Chemical Exam of Urine - Ketones

- **Ketone Bodies**
  - **Origin**
    - Products of fat catabolism
    - Breakdown of fat into CO2 and water
    - Not normally present in detectable amounts
    - They appear when carbohydrates are not available and the body utilizes fats as an alternative source of energy.

- **Definitions**
  - Ketonuria - ketones in the urine
  - Ketonemia - ketones in the blood
  - Ketosis - disease state, when patient has increased amount of ketones.
  - Acidosis - state when blood pH is decreased, an accumulation of acids; commonly occurs as a result of ketosis
  - Ketoacidosis - blood acidosis as a result of increased levels of ketones.
Chemical Exam of Urine - Ketones

- Three forms:
  - Acetone
    - constitutes 2%
    - Acetone is volatile, & excreted primarily through the lungs
  - Diacetic Acid (Acetoacetic)
    - the first formed
    - both acetone and beta hydroxybutyric acid are produced from diacetic acid.
    - Diacetic acid is the form detected by most ketone test procedures.
    - Makes up 20% of total.
  - Beta hydroxybutyric Acid
    - majority formed
    - although most of the ketones are this form, it is not detected by routine test.
    - Only Hart's test, an old 'wet chemical' test that is designed to detect B-hydroxybutyric acid

Chemical Exam of Urine - Ketones

- Clinical Significance
  - Health - formed in liver and completely metabolized
  - Disease - excessive formation and accumulation
    - Disturbance of carbohydrate metabolism
      - when there is a decrease of carbohydrate metabolism, then
        the body stores of fat must be metabolized to supply energy.
      - As a result of this increased fat metabolism ketones will be
        found in the urine.
    - Low carbohydrate diets (Atkins types)
    - Diabetics not in control

Chemical Exam of Urine - Ketones

- Other conditions
  - Persons exposed to cold / severe exercise
  - Febrile conditions
  - High fat diets / ketogenic diets
  - Starvation / malnutrition
  - Vomiting and diarrhea, esp in children
  - Van Gierke's Disease - glycogen storage disease
    - An error in carbohydrate metabolism, results in limited availability of carbohydrates.
  - Pyloric stenosis (sometimes in babies)
    - Affected infants have prolonged loss of gastric contents
      - resulting in starvation = ketones.
    - But also a frequent loss of the HCl from the stomach means
      loss of HCl - results in overall alkalosis instead.
    - So - while ketosis is most often associated with acidosis, when
      caused by pyloric stenosis - can result in overall alkalosis.
Chemical Exam of Urine - Ketones

- Physiological Effect
  - 2 of the 3 ketones are metabolic acids.
  - Can you name them?

- pH of the blood lowered
  - Normally the blood pH is 7.40,
  - but the presence of increased keto-acids lowers both blood and urine pH. (condition is called ketoacidosis)

- Excessive acid excreted in urine (lowers urine pH)
  - Urine ketones can be found before significant levels can be seen in the blood, increasing the importance of urine screening, especially in emergency situations.

- Toxicity - brain damage by
  - acetoacetic / diacetic acid
  - and acetone

Screening / checking for Ketonuria

- Diabetic Ketonuria
  - Diabetes mellitus
    - Out of control diabetic will have ketones in their blood and urine.
    - Checking for ketones in urine - Provides clue to early diagnosis of ketoacidosis and diabetic coma
    - Pregnant diabetic - fetal death due to ketoacidosis

- Others
  - Monitor a patient who is trying to change from insulin to an oral hypoglycemic agent
  - Ketonuria shows poor response
  - Also, oral agents lose effectiveness if the patient has a current infection.
  - Ketones in the urine would demonstrate that the patient’s oral hypoglycemic medication is not working
Chemical Exam of Urine - Ketones

• Typical urine of the diabetic patient
  • Low pH - from keto acids
  • High specific gravity - the presence of increase glucose
  • High glucose - positive test
  • Pale and maybe somewhat greenish color
  • Ketones - positive test
  
  (what would you look for in the microscopic?)

Chemical Exam of Urine - Ketones

• Ketone Tests
  • most use nitroprusside
  • which detects diacetic acid and a small amount of acetone,
  • but does not detect β-hydroxybutyric acid.

Chemical Exam of Urine - Ketones

• Acetest - tablet
  • Reagents
    • Sodium nitroprusside
    • Aminoacetic acid (glycine)
    • Disodium phosphate - provides optimal pH
    • Lactose
  • Chemistry
    • Reacts with AA and acetone to give purple color
    • Very sensitive (10 mg/dL in urine)
    • Most sensitive to diacetic acid / acetoacetic acid (10 X)
    • Also can detect acetone (7 X)
    • Not at all sensitive to beta hydroxybutyric acid
  • Can be used for urine, serum, EDTA plasma, or whole blood.
Chemical Exam of Urine - Ketones

- **Urine dipsticks**
  - Reagents - same as Acetest (primarily sodium nitroprusside)
  - Chemistry - similar to Acetest
  - Used for serum or urine

![Chemical Exam of Urine - Ketones Diagram]

**Urine ketone: false positive or atypical color**

- Highly pigmented urines
- Combination of high specific gravity and a low pH
- Levodopa metabolites
- Sulfhydryl groups
- Phenylketones
- Phthalein compounds
- Positive and questionable results may be confirmed with a tablet test.

**Urine ketone: false negative**

- Controls solutions that use acetone.
- **Old specimens**
- **Specimens that have been heated.**

General precaution: always test fresh specimens.
Reference Listing

- Please credit those whose work and pictures I have used throughout these presentations.
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