First 2008
VIVA 1

You are considering starting a patient on captopril. Discuss the pharmacology of this drug.

"Please discuss the mechanism of action of ace inhibitors"

The essential effect of these agents on the renin–angiotensin system is to inhibit the conversion of Angio tensin I to the active Angiotensin II, Thus, ACE inhibitors attenuate or abolish responses to AngI but not to AngII. They do not interact directly with other components of the renin–angiotensin system, and their principal pharmacological and clinical effects all apparently arise from suppression of AngII synthesis. Nevertheless, ACE is an enzyme with many substrates, and inhibition of ACE may induce effects unrelated to reducing the levels of AngII. Since ACE inhibitors increase bradykinin levels and bradykinin stimulates prostaglandin biosynthesis, bradykinin and/or prostaglandins may contribute to the pharmacological effects of ACE inhibitors. In a healthy, Na^+ replete person, a single oral dose of an ACE inhibitor has little effect on blood pressure, but repeated doses over several days cause a small reduction in blood pressure. By contrast, even a single dose of these inhibitors lowers blood pressure substantially in normal subjects when they have been depleted of Na^+.

"How do ACEI differ within their class?"

(1) potency (ramipril >lisinopril>captopril),
(2) whether ACE inhibition is primarily a direct effect of the drug itself or the effect of an active metabolite
captopril has active metabolites, ramipril is a prodrug and lisinopril itself is active
(3) pharmacokinetics Captopril has a much shorter half life and duration c/w ramipril and lisinopril.

"Please discuss the pharmacokinetics of captopril"

ABSORPTION bioavailabilty rapidly absorbed, bioavailability of 60-70% (ramipril and lisonpril less)
routes of administration oral
doses commenced at 6.25mg TDS and uptitrated
potency moderately potent
DISTRIBUTION protien binding 25% protien bound
METABOLISM mechanism oxidised in the liver and coverted to sulphides
ELIMINATION half life 2-4 hours
excretion urine both as active metabolites and unchanged

"What is the EC50 of a drug?"

EC50 represents the concentration of the drug which results in 50% of the maximal effect (Emax)

"What is the ED50 of a drug?"

The 50% of population with a quantal response represents the ED50. (effective dose). Animal studies are used to determine the 50% lethal dose LD50 (or 50% toxic dose TD50).

"What is the therapeutic index?"

The therapeutic index represents the ratio of LD50 to ED50. The higher the therapeutic index the greater the range of safety.