

March 2009
QUESTION 10

Describe the calculations involved in determining the loading dose and maintenance dose for an intravenous infusion (50% of marks).
What factors may affect these values in the critically ill (50% of marks)?

Volume of distribution

the apparent volume into which a drug disperses in order to produce the observed plasma conc.

The physicochemical properties of a drug influence V_d

lipid solubility - highly lipid soluble drugs have larger V_d

charge characteristics - highly charged drugs have smaller volumes of distribution

tissue binding may result in increased V_d

pathology - renal and hepatic disease leads to increased V_d due to fluid changes

Plasma concentration

is the amount of drug/volume within which it is diluted

Clearance

is the volume of plasma from which the drug is cleared from per unit time (usually ml/min)

it is also the dose/area under the curve

Loading dose

aims to achieve a required plasma concentration

therefore = volume of distribution x desired plasma concentration (divided by bioavailability if not IV)

Maintenance dose

aims to achieve a constant plasma concentration range

is equal to the elimination of the drug

Is clearance x desired plasma concentration

Factors which affect in critically ill

Volume of distribution

derangement of pH leads to altered ionisation depending on pKa

variation in lean body mass:total body mass for different drugs

renal and hepatic disease can increase the V_d

protein binding creates a larger central compartment in multicompartment models

decreased protein in critically ill will alter this

Clearance

may be influenced by other medications used in critically ill

inducing CYP enzymes - phenytoin, carbamazepine

inhibiting CYP enzymes - amiodarone, metronidazole

by renal impairment if the drug is renally excreted - aminoglycosides

by hepatic impairment

at the extremes of age