Second 2010
VIVA 5

This viva will explore your knowledge of Cerebral Blood Flow and the pharmacology of benzodiazepines.
What is the normal Cerebral Blood Flow and what are its determinants? Candidates had a good knowledge of cerebral blood flow, although struggled to graphically represent the relationship of CBF with, for example changes in PaCO2. Questions relating to effects of benzodiazepines were also well answered.

"Describe cerebral blood flow"

is 750ml minute (15% CO)
O2 consumption is 3ml/100g which given a weight of 1400g is about 50ml (20%)
it is determined by the Cerebral Perfusion Pressure / Cerebrovascular Resistance
CPP is calculated by MAP - CVP, or in pathological states MAP - ICP (starling resistor model)

"How is CBF measured?"

measurement is via the Fick principle using the Kety-Schmidt method
fick principle states that the amount taken up by the organ/[arterial]-[venous] = flow
K-S used NO (highly inert and diffusable) and measured uptake/artial-venous conc diff

"What factors alter CBF?"

intrinsically it demonstrates autoregulation
primarily myogenic stretch factors
local metabolic control is more specific to regional distribution rather than total flow
extrinsically
hypoxia results in increased flows when it drops below 50mmHg
raised CO2 shows a near linear increase in blood flow 20mmHg to 80mmHg

"What is the mechanism of action of benzodiazapienes?"

Benzodiazepines appear to produce all their pharmacologic effects by facilitating the actions of gamma-aminobutyric acid (GABA), the principal inhibitory neurotransmitter in the CNS. Benzodiazepines do not activate $GABA_A$ receptors but rather enhance the affinity of the receptors for GABA. As a result of this drug-induced increased affinity of GABA receptors for the inhibitory neurotransmitter, an enhanced opening of chloride gating channels results in increased chloride conductance, thus producing hyperpolarization of the postsynaptic cell membrane

"How are the benzodiazepines classified?"

they are usually classified by their duration of action
short (<12hrs) - midazolam, intermediate (12-24hrs) - lorazepam, and long (24hrs+) diazepam

"Describe briefly midazolam"

Midazolam is a water-soluble benzodiazepine with an imidazole ring in its structure that accounts for its stability in aqueous solutions and its rapid metabolism. Compared with diazepam, midazolam is two to three times as potent. As with other benzodiazepines, the amnestic effects of midazolam are more potent than its sedative effects. It also has anticonvulsant properties. Midazolam is presented as a clear solution at a pH of 3.5. At this pH is almost completely ionised and therefore water soluble. Since its pKa is 6.5 it is 89% un-ionised at physiological pH and can therefore cross lipid membranes. It has a short half life and is metabolised in the liver via hydroxylation then gluronidation.

"How would you manage an overdose of benzodiazepines?"

early recognition, ABCDs, protection of airway, high flow O2 initially, cardiovascular assessment
request help
reduce further ingestion by considering activated charcoal if it is an oral overdose
consideration of a BDZ antagonist such a flumenzil if appropriate