MAYO CLINIC LABORATORIES

Test Definition: PNYF

Phenytoin, Free, Serum

Overview

Useful For

Monitoring for appropriate therapeutic concentration of free phenytoin: free phenytoin level is the best indicator of adequate therapy in renal failure

Assessing compliance and toxicity

Method Name

Membrane Separation/Kinetic Interaction Microparticles in Solution (KIMS)

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Collection Container/Tube: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial within 2 hours of collection.

Forms

If not ordering electronically, complete, print, and send a Therapeutics Test Request (T831) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	7 days	
	Ambient	7 days	

	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Phenytoin is the drug of choice to treat and prevent tonic-clonic and psychomotor seizures. If phenytoin alone will not prevent seizure activity, coadministration with phenobarbital is usually effective.

Phenytoin is highly protein-bound (90%), mostly to albumin. Ten percent of the phenytoin circulates in the free, unbound form. Free phenytoin is the active form of the drug, available to cross biologic membranes and bind to receptors. Increased free phenytoin produces an enhanced pharmacologic effect. At the same time, the free fraction is more available to the liver to be metabolized, so it is cleared more quickly.

Concurrent use of phenytoin and valproic acid (another frequently used antiepileptic) may result in altered valproic acid levels and/or altered phenytoin levels. Due to the complex situation involving displacement of protein-bound phenytoin and inhibition of phenytoin metabolism, as well as the potential for decreased valproic acid concentrations, patients should be monitored for both phenytoin toxicity and therapeutic efficacy. Free phenytoin levels should be measured to provide the most accurate assessment of phenytoin activity early in therapy. At steady-state, free phenytoin and free valproic acid concentrations should be normalized.

In renal failure, the opportunity for the free phenytoin fraction to be cleared is significantly reduced. The end result is that both the total and free concentration of phenytoin increase, with the free concentration increasing faster than the total. Dosage must be reduced to avoid toxicity. Accordingly, the free phenytoin level is the best indicator of adequate therapy in renal failure.

Toxicity is a constant possibility because of the manner in which phenytoin is metabolized. Small increases in dose can lead to very large increases in blood concentration, resulting in early signs of toxicity such as nystagmus, ataxia, and dysarthria. Severe toxicity is typified by tremor, hyperreflexia, lethargy, and coma.

Reference Values

Therapeutic: 1.0-2.0 mcg/mL
Critical value: > or =2.5 mcg/mL

Interpretation

Dose should be adjusted to achieve steady-state blood concentration of free phenytoin between 1.0 and 2.0 mcg/mL. The range for percent free phenytoin is 8% to 14%.

Severe toxicity occurs when the free phenytoin concentration is > or =2.5 mcg/mL. However, response and side effects will be individual.

Cautions

No significant cautionary statements

Clinical Reference

Richens A: Clinical pharmacokinetics of phenytoin. Clin Pharmacokinet 1979;4:153-169

Performance

Method Description

Fresh serum subjected to ultra-filtration to generate a protein-free filtrate, which is then analyzed for free phenytoin by the kinetic interaction of microparticles in a solution (KIMS). Phenytoin antibody is covalently coupled to microparticles and the drug derivative is linked to a macromolecule. The kinetic interaction of microparticles in solutions is induced by binding of drug-conjugate to the antibody on the microparticles and is inhibited by the presence of phenytoin in the sample. A competitive reaction takes place between the drug conjugate and phenytoin in the serum sample for binding to the phenytoin antibody on the microparticles. The resulting kinetic interaction of microparticles is indirectly proportional to the amount of drug present in the sample.(Package insert: Roche Phenytoin reagent, Roche Diagnostic Corp, Indianapolis, IN)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

Same day/1 day

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

80186

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PNYF	Phenytoin, Free, S	3969-3

Result ID	Test Result Name	Result LOINC® Value

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