Clinical chemistries of small mammals

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Clinical chemistries

- In general, interpretation of biochemical profiles in small mammals and non-domestics is the same as for the common domestic mammals.
Blood sampling considerations

- Small sample size
  - 1% of the body weight
- Collect in lithium heparin
- Rats
  - 16 hr fast needed to obtain a non-lipemic plasma sample
- Rabbits
  - 16 hr fast results in hypoglycemia

Blood sampling considerations

- Blood collected via cardiocentesis
  - Contaminated with muscle enzymes
    - CK, AST, LD, ALT
- Mice
  - Orbital sinus blood
    - Higher plasma calcium

Rodents

- Laboratory evaluation of kidney
  - Same as domestic mammals
  - BUN
  - Creatinine
  - Electrolytes
  - Urinalysis
BUN in rodents

- Plasma urea nitrogen concentration is influenced by
  - Diet
  - Liver function
  - Gastrointestinal absorption
  - Hydration
  - Renal function

Increases in BUN

- When greater than 75% of renal function is compromised
  - Test lacks sensitivity for renal disease
  - High protein diets
    - Increased nitrogen metabolism rather than renal disease

Other laboratory abnormalities with renal disease

- Hyperphosphatemia
  - Decreased glomerular filtration
- Hypoproteinemia
  - Glomerular disease
  - Urinary protein loss
- Increased creatinine
  - Decreased glomerular filtration
### Enzymes with high kidney tissue activity

- Gamma-glutamyltransferase
- N-acetyl-β-D-glucosaminidase
- Alkaline phosphatase (AP)

- Measurement of these in urine may improve the sensitivity of clinical chemical testing for renal disease in rodents

### Creatinine clearance in rodents

- Testing of endogenous creatinine clearance
  - May provide a specific and sensitive test for decreased glomerular filtration
  - Before plasma urea nitrogen and creatinine concentrations are increased

### Renal azotemia in rodents

- Common causes
  - Amyloidosis
  - Immune complex disease
  - Polycystic disease

- Age-related increases in BUN
Urinalysis in rodents
- Often spontaneously urinate when handled
  - Clean sample
- Cystocentesis
  - Eliminates artifact
  - May have blood contamination
- Perform urinalysis within 2 hours of collection
  - Urine may be refrigerated at 4°C up to 48 hours
    - Refrigerated urine
      - Warm to room temperature before testing

Urinalysis of rodents
- pH is influenced by diet
- Acidic urine
  - Catabolic conditions
    - Starvation
    - Ketosis
    - Fever

Urinalysis of rodents
- Specific gravity and osmolality
  - Evaluate kidney’s ability to concentrate or dilute urine
  - Water-deprivation test
    - Withhold water for 24 hr
    - Specific gravity >1.030 is normal
  - Osmolality is the definitive method
    - Rat urine: 331 - 445 mOsm/kg is normal
    - Hamster urine: 307 - 355 mOsm/Kg is normal
Urinalysis of rodents

- Normal trace glucose
- False-negative results
- Ascorbic acid in urine
- Proteinuria is common
  - Variety of normal urine proteins
  - Increases with age
  - Males tend to be more proteinuric than females

Urinalysis of rodents

- Urine sediment
  - < 5 rbc/ hpf
  - < 5 wbc/ hpf

Rodent: liver evaluation

- Same as domestic mammals
- Enzymes
  - AP, GGT, AST, ALT, LD, SD
  - ALT is liver-specific in rats
  - ALT is not useful in guinea pigs
- Bilirubin
- Bile acids
- Cholesterol
Alkaline phosphatase

- A membrane-bound enzyme
- Highest activity in
  - Osteoblasts
  - Biliary epithelium
  - Epithelial cells of kidneys and intestines

Increased serum or plasma AP activity in rodents

- Hepatic cholestasis
  - Ligation of the bile duct in rats
    - Elevation of both hepatic and intestinal AP isoenzymes
  - More sensitive test than bilirubin or ALT for detection of hepatic disease in hamsters

Increased serum or plasma AP activity in rodents

- Drugs that increase AP synthesis and plasma activity in rats
  - Cortisol
  - Phenobarbital
  - Theophylline
Plasma GGT activity in rodents

- Experimentally induced hepatic injury resulting in cholestasis
  - Increased plasma GGT in hamsters and rats

- Guinea pigs have higher hepatic GGT activity than rats
  - Higher plasma GGT activities with cholestasis
  - Increased serum GGT activity in guinea pigs after in vitro blood clot formation
    - Avoided with use of plasma for enzyme testing

High GGT activity in kidneys of rodents

- The kidneys of rats have 200- to 300-fold the GGT activity of the liver
- Not detectable in the plasma or serum of most rodents
Aspartate aminotransferase (AST)
- Mitochondrial and cytosolic enzyme
- High activity in:
  - Liver
  - Heart
  - Skeletal muscle
  - Kidney
- Low activity in:
  - Intestines
  - Brain
  - Lung
  - Testes
- Increases in plasma or serum AST activity
  - Hepatic injury
  - Cardiac muscle injury
  - Skeletal muscle injury

Alanine aminotransferase (ALT)
- Cytosolic and mitochondrial isoenzymes
- ALT activity in rodents
  - Intestines
  - Kidneys
  - Heart and skeletal muscle
  - Brain
  - Skin
  - Pancreas
Alanine aminotransferase (ALT)

- Rats and mice
  - Highest activity in the liver
- Cytosolic to mitochondrial ratio of ALT isoenzymes in rats
  - Liver is 5:1
  - Heart muscle 50:1
- Guinea pig ALT activity
  - Heart is equal to liver

Increased plasma and serum ALT activity

- Hepatocellular damage in most rodents
- Liver specific in rats and mice
- No diagnostic value for hepatic disease in guinea pigs
  - Have only half the hepatic ALT activity of rats and mice
- Increases in serum ALT activity correlate with the degree of hepatic necrosis in rats
- A threefold increase in plasma ALT activity occurs in mice restrained by holding the body compared to the tail

Lactate dehydrogenase (LD)

- Cytosolic enzyme
- Highest activity in skeletal muscle
  - Cardiac muscle
  - Liver
  - Kidney
  - Intestines
- Five isoenzymes in mouse
  - LD-1 and LD-2 in cardiac muscle
  - LD-5 in the liver and skeletal muscle
  - LD-3 in most other tissues
Lactate dehydrogenase (LD)
- Elevated serum or plasma LD activity
  - Hepatocellular disease in rodents
  - Normal values are highly variable
  - Depend on the analytic method used

Sorbitol dehydrogenase (SD)
- Cytosolic enzyme
- Mice
  - Liver
  - Kidney
  - Seminal vesicles
- Liver specific in rats

Sorbitol dehydrogenase (SD)
- Increases in serum or plasma
  - Hepatic disease in rodents
  - More sensitive test than ALT for detection of hepatocellular disease in rats
- Usually not offered by veterinary laboratories
Increased serum and plasma total bilirubin in rodents

- Hepatobiliary disease
- Extra-hepatic biliary obstruction
- Hemolysis

Total serum and plasma bile acid concentration

- Sensitive and specific test for hepatobiliary disease
- Disorders of the enterohepatic circulation
- Excellent potential for detecting hepatobiliary disease in rodents
  - Especially rats with a high concentration of circulating bile acids

Plasma cholesterol concentration

- Increases in rodents with extrahepatic biliary obstruction
- Mice
  - Normal plasma cholesterol concentration varies between strains
- Hypercholesterolemia often is associated with fatty infiltration of many tissues
- Guinea pigs
  - Intestine not liver is primary site of cholesterol production
Normal plasma cholesterol concentration of hamsters

- 112-210 mg/dL or 2.90 - 5.43 mmol/L
- Higher than that of other rodents
- Decreases during short photoperiods
- Increases with cold temperatures

Rabbits

- Kidney evaluation
  - Urea and creatinine
    - Requires 50 to 75 % loss of function

Rabbits

- Renal failure often associated with increased
  - BUN
  - Creatinine
  - Calcium
  - Phosphorus
  - Potassium concentrations
Rabbits
- Renal failure may exhibit
  - Isothienuria
  - Nephritis
    - Proteinuria
    - Ketonuria
    - Pyuria
    - Cast formation

Rabbits: Calcium
- Normal: 13 - 15 mg/dl
- Mean urinary fractional calcium excretion is 45%
  - Note: less than 2% in other mammals

Rabbits
- Liver evaluation
  - ALT, AST, LD, AP, GGT
    - Plasma ALT is liver-specific
    - Normal plasma ALT is less than half of that of the dog
  - Bilirubin
  - Cholesterol
Rabbits: Liver evaluation

- Marked increase in plasma bilirubin
  - Biliary obstruction

Rabbit alkaline phosphatase

- 3 AP isoenzymes
  - 1 intestinal form
  - 2 liver/kidney forms
    - Major form similar to intestinal form of other mammals
    - Minor form is similar to liver/kidney/bone form of other mammals

Rabbit cholesterol

- May increase with extrahepatic biliary obstruction
- Rabbits used for cholesterol metabolism research
  - Rapidly develop cholesterolemia with high-cholesterol diets
Ferrets

- **Kidney evaluation**
  - BUN, creatinine, protein, electrolytes, urinalysis
  - Normal ferrets and those with azotemia
    - Lower creatinine than dogs and cats

Ferrets

- **Liver evaluation**
  - Same as dogs and cats
  - ALT is a sensitive and specific test for hepatocellular disease in ferrets

Ferrets: Glucose

- 4- to 5-hour fasting plasma glucose
  - < 60 mg/dL (3.33 mmol/L): presumptive diagnosis of insulinoma
  - 60 - 90 mg/dL (3.33-5.0 mmol/L) merely suggestive
  - > 90 mg/dL (5.0 mmol/L) are normal
Ferrets: Insulinoma

- Normal serum immune-reactive insulin
  - 4.6 to 43.3 µU/mL (SI units, 33-311 pmol/L)

- Normal insulin: glucose ratio
  - 3.6 to 34.1 µU/mg (SI units, 4.6-44.2 pmol/mmol)

- Results may vary among laboratories

Ferrets: Insulinoma

- Amended insulin:glucose ratio (AIGR)
  - Insulin (µU/mL) x 100/fasting glucose (mg/dL) - 30
  - > 30 suggestive of hyperinsulinism
  - Rarely used

Ferrets: other caused for hypoglycemia

- Delayed separation of plasma from erythrocytes
- Starvation
- Chronic hepatic disease
- Septicemia
- Endotoxemia