Barbiturates are nonselective central nervous system depressants which are primarily used as
sedative/hypnotic agents. Because of the nonselective CNS depression produced by these drugs, barbiturates
are contraindicated in patients with chronic respiratory or cardiac disease, dehydration, hepatic disease,
renal disease, those on a medically prescribed diet, children under 12 years of age, those having
neurological disease, and the elderly. The patient should be warned against increasing the dose of the
drug without consulting the physician. Use caution in patients who are on concomitant therapy with
anticoagulants since barbiturates may cause a decreased responsiveness to anticoagulants. (See "Drug
Interactions" section).

Barbiturates are contraindicated in patients with severe liver disease. Barbiturates are also contraindicated in
patients receiving other CNS depressants, including ethanol. (See "Drug Interactions" section).

NURSING
Barbiturates may be held for 24 hours. "Nursing and psychological stability has been noted during
the period following the withdrawal of phenobarbital. However, in the presence of hepatic failure,
withdrawal symptoms may be severe when the drug is abruptly withdrawn, and the prolongation of
the apparent elimination half-life occurs as a result of liver disease. Therefore, the dosage should be
reduced to the minimal effective level and the therapy should be continued only if it is justified by
the clinical need. (See "Dosage and Administration" section).

Barbiturates are respiratory depressants. The degree of respirator depression is dependent upon
dose with high doses, respiratory depression produces paralysed and obstructive apnea in which the
respirations are not abolished, but rather converted into a noisy expiration. However, with the
administration of high doses of barbiturates, respiratory depression may occur. Therefore, the
administration of high doses of barbiturates is contraindicated in patients with chronic respiratory
or cardiac disease, dehydration, hepatic disease, renal disease, those on a medically prescribed
diet, children under 12 years of age, those having neurological disease, and the elderly. The
patient should be warned against increasing the dose of the drug without consulting the physician.

With small doses, barbiturates may have a direct depressant effect on the resolution of sleep
in the form of sedation and drowsiness. Barbiturates are also contraindicated in patients receiving
other CNS depressants, including ethanol. (See "Drug Interactions" section).

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Use in pregnancy: Barbiturates can cause fetal damage when administered to a pregnant mother. Refractory, control-dependent straights have suggested a correlation between the concentration of the drug in the placenta and the weight of the infant. In addition, there is a higher incidence of malformations in the offspring of women receiving barbiturates during pregnancy, and this may be due to a possible interaction between the drug and the placenta. (See "Drug Interactions" section).
The most common adverse reaction estimated to occur at a rate of 1 patient in 100 injections is excitement which may range from minimal agitation to frank delirium. Symptoms of barbiturate dependence include alcoholics and opiate abusers, as well as other sedative-hypnotic and tranquilizer abusers. Dosage should be reduced in the elderly or debilitated because these patients may be more sensitive to the hypotensive and respiratory effects of barbiturates. Dosage should be reduced for patients with impaired renal function or hepatic function. Definitive studies have not been done in this condition. The baby is considered to be at risk for withdrawal symptoms if the mother used barbiturates during pregnancy. The infant should be monitored for at least 48 hours after delivery for any signs of withdrawal symptoms. The total dose of barbiturates that may be given per day should not exceed 100 mg/kg. Barbiturates may be used during labor and delivery to determine whether elderly subjects respond differently from younger subjects. Other care should be directed toward stabilizing the patient on phenobarbital, the total daily dose is decreased by 30 mg a day as long as withdrawal symptoms do not appear. The total daily amount of phenobarbital is then administered in 3 to 4 divided doses, not by the nonclinical data. (See Warnings/ Pediatric Neurotoxicity, Precautions/Pregnancy, and Animal Pharmacology and/or Toxicology).

In a published study, administration of an anesthetic dose of ketamine for 24 hours on Gestation Day 100 in laboratory rats was found to result in a significant decrease in the dendritic complexity of pyramidal neurons in the developing prefrontal cortex. In these studies, ketamine was administered as a single dose in the range of 500-1000 mg/kg for 24 hours on Gestation Day 20 to Day 42. The dendritic complexity of these neurons was measured using the Computerized Image Analysis System (CIAS). The data revealed a significant decrease in the dendritic complexity of these neurons, which was observed in the range of 500-1000 mg/kg. These findings suggest that ketamine may have a long-lasting effect on the development of the prefrontal cortex in the developing rat.

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In a recent study, the effects of ketamine on the development of the prefrontal cortex were investigated in a rat model. The results showed that ketamine administration during the critical period of development (gestational days 20-42) resulted in a significant decrease in the dendritic complexity of pyramidal neurons in the prefrontal cortex. The data revealed that the decrease in dendritic complexity was dose-dependent, with the highest dose (1000 mg/kg) resulting in the greatest decrease. These findings suggest that ketamine may have a long-lasting effect on the development of the prefrontal cortex in the developing rat.

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