Lamictal Narrations

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"Severe head trauma, stroke, and central nervous system infections are the most common risk factors for epilepsy. In infants, seizures can be caused by hypoxia, genetic metabolic or developmental brain defects, or perinatal injuries, meningitis or encephalitis. Moderate or severe head trauma is a major cause of epilepsy in young adults; in the case of the elderly, cerebral stroke may be the most common cause."

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"Seizures are of two types, partial and generalized. The initiation of partial seizures is confined to a discrete part of one cerebral hemisphere, associated with excessive focal neuronal discharges, and can be divided into two types, simple or complex. Generalized seizures involve both cerebral hemispheres and usually cause impairment of consciousness. Seizures may evolve from simple, complex or partial seizures to generalized tonic-clonic seizures."

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"Many patients experience more than one type of seizure. In patients under 15, generalized seizures occur about 50 percent of the time; but this percentage decreases drastically with age, with patients between 35 and 64 experiencing these seizures just six percent of the time. In patients of all ages, myoclonic seizures account for about five percent; and absence seizures are rare after adolescence."

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"The incidence of partial seizures increases with age, especially those with complex symptomatology. About 50 percent of all new cases of epilepsy in patients over 65 are manifested by partial seizures."

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"Ideally a single antiepileptic drug should be used to treat epileptic seizures once the specific seizure type has been identified. Drug interactions can complicate the overall management of epilepsy. Most antiepileptic drug interactions increase serum concentrations, thereby promoting toxicity, or decrease serum concentrations, resulting in therapeutic failure. However, if seizure control remains poor with monotherapy, a second drug may be added."

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"Several antiepileptic drugs are now available to treat seizures. Phenytoin and the barbiturate primidone are commonly used to treat generalized tonic-clonic seizures, while ethosuximide is highly effective in treating uncomplicated absence seizures. Valproic acid has a broader spectrum of clinical activity in the treatment of generalized seizures."

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"Drugs used to treat generalized seizures can also be used for complex partial seizures and partial seizures secondarily generalized. However, carbamazepine and phenytoin are preferred as initial therapy since they are effective and have few long-term adverse effects."

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"Patients with childhood-onset or primary generalized epilepsy or normal neurologic and EEG findings are good candidates for seizure control. Patients who have a long duration of untreated or inadequately treated epilepsy, frequent seizures, partial seizures, or a neurologic or cognitive handicap usually do poorer. In newly diagnosed patients, seizure control in the first two years of treatment is predictive of subsequent remission."

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"As many as 50 percent of all patients with epilepsy have poorly controlled seizures. Reasons for this vary and include lack of compliance with the prescribed drug therapy and intercurrent or underlying illness. Patients may also be ignoring precipitating or triggering factors such as alcohol, lack of sleep, or stress. In addition, errors in diagnosis or treatment can contribute to incomplete seizure control."

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"Efficacy in a broad spectrum of seizure types and long-term seizure control are two of the most important characteristics that an antiepileptic drug must possess. Other features include a consistent rate of absorption and a long duration of action that permits the patient to take the drug just once or twice daily, thereby improving compliance. An ideal drug must also be well tolerated, have relatively few drug interactions, and be free of serious adverse side effects."

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"Four phases describe a drug's pharmacokinetics and are ultimately responsible for achieving appropriate therapeutic concentrations--absorption, distribution, metabolism, and excretion. Absorption is the process by which a drug gets from its dosage form to the bloodstream; while distribution occurs after the drug is absorbed into the bloodstream. Metabolism and excretion are defined in terms of a drug's half-life, the time it takes to reduce the concentration of a drug in the bloodstream by 50 percent."

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"Here we see the various phases of pharmacokinetics after a single dose of a drug. Note, the time it takes for the concentration to decrease from 2ug/mL to 1 ug/mL is 24 hours, thus the half-life is 24 hours. There is an advantage to a drug such as Lamictal that has predictable, linear pharmacokinetics, particularly in light of the fact that many AEDs have non-linear pharmacokinetics."

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"When examining drug interactions, the mechanism of the interaction must be considered. Does it involve absorption, distribution, metabolism, or excretion? Further, both antiepileptic drugs and non-antiepileptic drugs may alter serum concentrations of concomitantly administered medications."

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"Changes in antiepileptic drug concentrations can lead to clinically significant changes in the patient's condition. A decrease in drug concentrations may result in seizures, while an increase may result in toxicity. Changes in total concentrations are often obvious when determined by routine serum monitoring; however, changes due to protein binding or patterns of elimination may not be as easily detected using this technique."

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"An increase in total serum concentration can be achieved by manipulating any of the four phases of a drug's pharmacokinetics. To improve absorption, remove a compound that impairs it from the patient's regimen; for better distribution, remove the displacer. In the case of metabolism and excretion, you can either remove an inducer drug or add an inhibitor drug."

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"To decrease total serum concentration, manipulate any one of the four phases of a drug's pharmacokinetics. You can add absorption interference or displacer. To decrease metabolism and excretion, either add inducer or remove inhibitor."

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"These are common drugs that affect absorption, distribution, metabolism, and excretion. Before adding or removing any of these drugs from a patient's regimen, you must consider how it will affect the antiepileptic drug concentration."

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"The addition of an antiepileptic drug affects concomitant medications. Here is a listing of common interactions. In most cases, the antiepileptic drug decreases the concentration and possibly the effectiveness of non-antiepileptic drugs. Thus, non-antiepileptic drug doses may need to be adjusted."

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"Various formulations of phenytoin are available. They have significant differences in bioavailability and should not be used interchangeably in a particular patient."

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"Many formulations of valproate are available, including capsules and enteric-coated tablets. Originally created to decrease gastrointestinal tolerance, enteric-coated tablets do not readily dissolve in the gastric acid pH of the stomach. Instead the coating of these delayed-release tablets dissolves in the more basic intestinal pH. This may lead to lags in the rate of absorption if the drug is taken on a full stomach."

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"Carbamazepine tablets are slowly absorbed after oral administration, with plasma concentrations peaking in four to eight hours. Since this drug is highly lipophilic and insoluble in water, no parenteral preparation is available."

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"Here we see an overview of the pharmacokinetics of phenytoin, valproate, and carbamazepine administered as monotherapy. If polytherapy is being administered, keep in mind that a particular therapy may change the pharmacokinetics of both therapies."

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"Available as a tablet, maximum serum concentrations for felbamate can be reached one to four hours after dosing."

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"Though rapidly absorbed, gabapentin exhibits dose-limited absorption. Higher doses of gabapentin may not be absorbed as well as lower doses, and in patients requiring high doses, multiple daily doses may be necessary."

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"Rapidly absorbed, Lamictal is available as a tablet formulation. It is rapidly absorbed, not highly protein bound, has a plasma half-life of 25 hours and excreted 100 percent as metabolite. The optimal concentration is greater than 2 micrograms per milliliter."

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"Alterations in serum concentrations caused by conventional antiepileptic drugs used concurrently with newer agents are summarized here."

Slide32.wav

"Alterations in serum concentrations caused by new antiepileptic drugs used concurrently with conventional agents are summarized here."

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"These are the structural formulas of older antiepileptic drugs. Many of these drugs are structurally related to phenobarbital, the oldest antiepileptic agent."

Slide35.wav

"These are the structural formulas of newer agents, some of which are in investigational use. They have novel chemical structures that differ from those of older agents."

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“Some of the most important acute adverse effects, including nausea and vomiting, sedation, dizziness, visual disturbances and rash, are compared for four commonly used drugs.”

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"All antiepileptic drugs can produce cognitive or behavioral syndromes, impairing attention, concentration, memory, and mental or motor speed. Hand tremor associated with valproic acid is most commonly seen with doses above 750 mg per day.."

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"Older antiepileptic drugs may cause idiosyncratic toxicity. Routine laboratory and clinical monitoring may be helpful for early detection of chronic adverse effects. However, until specific markers that identify susceptible patients are available, this approach won't predict acute idiosyncratic adverse effects."

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"Phenytoin is less often administered to women and children over five since it causes coarsening of facial features, hirsutism, and gingival hyperplasia. Barbiturates may exert subtle effects on cognitive ability in both children and adults."

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"Several new agents are available for the treatment of epilepsy. Here we see a summary of their associated side effects."

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"Preclinical animal studies were conducted on three new drugs: felbamate, gabapentin, and Lamictal. As shown in these study results, an increase in the incidence of pancreatic cancer in male rats was seen with gabapentin. However, animal studies are not always predictive of human response."

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"The chemical structure and proposed mechanism of action of Lamictal brand of lamotrigine are unrelated to those of other antiepileptic drugs. A phenyltriazine derivative, Lamictal displays marked anticonvulsant activity with very weak antifolate properties. This drug inhibits the tonic seizure component of supramaximal electrical and pentylenetetrazol-induced seizures."

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"Disturbances in excitatory amino acid transmission may be partially responsible for the underlying biochemical abnormalities seen in epilepsy. Lamictal acts at voltage-sensitive sodium channels to stabilize neuronal membranes and normalize the excessive release of excitatory amino acids, such as glutamate and aspartate."

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"Both preclinical and clinical findings confirm that Lamictal possesses good anticonvulsant activity against partial seizures with or without generalized tonic-clonic seizures. These studies also point to Lamictal's potential use as a treatment for other seizure types."

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"This screen summarizes the results of preclinical and clinical findings for Lamictal. These results suggest that therapy with this drug should result in few drug--drug interactions, an important consideration since polytherapy is often used to control epilepsy in many patients."

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"When prescribing polytherapy for an epileptic patient, a major concern for physicians is the effect of each drug on the serum concentrations of other drugs. Lamictal doesn't alter the serum concentrations of concomitant antiepileptic drugs. As a result, it can be added to an ongoing drug regimen without making major adjustments in the doses of concomitant antiepileptic drugs."

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"The results of pharmacokinetic studies of Lamictal, which investigated the effect of concomitant antiepileptic drugs on the serum concentrations of Lamictal at steady state are shown here. The studies conclude that dosing should be adjusted depending on the concomitant antiepileptic drug, enzyme inducers, valproic acid or enzyme inducers plus valproic acid."

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"Numerous clinical studies have been conducted with Lamictal. The findings have established the drug's efficacy and safety in patients with simple or complex partial seizures with or without generalized tonic-clonic seizures."

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"In eight placebo-controlled parallel and crossover studies, over 700 patients were treated with Lamictal. The mean duration of epilepsy was 22 years with a mean seizure frequency per week of 6.6. The most common concomitant AEDs included carbamapezine, phenytoin, primadone and phenobarbital."

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"This diagram shows the basic structure of the study design for US 05. After screening and a baseline evaluation, the patients were divided into three groups. One received 500 mg of Lamictal per day; a second group received 300 mg of Lamictal per day; and a third group received placebo. Therapy was tapered during the follow-up period from 36 to 39 weeks."

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"Here are the results of a 39-week double-blind, placebo-controlled, parallel study with Lamictal as add-on therapy in patients with refractory simple or complex seizures with or without generalized tonic/clonic seizures. All patient groups had similar baseline seizure frequencies."

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"This diagram shows the basic crossover design for study US 06."

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"We can see the percent median change in partial seizure frequency with Lamictal as add-on therapy in patients with refractory partial epilepsy in six placebo-controlled, crossover studies. In these studies, the frequency of seizures was reduced in 63% to 86% of the patients receiving Lamictal."

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"Generally, adverse experiences in Lamictal-treated patients were mild or moderate and resolved without discontinuation of Lamictal treatment."

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"This is a summary of the adverse experiences commonly reported in the placebo-controlled add-on clinical trials. Note the small percentage of add-on Lamictal patients who were discontinued for any of these reactions."

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"Here is a summary of the results from a study on the long-term efficacy of Lamictal in patients with partial seizures."

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"Here we can see a description of the efficacy of the novel antiepileptic drug, Lamictal. More than 400 patients have been included in long-term continuation studies; many of these have been maintained on Lamictal for up to seven years."

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"Lamictal as add-on therapy is well tolerated by the majority of patients, making it a valuable addition to the therapeutic armamentarium for treatment of refractory partial seizures. Note that serious adverse experiences were uncommon."

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"The efficacy of Lamictal in the treatment of patients with refractory partial seizures was established in seven placebo-controlled studies in which Lamictal was added to other antiepileptic drug therapy twice daily. This list of dosing recommendations resulted; dosing should be based on therapeutic response, not plasma concentration."

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"These are several key conclusions drawn about this novel antiepileptic drug, Lamictal."

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"Lamictal has a low incidence of adverse events."