Self Study: Metabolic Disease  KEY

For each of the following disorders, state the causal metabolic defect, clinical symptoms and expected key laboratory findings.

1. **Phenylketonuria (PKU)**
   Causal metabolic defect: The conversion of phenylalanine to tyrosine is blocked due to an enzyme deficiency (phenylalanine hydroxylase), resulting in accumulation of phenylalanine in the blood and phenylpyruvic acid (a ketone) in the urine.

   Clinical symptoms: If not treated it causes severe mental retardation in babies that appear normal at birth. Symptoms: delayed development, vomiting, decreased skin pigmentation.

   Key laboratory findings: The urine has a characteristic barny (mousy, musty) odor. Urine tests for phenylpyruvic acid are based upon the Ferric Chloride reaction (non-specific) (metabolic acidosis)

2. **Galactosuria/galactosemia**
   Causal metabolic defect: Accumulation of galactose in the blood and urine due to an enzyme defect in the galactose metabolic pathway (galatose 1-phosphate uridyltransferase, galactokinase, uridine diphosphate epimerase). Galactose, which is obtained from lactose (milk) cannot be converted to glucose

   Clinical symptoms: Infants will demonstrate a failure to thrive, diarrhea, vomiting, liver dysfunction, cataracts, mental retardation.

   Key laboratory findings: The Clinitest can be used as a screening test: positive clinitest and negative glucose dipstick.

3. **Alkaptonuria**
   Causal metabolic defect: When the liver enzyme homogentisic acid oxidase is deficient or absent, homogentisic acid is unable to be metabolized properly, resulting in an accumulation of homogentisic acid in cells and body fluids and excretion into the urine (homogentisic acid is not normally found in urine)

   Clinical symptoms: Accumulation of homogentisic acid in tissues causes an abnormal dark blue or black tissue pigmentation and development of degenerative arthritis. The urine will darken after becoming alkaline from standing at room temperature, exposure to air or sunlight, or the addition of alkali.

   Key laboratory findings: The ferric chloride test can be used (non-specific), or alkali or silver nitrate and ammonium hydroxide can be added to the urine and look for a darkening of the urine color.
4. **Maple Syrup urine disease**
   Causal metabolic defect: A disorder characterized by the accumulation of the branched-chain amino acids (leucine, isoleucine, valine) in blood, CSF, urine due to an enzyme defect or deficiency.

   Clinical symptoms: Newborns with this disease show failure to thrive at an early age. Symptoms: acute ketoacidosis, vomiting, seizures, lethargy, mental retardation, death.

   Key laboratory findings: The accumulation of keto acids in the urine produces a strong smell of maple syrup. (metabolic acidosis)

5. **Cystinuria**
   Causal metabolic defect: Inherited autosomal recessive disorder that results in increased levels of cystine in the urine due to the inability of the tubules to reabsorb cystine (and also arginine, lysine, ornithine) filtered by the glomerulus.

   Clinical symptoms: none found intextbook

   Key laboratory findings: Cystine crystals may be seen in the urine sediment.

6. **Cystinosis**
   Causal metabolic defect: Metabolic disease that involves the intracellular deposition of cystine in the lysosomes of all cells of the body.

   Clinical symptoms: This causes extensive renal damage, resulting in polyuria, polydipsia, aminoaciduria, glucosuria, and inability to concentrate or acidify the urine, growth retardation, rickets, acidosis. Without treatment, these patients die by age 10 due to extensive renal damage

   Key laboratory findings: Cystine crystals may be seen in the urine sediment

7. **Tyrosinuria**
   Causal metabolic defect: Due to overflow of this amino acid from the blood plasma; most often seen as a transient condition in neonates, but can also be seen with severe liver disease in which case a generalized aminoaciduria develops.

   Clinical symptoms: Tyrosine is a metabolic precursor of melanin, thyroxine and catecholamines and thus various defects may affect one product and not another

   (see Brunzel, figure 9-3)

   Key laboratory findings: may see tyrosine crystals in urine sediment
8. **Melanuria** –
Causal metabolic defect: Overproduction of melanin by a malignant neoplasm of melanocytes (called melanoma) in skin, mucous membranes or retina will result in melanuria.

Clinical symptoms: Melanin is produced from tyrosine by melanocytes and is the pigment responsible for the color of hair, skin and eyes. Inherited defects in melanin production result in albinism (see Brunzel, figure 9-3)

Key laboratory findings: Urine color will darken (black color is extreme case) upon exposure to air or sunlight if melanin present.