INBORN ERRORS (DISEASES) OF PHENYLALNINE AND TYROSINE DEGRADATION

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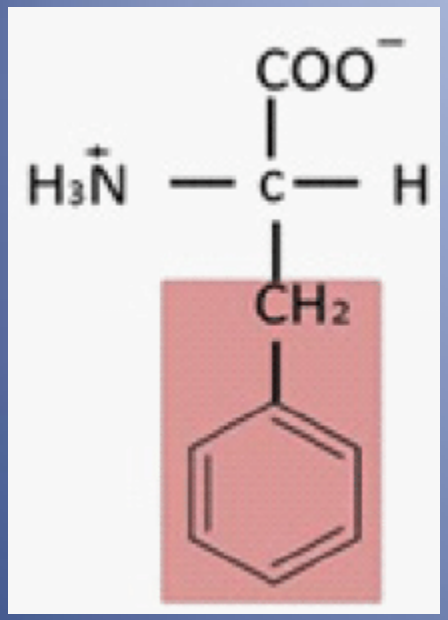
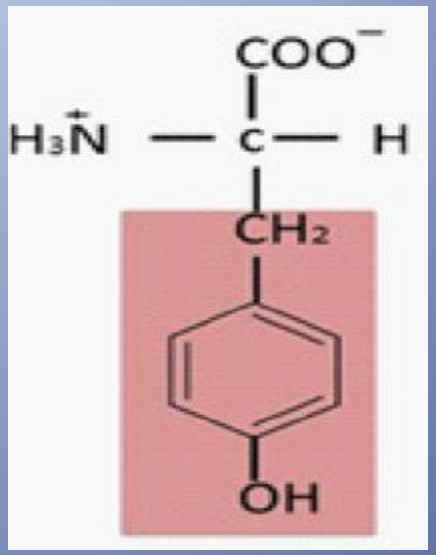
PHENYLALANINE



TYROSINE

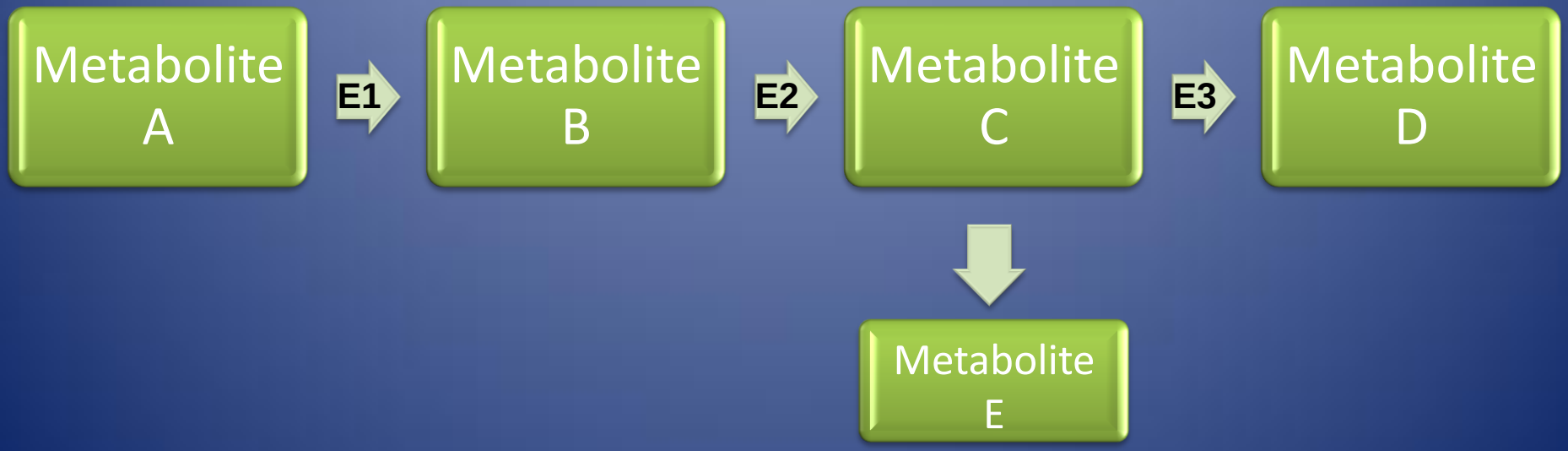


- IN HEALTHY HUMANS THE SURPLUS PHENYLALANINE OR TYROSINE IS CATABOLIZED TO FUMARATE AND ACETOACETATE AFTER PASSING THROUGH MULTIPLE INTERMEDIATES.

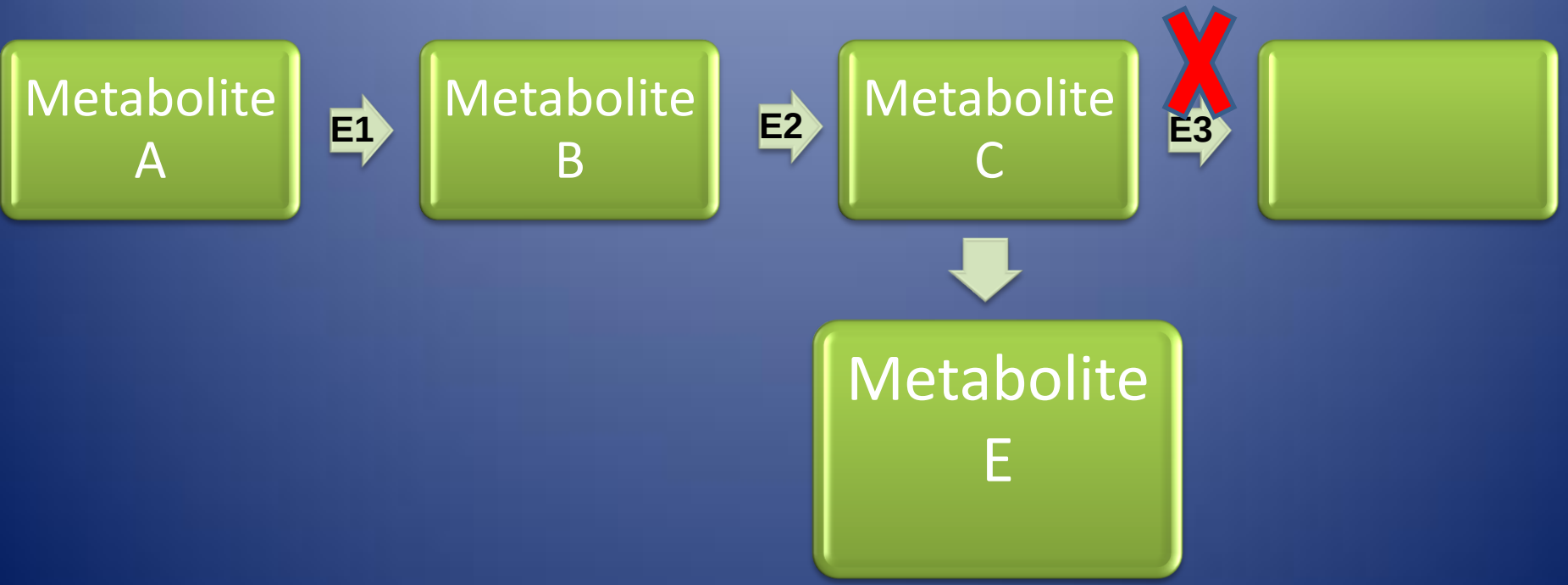
- IF AN INDIVIDUAL IS NOT PRODUCING ENZYMES OF ABOVE DEGRADATION PATHWAY DUE TO DEFECTIVE GENE, THEN SUBSTRATE OF THAT ENZYME WILL ACCUMULATE AND PRODUCT WILL NOT FORM

EFFECT OF A DEFECT IN ENZYME SYNTHESIS ON METABOLIC PATHWAY

IN HEALTHY HUMANS



IN CASE OF A DEFECTIVE ENZYME



DISEASES OF DEFECTS IN PHENYLALANIE AND TYROSINE DEGRADATION PATHWAY

- PHENYLKETONURIA
- ALKAPTONURIA
- TYROSINEMIA TYPE I
- TYROSINEMIA TYPE II
- TYROSINEMIA TYPE III

PHENYLKETONURIA

In this disease phenylalanine is not converted into tyrosine

Consequences

Phenylalanine would accumulate in all body fluids and will be metabolized by alternate pathway

Tyrosine formation would be severely affected, required for the synthesis of T3, T4, melanin, epi/nor-epinephrine , dopamine

Clinical Picture

Urine, hair and skin of patients would smell like a dead mouse due to phenylacetate which is produced from Phenyalanine degradation via alternate pathway

Phenylketourics are severely mentally retarded and myelination of their nerves is defective

ALKAPTONURIA

In Alkaptonuria conversion of homogentesic acid into malelyacetoacetate is blocked due to homogentisate oxidase enzyme deficiency

Homogensetic acid is excessively increased spills into urine
The patients urine on exposure to air becomes black due to oxidation and polimerization of homogesetic acid into melanin-like substance called Alkaptons— hence the name ALKAPTONURIA

ALKAPTONURIA

The homogensitic acid in alkaptonuric may be also oxidized within the body and converted into benzoquinone acetate (BA)— This compound is not excreted into urine rather it is deposited on cartilages, ear pinnae, nose etc.

BA may also deposits in large joints and cause ochronotic arthritis which is different from other forms of arthritis namely rheumatoid arthritis and gouty arthritis

It may be noted that biochemical markers of above three forms of above three forms of arthritis are different

TYROSINEMIA TYPE I

In this genetic disease fumarlyacetoacetase enzyme is lacking this causes accumulation of large quantities of fumarlyacetoacete which is converted into succinyl acetone, a powerful hepatotoxin as a result the patient develops jaundice and complains of nose bleeding.

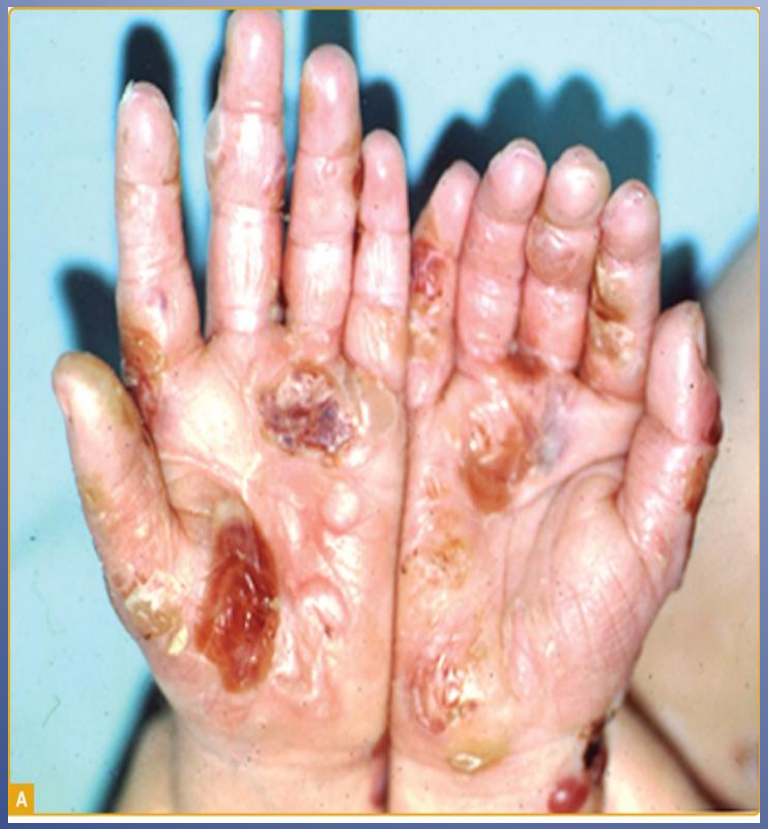
The urine and blood of the patients smells like cabbage
The patient may go into liver failure

TYROSINEMIA TYPE II

In this variant of tyrosinemia tyrosine transaminase is absent

Clinical Picture

Pain and redness of eyes
Uniform/ Scattered thickning of skin of palms of hands and soles of feet known as PALMOPLANTAR HYPERKERATOSIS OR PALMOPLANTAR KERATODERMA
Due to thickening of soles the patient has great difficulty in walking
Tearing of skin may occur and become infected
(In this disease only secondary infections can be treated)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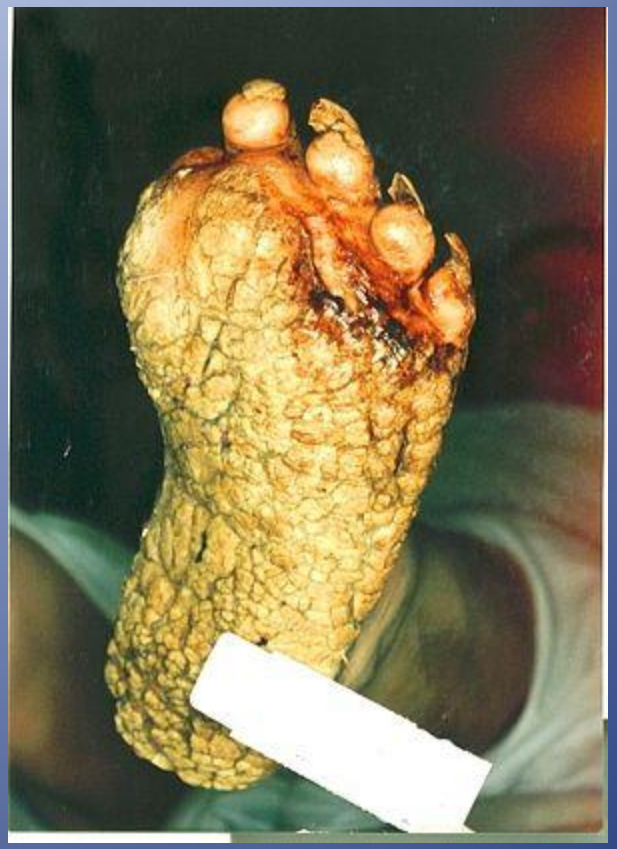

TYROSINEMIA TYPE III

In tyrosinemia type III hydroxy phenylpyruvate dioxygenase enzyme is missing

Clinical Picture

The patient develops seizures, intellectual deficiency and notable intermittent ataxia (poor coordination and balance)

Let us all pray that no child is born with a congenital defect

Thank you!