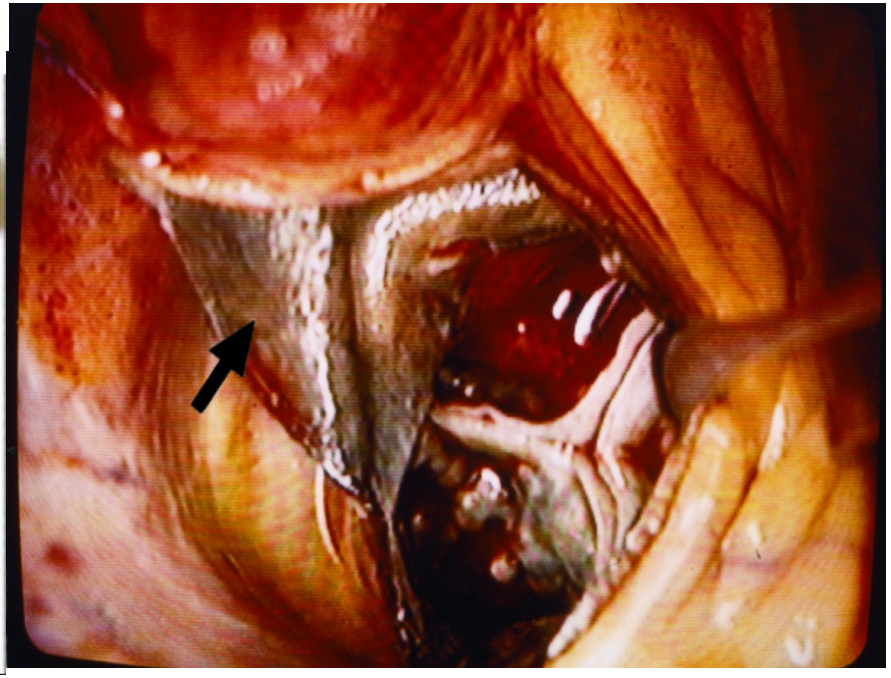
Accumulation of oxidized homogentisic acid in connective tissue



Arthritis of the Spine



Urine turns a black color upon exposure to air

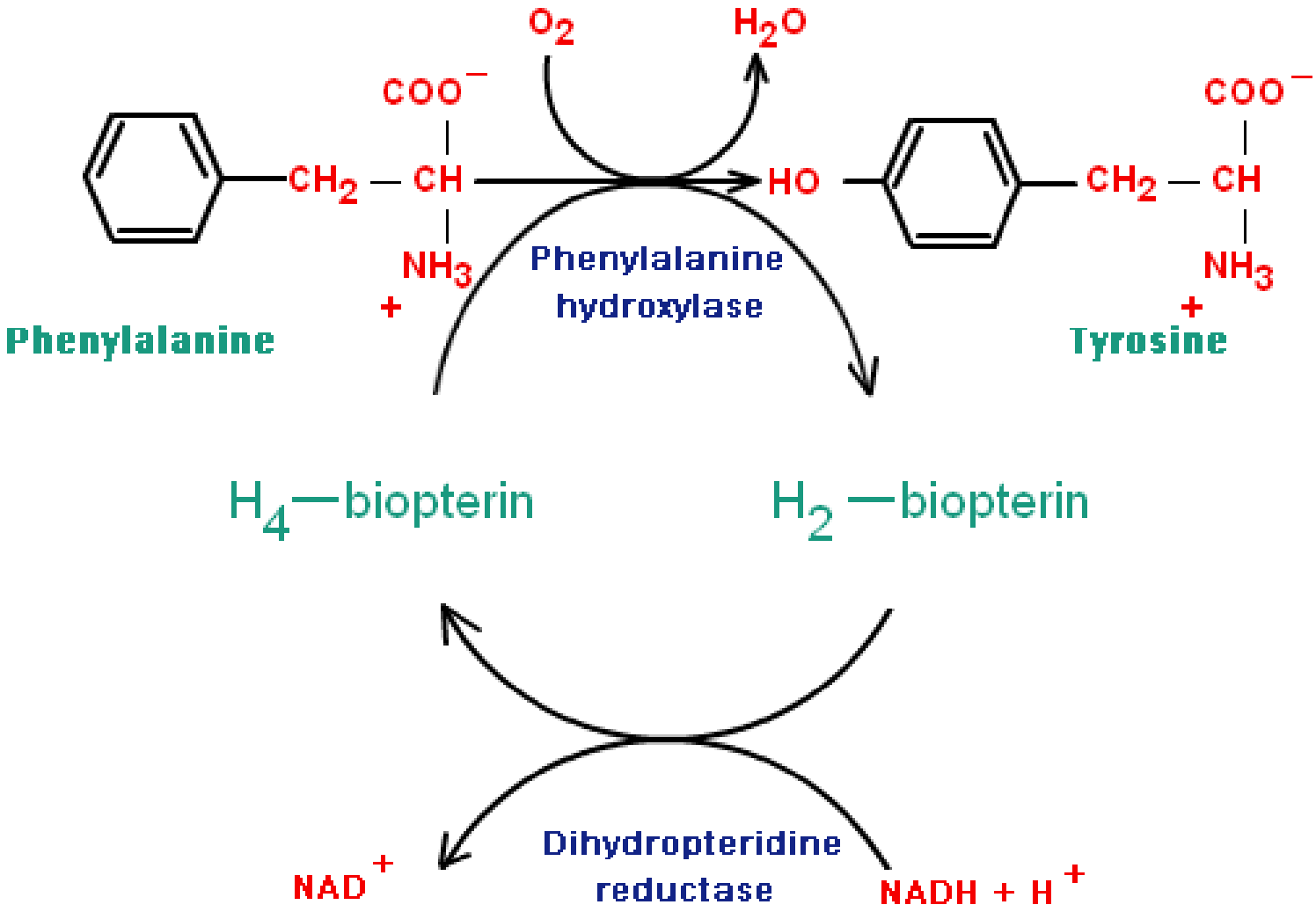


Aortic valve Stenosis

Diagnosis

- Benedict Test
  - Urine Sample = Homogentisic Acid
  - Positive test
- Imaginary Study
- Chromatography

Phenylalanine to Tyrosine



Phenylketonuria = Biochemical Alteration

- No Dopamine
  - Extrapyramidal manifestration (Parkinosonism)
  - Seizure
  - Hypotonia
  - Tremor
- No Epinephrine
- No Norephnephrine
- No Melanine
  - Light colour skin
  - Eye abnormality = Hypopigmetation
- No Thyroid hormone
  - Physical & Mental Growth retardation

Phenylketonuria = Biochemical Alteration

- Accumulation of Phenyalanine (Large Neutral)
  - Restrict entry of some other Large neutral AA
  - Decrease synthesis of Other Neurotransmitter
  - Decrease Interactuall activity
- Accumulation of Phenylacetate
  - “Musty Odour” Urine & Sweat

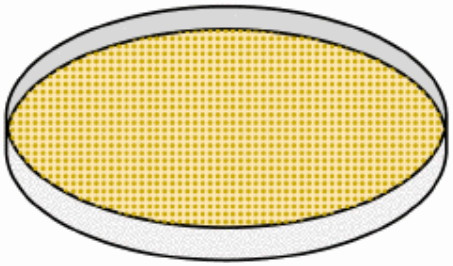
Phenylketonuria Diagnosis

- Ferric Chloride Test
- Guthrie test = Screening Neonate
- Tandem Mass spectroscopy
- Genetic Study

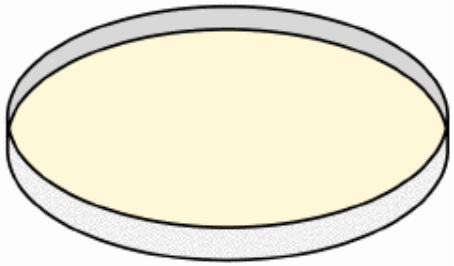
Guthrie Test

Screening by Bacterial Inhibition

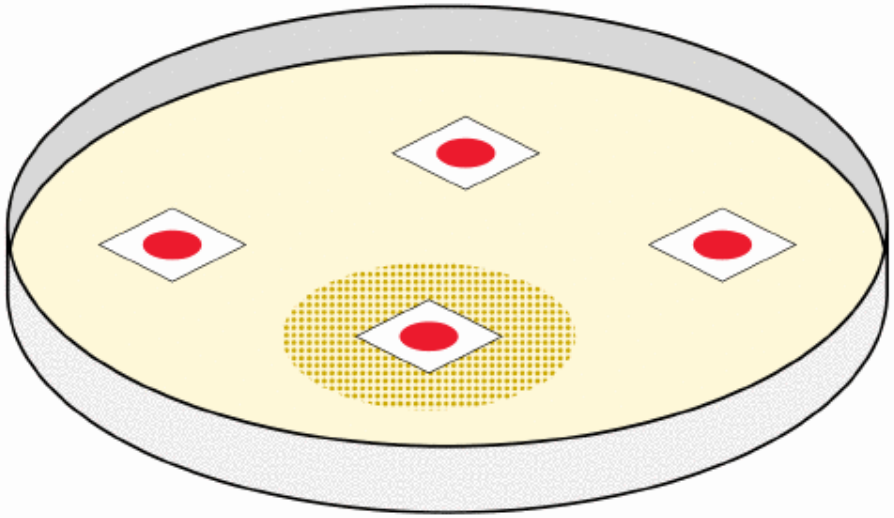
Grown E.Coli on Media
With Phenylalanine



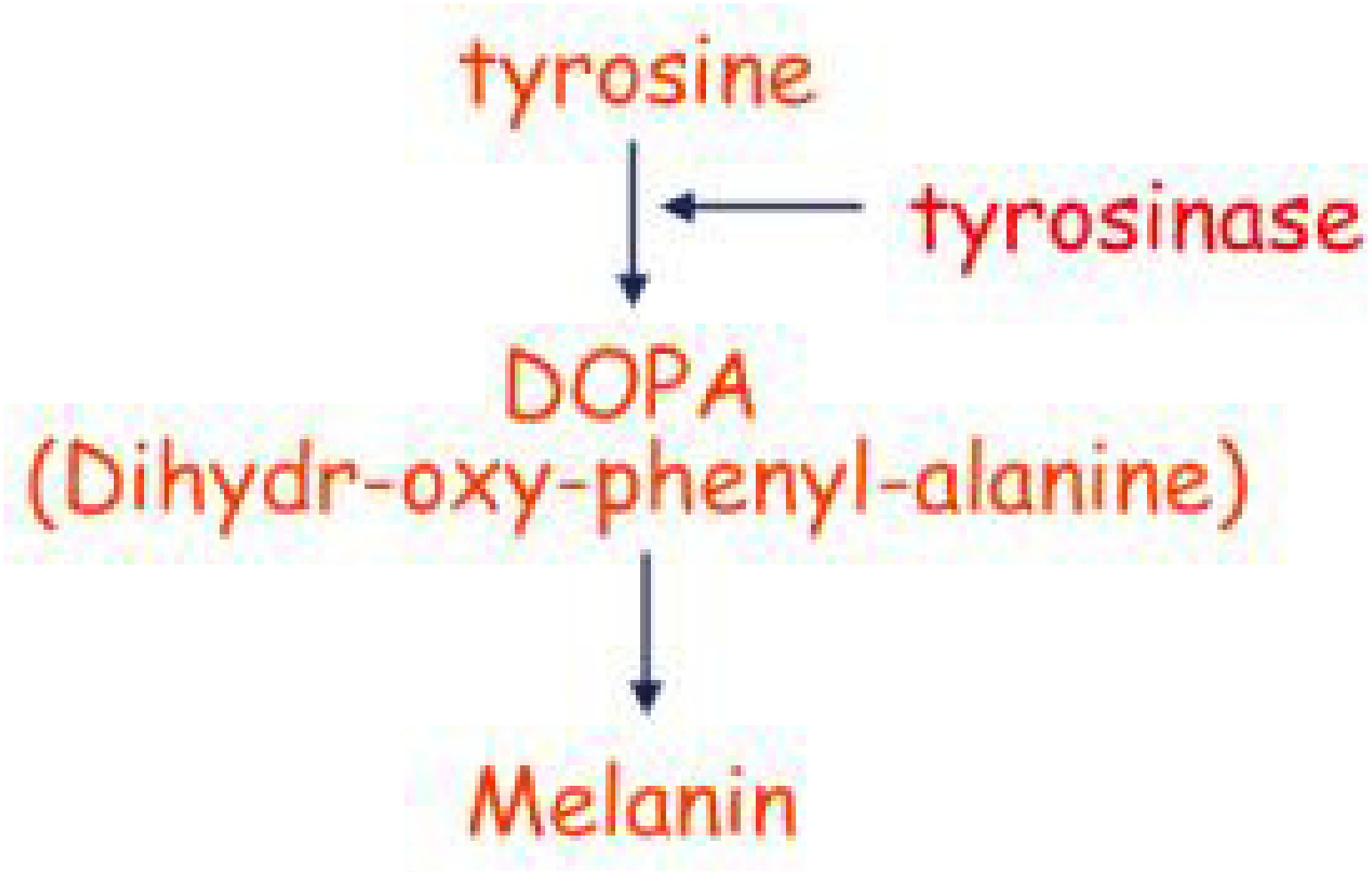
E.Coli on Media with
Beta 2thienylalanine (Inhibit Bacteria Growth)



If Patient sample has Excess
Phenylalanin,
It counter inhibition
and E.Coli will grow

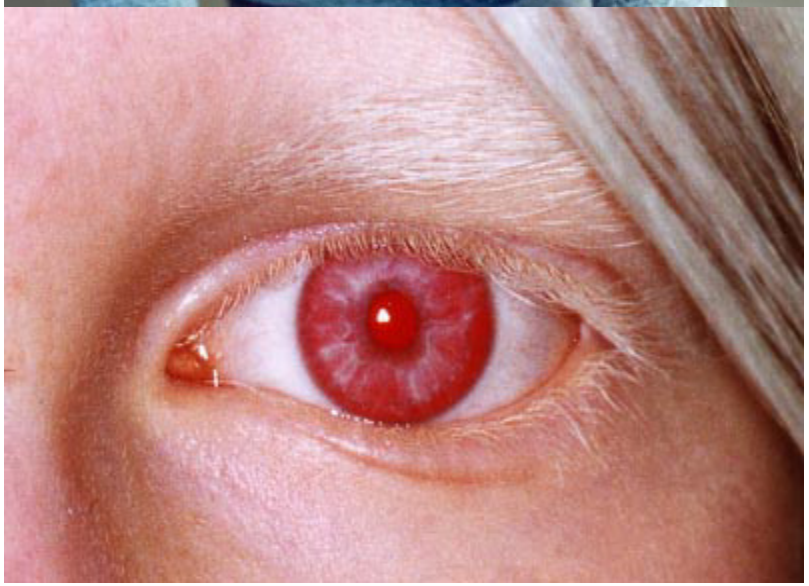


Albinism = Deficiency of Tyrosinase

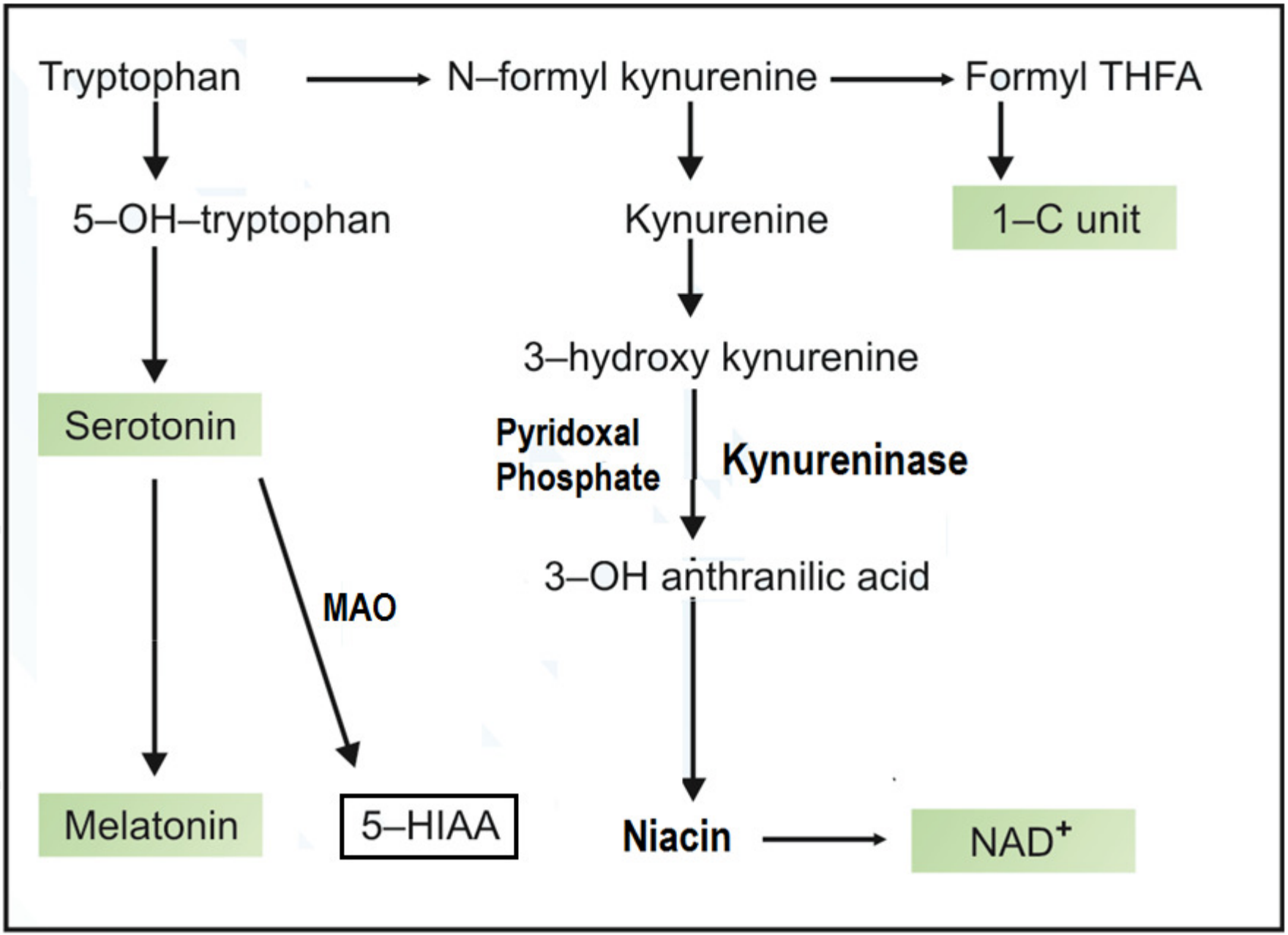


Symptoms of Albinism

- lack of melanin in skin, hair, eyes
- Increased sensitivity to sunlight



Tryptophane Metabolism



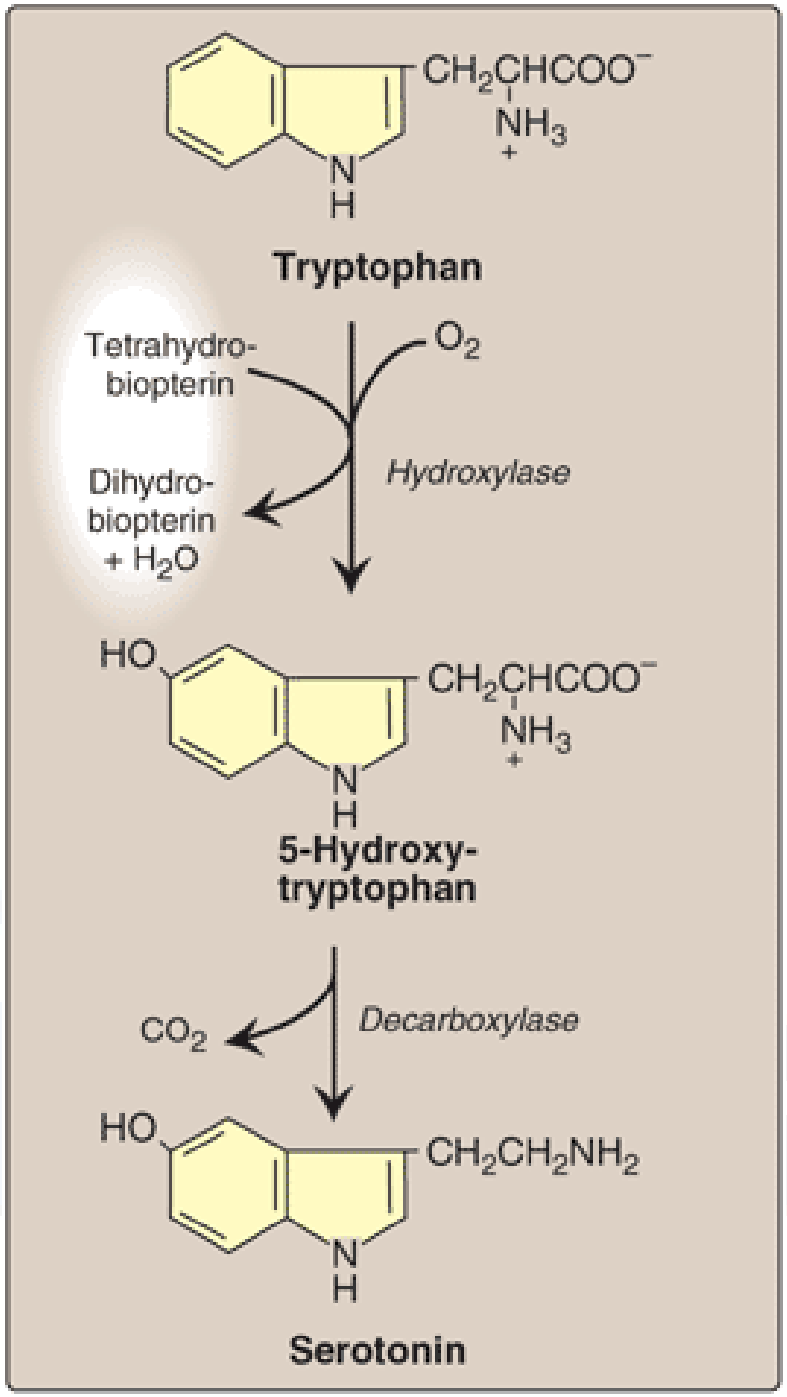
Carcinoid Syndrome

- Carcinoid Tumour = Tumour of Endocrine gland

- Paraneoplastic Syndrome
  - This Malignant cell produce “Hormone”

- In Carcinoid Tumor = Paraneoplastic Syndrome
  = Carcinoid Syndrome

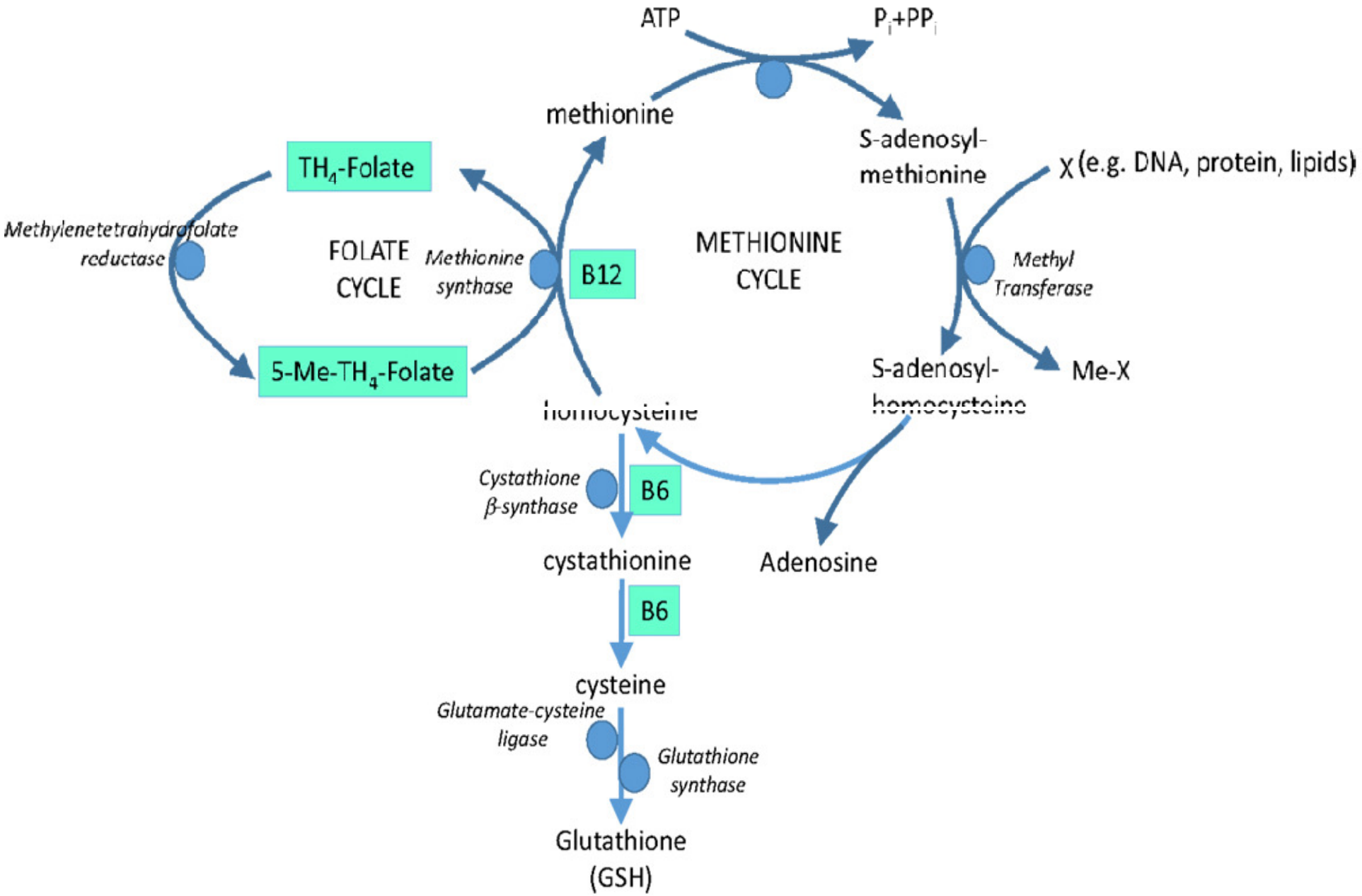
- Increase Production of Serotonin from Tryptophan
- Decrease Production of Niacin
- **Patient Suffer from Pellagra**


CH2CHCOO−
NH3+
N
H
Tryptophan
Tetrahydro-
biopterin
O2
Hydroxylase
Dihydro-
biopterin
+ H2O
HO
CH2CHCOO−
NH3+
N
H
5-Hydroxy-
tryptophan
CO2
Decarboxylase
HO
CH2CH2NH2
N
H
Serotonin

Monoamino Oxidase Inhibitor

- Decrease Break down of Serotonin
- Increase Level of Serotonin
- Clinical Useful in
  - Depression
  - Schizophenia
- As well As Increase level of
  - Epinepherin
  - Norepinepherin
  - Dopamine

Methionine Metabolism

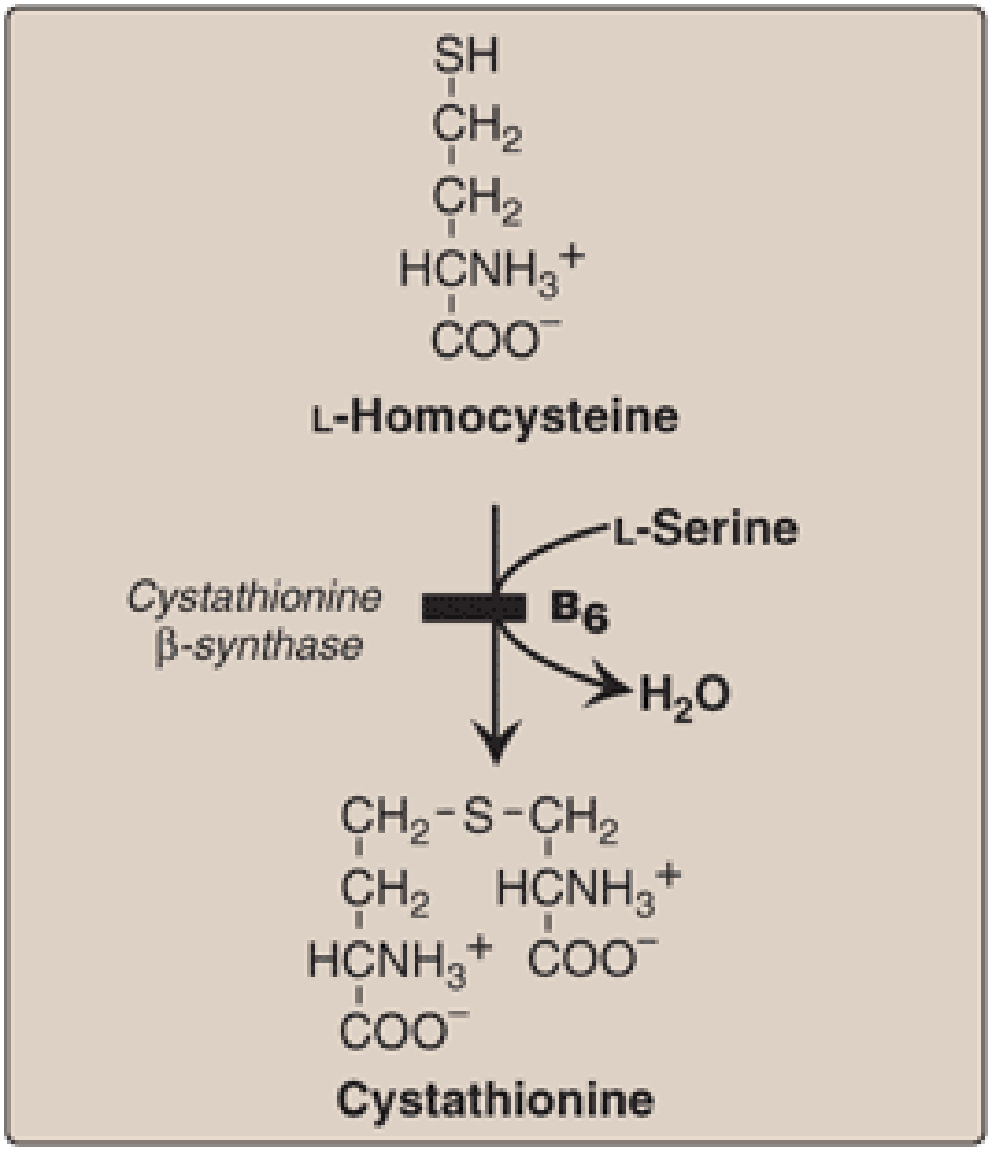


Folate Trap

- Vitamin B 12 deficiency
- Decrease Methionine synthase activity
- 5 – methyl- THF can not converted to THF
- No methyl group transfer
- No Methionine
- No SAM
  - DNA replication affected
  - Increase Homocysteine level

Hyperhomocysteinemia

Ectopia lentis = Dislocation of Eye lens



Hartnup Disease

Etiology

- Genetic Disorder
- Autosomal Recessive

Pathogenesis

Failure of Amino Acid (Non-Polar Amino acid)Transport

- In Intestine
- In Kidney

Decrease absorption of Tryptophan

Decrease Reabsorption of Tryptophan

Increase Loss of Tryptophan

Clinical Feature

- Pellagra

Fanconi Syndrome

Etiology

Congenital or Acquired

Hartnup Disease

Etiology

- Genetic Disorder
- Autosomal Recessive

Pathogenesis

- Failure of Amino Acid (Non-Polar Amino acid) Transport
  - In Intestine & Kidney
- Decrease absorption of Tryptophan
- Decrease Reabsorption of Tryptophan
- Increase Loss of Tryptophan

Clinical Feature

- Pellagra

Fanconi Syndrome

Etiology

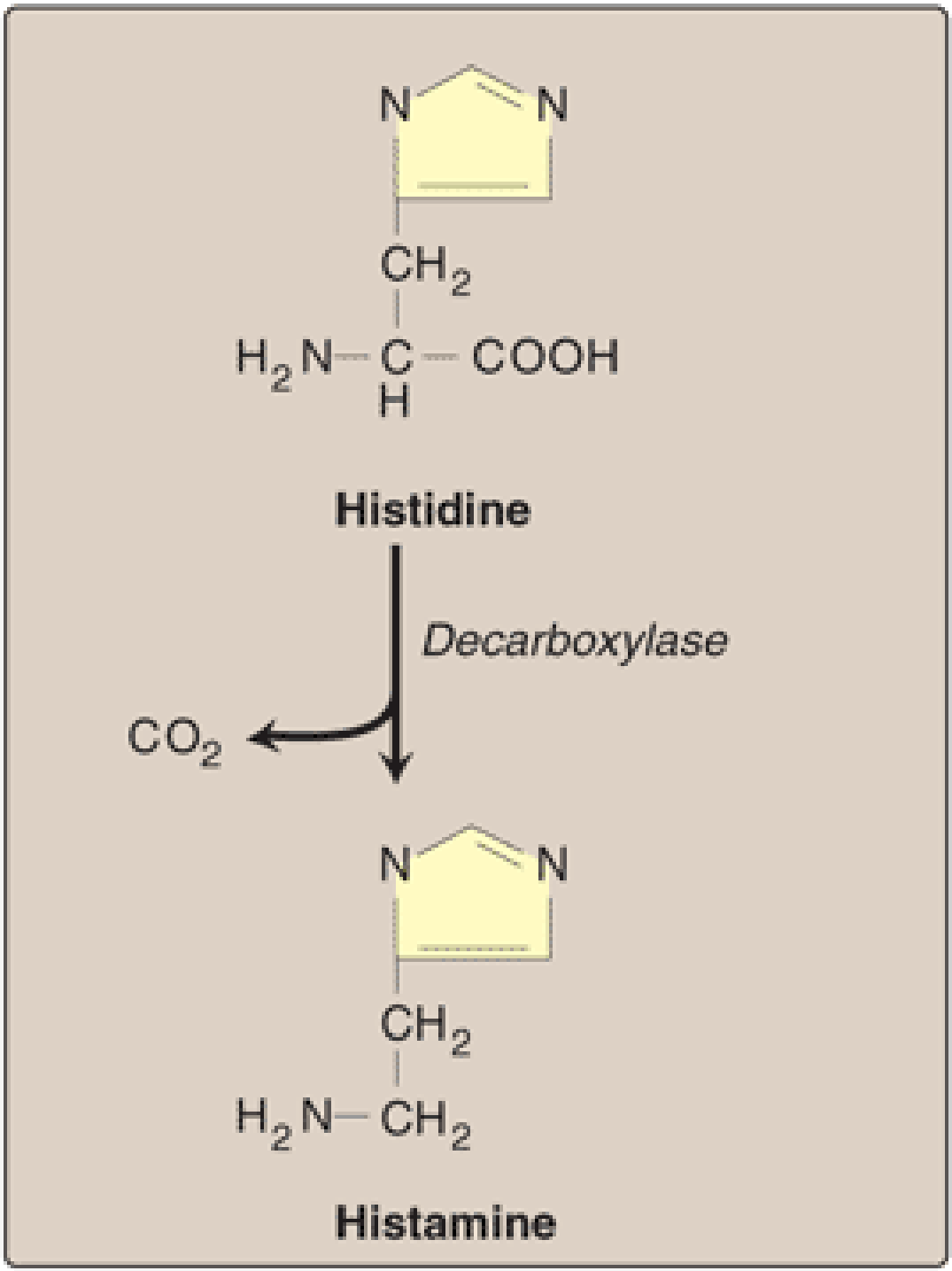
- Congenital or Acquired

Pathogenesis

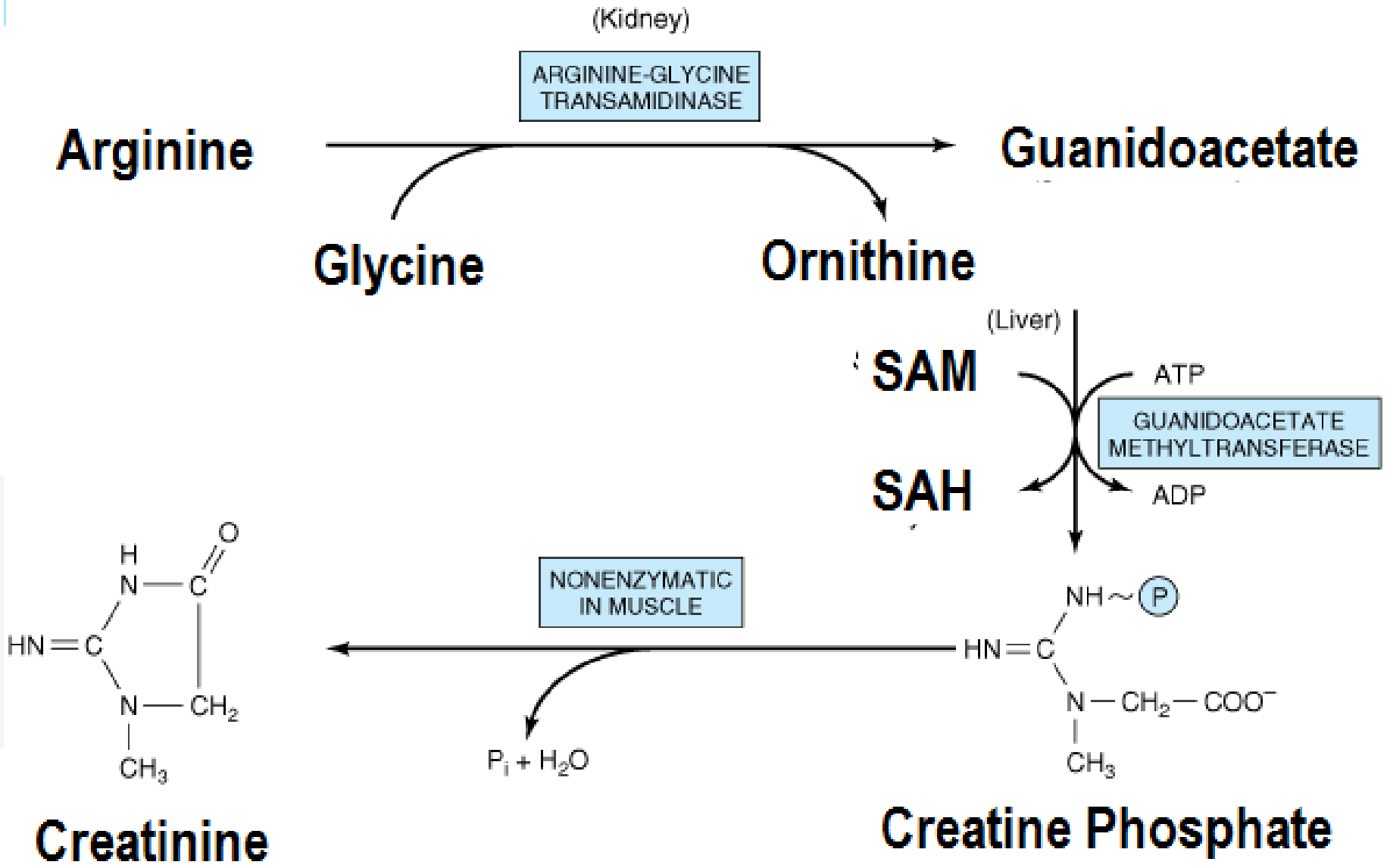
- Inadequate absorption in Proximal Renal Tubules
- Reabsorption of Amino acid ,Glucose, Uric acid , Phosphate , Bicarbonate

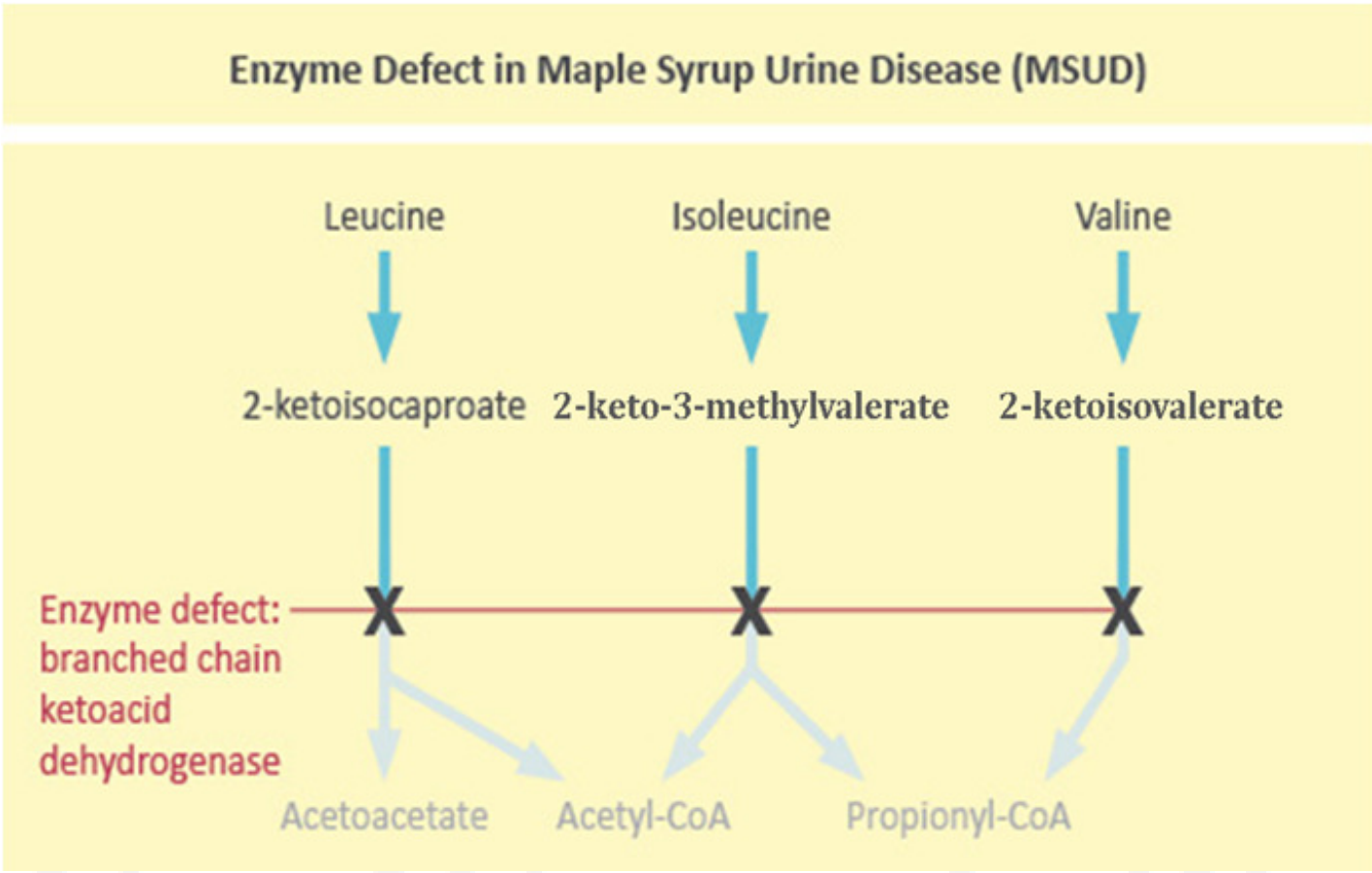
Clinical Feature

- Polyuria , Polydipsia & dehydration
- Hypophosphatemia
- Rickets.
- Osteomalacia (in adults)
- Growth failure
- Metabolic Acidosis
- Hypokalemia
- Hyperchloremia

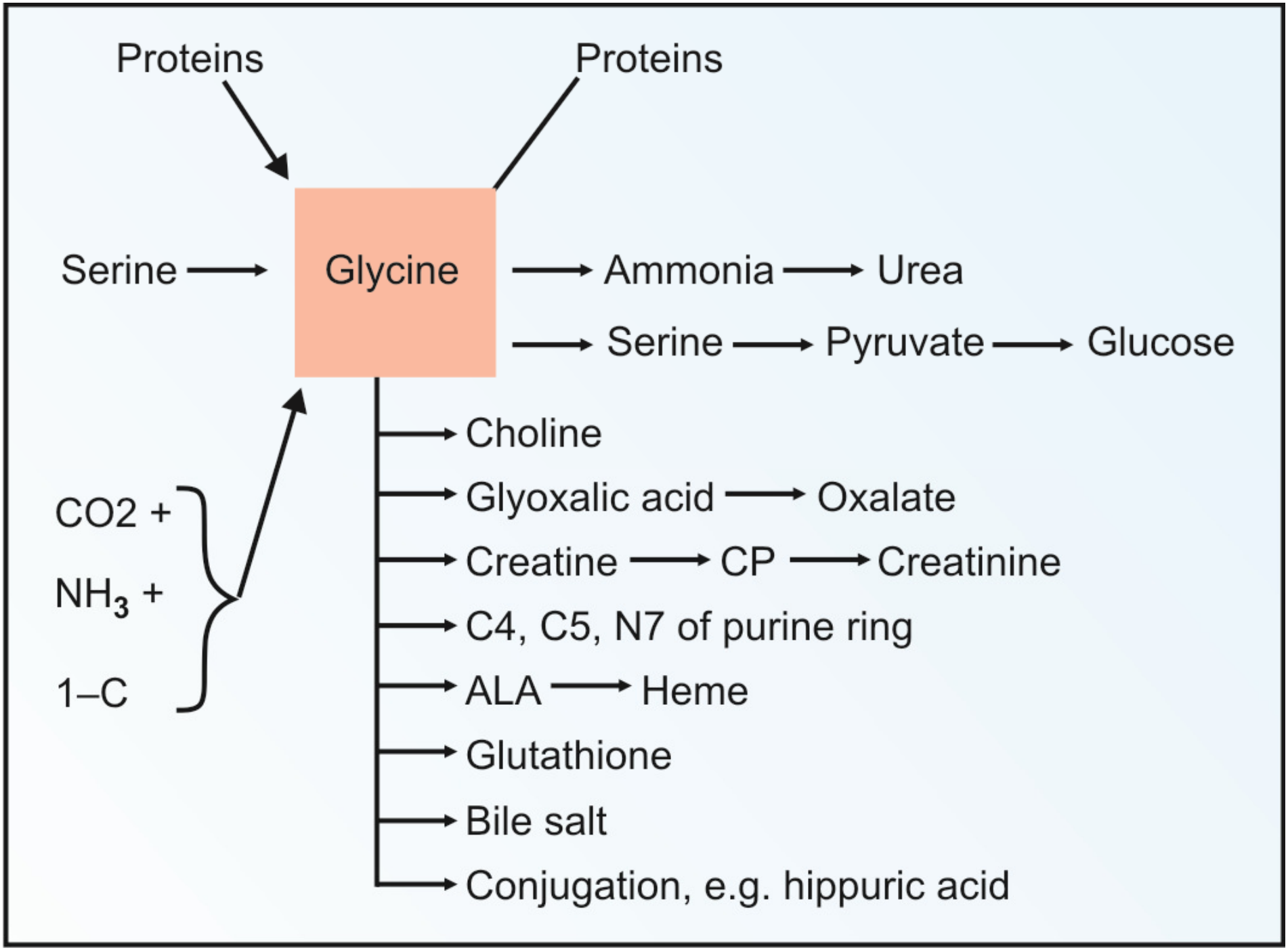

N
N
CH2
H2N
C
H
COOH
Histidine
Decarboxylase
CO2
N
N
CH2
H2N
CH2
Histamine

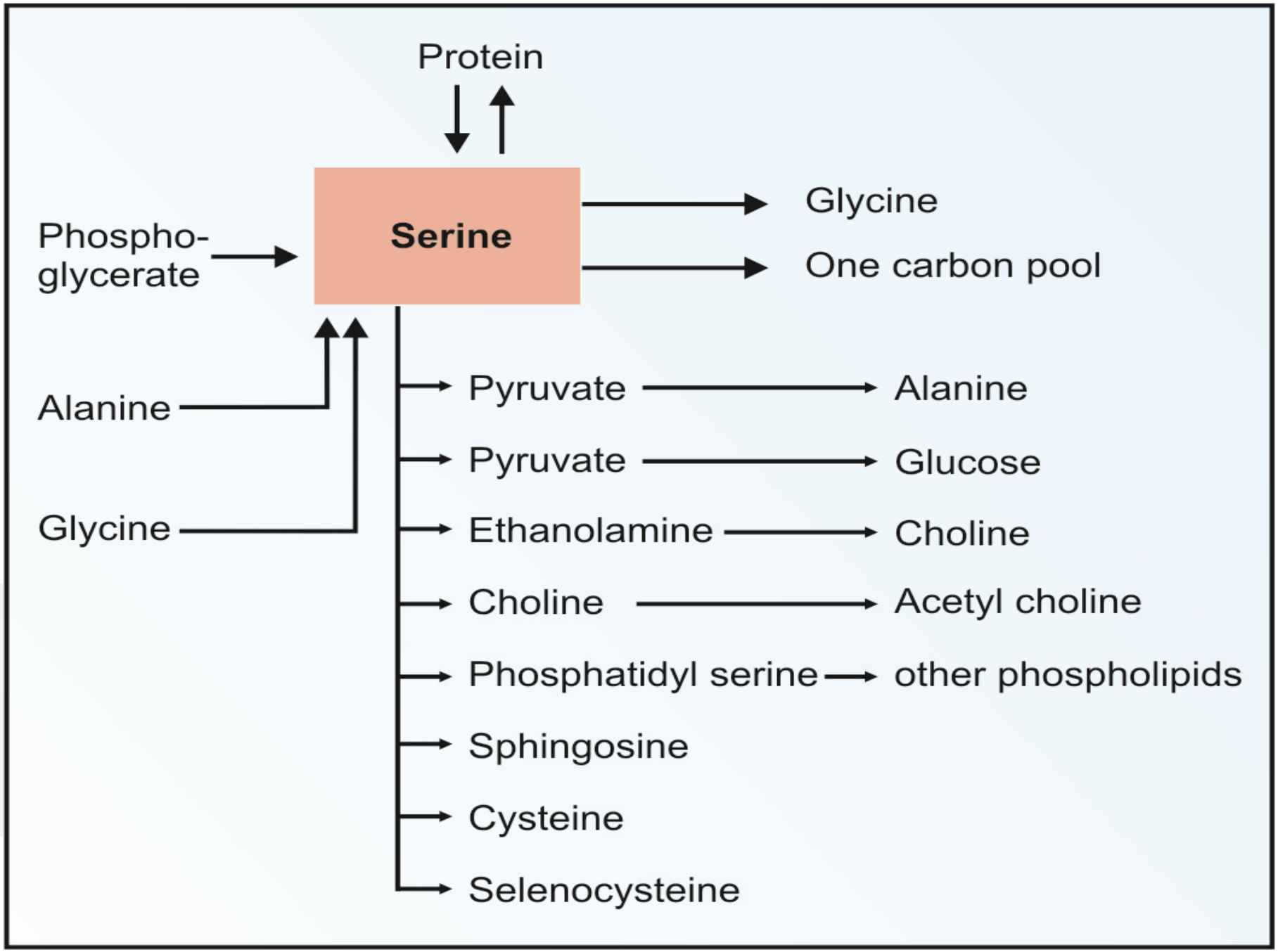
Creatine & Creatinine Synthesis





Neurological Symptoms – Cerebral damage
Diarrhea , Vomiting, Weight Loss, Anorexia


Proteins
Proteins
Serine
Glycine
Ammonia
Urea
Serine
Pyruvate
Glucose
Choline
CO2 +
Glyoxalic acid
Oxalate
NH3 +
Creatine
CP
Creatinine
C4, C5, N7 of purine ring
1–C
ALA
Heme
Glutathione
Bile salt
Conjugation, e.g. hippuric acid


Protein
Serine
Phospho-
glycerate
Glycine
One carbon pool
Alanine
Glycine
Pyruvate
Alanine
Pyruvate
Glucose
Ethanolamine
Choline
Choline
Acetyl choline
Phosphatidyl serine
other phospholipids
Sphingosine
Cysteine
Selenocysteine