QUESTION 100

Which of the following anticonvulsant drugs is most likely to cause a clinically important interaction with lamotrigine?

A. Clonazepam  
B. Gabapentin  
C. Vigabatrin  
D. Carbamazepine  
E. Sodium valproate

Lamotrigine:

- Stabilises presynaptic neuronal membranes by blocking voltage-dependent and use-dependent sodium channels
- Used for partial and generalised seizures
- Severe skin reactions (eg: Stevens-Johnson syndrome) can occur in 1 in 50-300 children and 1 in 1000 adults
- More likely if also taking valproate or with rapid dose escalation of lamotrigine
- Stop treatment immediately if rash occurs
- Other common side effects include diplopia, dizziness, ataxia, headache, somnolence, hyperkinesia, nausea, vomiting
- Rare side effects: multi-organ hypersensitivity syndrome, neutropaenia, thrombocytopaenia

Carbamazepine decreases lamotrigine concentration, reducing its efficacy. Lamotrigine may increase the concentration of carbamazepine epoxide, increasing adverse CNS effects of carbamazepine. May need to adjust doses

Valproate increases lamotrigine's concentration and toxicity, including rashes. Stop immediately if rash occurs.

No interaction with clonazepam, gabapentin or vigabatrin.

Correct answer is E – valproate.

While carbamazepine can interact and cause changes in concentrations, the increased risk of severe skin reactions with valproate is much more clinically important.
Category A
Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Category B1
Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage. (Animal studies submitted in support of new drug applications must conform to the Australian Guidelines on the Registration of Drugs - Volume 1, Prescription and Other Specified Drug Products, 2nd edition.)

Category B2
Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage. (Animal studies submitted in support of new drug applications must conform to the Australian Guidelines on the Registration of Drugs - Volume 1, Prescription and Other Specified Drug Products, 2nd edition.)

Category B3
Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans. (Animal studies submitted in support of new drug applications must conform to the Australian Guidelines on the Registration of Drugs - Volume 1, Prescription and Other Specified Drug Products, 2nd edition.)

Category C
Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.

Note that Category C in the Australian and Swedish Categorisations of Risk is a pharmacological effect category and differs from that in the FDA Categorization (where Category C indicates greater likelihood of risk than in B on the basis of adverse effects of any type in animal studies).

Category D
Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Accompanying texts should be consulted for further details.

Category X
Drugs which have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy.