# Phenobarbital

## Interpretive Summary

**Description**: Phenobarbital is a barbiturate that is primarily used for seizure control. Serum phenobarbital concentrations are assessed to help determine if the drug is reaching therapeutic levels and to assess for toxic levels.

### Below Therapeutic Level

#### Common Causes

- Low dose of phenobarbital
- Artifact
    - Using a serum separator tube for blood collection/transport

#### Uncommon Causes

- Severe malabsorption due to gastrointestinal disease
- Alkaline urine
    - Urine pH > 7.0
- Increased urine flow can increase phenobarbital clearance
    - Mannitol
- Medications
    - Rifampin

### Above Therapeutic Level

#### Common Causes

- High dose of phenobarbital

#### Uncommon Causes

- Severe anuric or oliguric renal failure
- Medications
    - Chloramphenicol
    - Felbamate
- Diet
    - Lower protein or lower fat diet may increase phenobarbital half-life

#### Related Findings

- Adverse effects of phenobarbital (more common at higher serum concentrations)
    - Increased ALP, ALT (dog)
    - Increased Spec cPL® with secondary pancreatitis
    - Decreased T4, free T4
    - Hepatotoxicity
        - Decreased albumin, increased bilirubin, bile acids with secondary hepatotoxicity
    - Bone marrow suppression (rare)
        - Anemia, decreased neutrophils, platelets
    - Coagulopathy (cats – rare)
        - Increased PT, PTT

## Additional Information

### Physiology

- Phenobarbital's exact mechanism of action on the CNS is unknown. Phenobarbital likely increases the effects of the inhibitory neurotransmitter GABA, and decreases the release of the excitatory neurotransmitter glutamate.
    - Phenobarbital can decrease the release of acetylcholine and norepinephrine.
- The drug has good oral absorption in dogs, cats, and horses.
- Approximately 40-60% of phenobarbital is protein bound.
- Peak levels occur 4-8 hours after oral administration in dogs.
- Steady state serum levels are achieved after 2-3 weeks.
- Timing of the blood collection for phenobarbital levels is not important in the majority of cases.
    - If there are signs of toxicity, it is recommended to get a peak sample 4-6 hours after the phenobarbital administration.
    - If there are signs of break through seizures, it is recommended to get a trough sample right before the next dose of phenobarbital.
- If phenobarbital levels are below the therapeutic range, the dose does not have to be increased in the face of good seizure control.
- If the phenobarbital level is above the therapeutic range, there is an increased risk for hepatotoxicity.
    - The dose of the phenobarbital should be decreased and another anti-epileptic drug may need to be started to maintain good seizure control.
    - Drugs that can increase the risk for phenobarbital-induced hepatotoxicity
        - Carprofen
        - Acetaminophen
- Phenobarbital induces hepatic microsomal enzyme activity, which can increase the metabolism of many drugs and decrease serum concentrations of those drugs.
    - Lists of these drugs can be found in most pharmacology texts

### References


- Boothe DM. *Small Animal Clinical Pharmacology and Therapeutics*, 2nd ed. Philadelphia, Pa: WB Saunders; 2001.


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