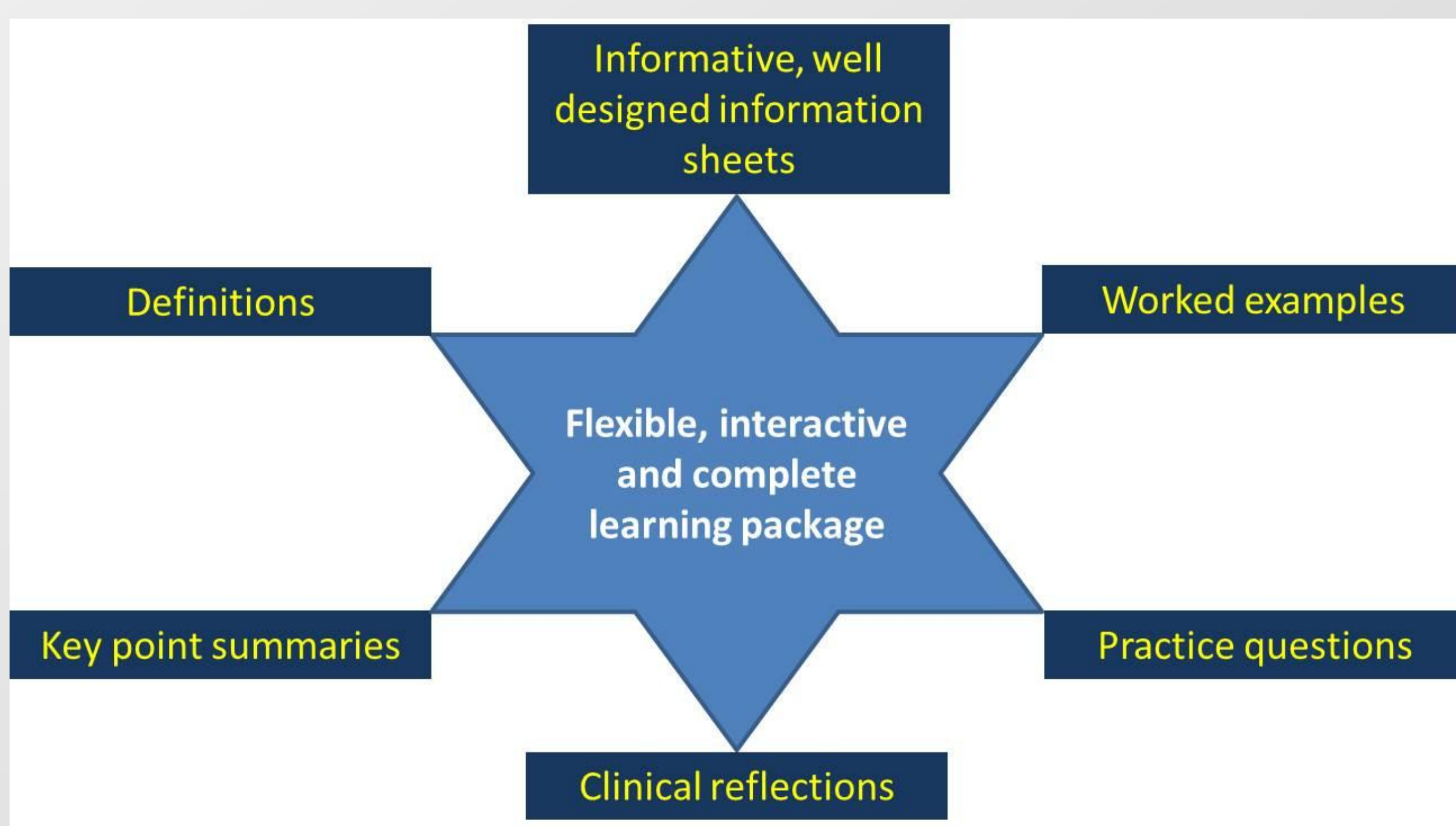


## Pharmacokinetics

- Pharmacokinetics describe the interaction between an organism and drugs administered to it – *i.e. what the body does to the drug*
- It involves graphical representation of drug data and the use of complex mathematical expressions.
- The mathematical nature of the subject matter often means that clinical and pharmacological meaning is lost and student feedback suggests a lack of understanding.
- In pharmacology (clinical and basic), pharmacokinetics is a key aspect of the curriculum in terms of drug development, design and administration.
- The aim of this QAA enhancement theme: developing and supporting the curriculum funded project was to develop a database of interactive, intuitive and innovative resources to support student learning in this area.
- The grant was used to employ a student intern with recent pharmacokinetic experience (Shelby Barnett) to develop these resources.

## Resource design

- A simple design involving a hierarchy of interlinking spreadsheets within Excel was chosen as this would be most flexible, accessible and compatible with the aim.
- By interlinking a variety of spreadsheet types (see below), an innovative and effective learning package was created:

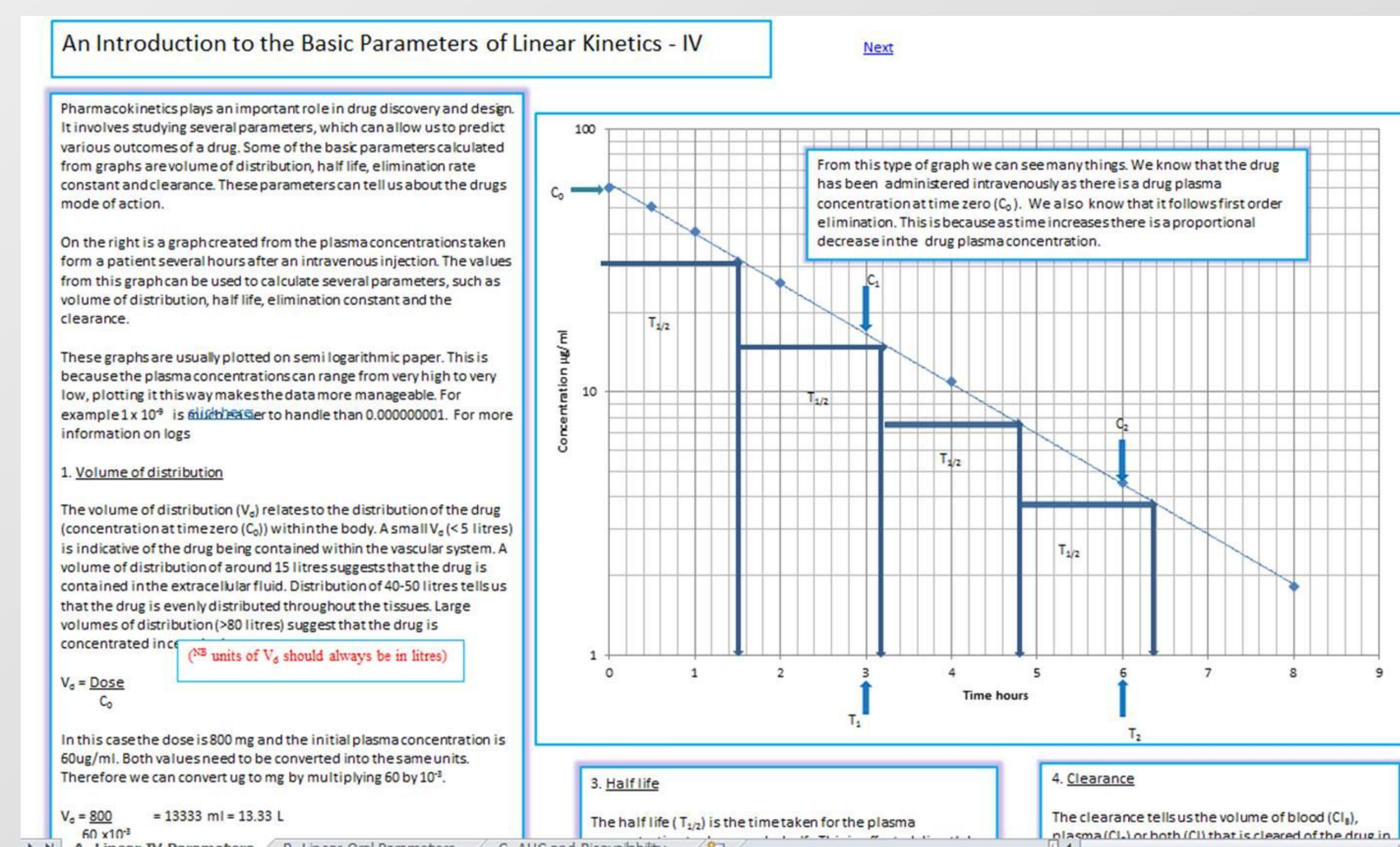


## The database

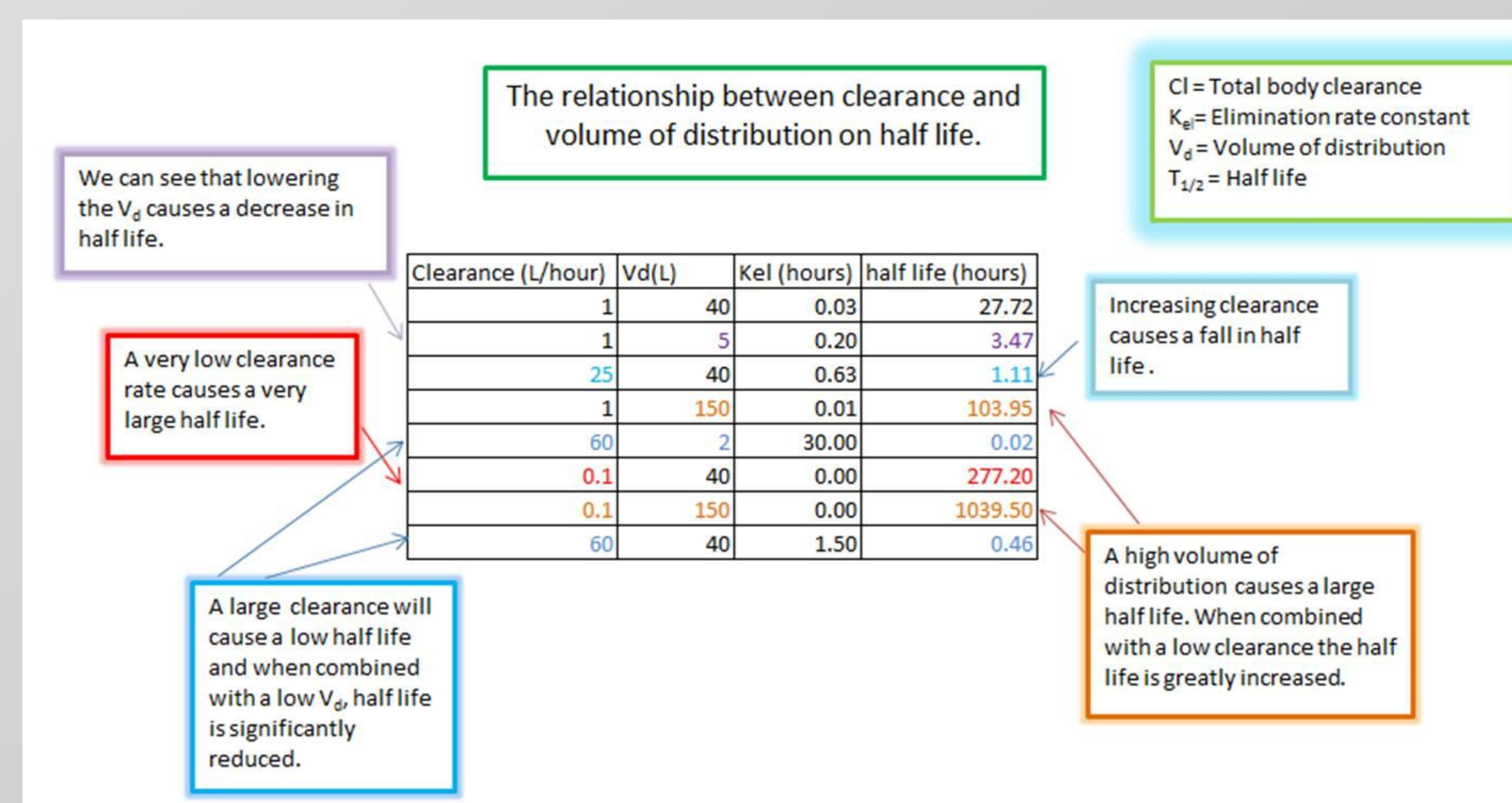
- The main pharmacokinetic topics relevant for UG and PG students are covered in detailed sections:

Section 1 - Basic Linear Pharmacokinetics	02/08/2013 15:41	File folder
Section 2 - Intravenous Infusion	02/08/2013 15:41	File folder
Section 3 - Intermittent Intravenous Infus...	02/08/2013 15:41	File folder
Section 4 - Multiple Oral Doses	02/08/2013 15:41	File folder
Section 5 - Two compartment models	02/08/2013 15:41	File folder
Section 6 - Non Linear Enzyme Kinetics	02/08/2013 15:41	File folder

- Concepts are covered thoroughly, with full explanation of graphs, formulae, provision of worked examples, links to other topics and reminders against common errors all evident in the example below:



- Precise relationships between parameters are summarised in clinical context using accessible and intuitive diagrams to enhance learning:



- Key definitions and equations are provided along with reference to practical clinical meaning:

Definitions	Equations
Volume of distribution (VD) is the distribution of the drug (concentration at time zero (C <sub>0</sub> )) within the body. A small VD (<5 litres) is indicative of the drug being contained within the vascular system. A volume of distribution of around 15 litres suggests that the drug is contained in the extracellular fluid. Distribution of 40-50 litres tells us that the drug is evenly distributed throughout the tissues. Large volumes of distribution (>80 litres) suggest that the drug is concentrated in certain tissues. VD = Dose/C <sub>0</sub>	Volume of distribution (VD) = Dose/C <sub>0</sub> L Concentration time zero (C <sub>0</sub> ) = C <sub>0</sub> = Dose/VD μg/ml or mg/ml Clearance = Cl = VD × K <sub>el</sub> L/hour Cl = rate of excretion / C <sub>0</sub> or Cl = k <sub>el</sub> × VD μg/ml or mg/ml Plasma concentration = C <sub>0</sub> = Dose/VD μg/ml or mg/ml Glomerular filtration = GFR = Urine concentration × volume / plasma concentration ml or L
Concentration time zero (C <sub>0</sub> ) is the plasma concentration at time zero after a drug has been administered.	Half life = T <sub>1/2</sub> = 0.693 / K <sub>el</sub> min or hour Elimination = -K <sub>el</sub> = (ln C <sub>0</sub> - ln C <sub>t</sub> ) / T <sub>1/2</sub> - T <sub>0</sub> or K <sub>el</sub> = 0.693 / T <sub>1/2</sub> min or hour Zero order = dA/dt = -K <sub>0</sub> First order = -dC/dt = K <sub>1</sub> C
Plasma concentration (C <sub>t</sub> ) is the concentration of the drug in blood plasma at any given time.	Steady state = C <sub>ss</sub> = (ln C <sub>0</sub> - ln C <sub>t</sub> ) / (A - A <sub>0</sub> ) / T <sub>1/2</sub> min or hour Absorption = K <sub>a</sub> = (ln C <sub>0</sub> - ln C <sub>t</sub> ) / (A - A <sub>0</sub> ) / T <sub>1/2</sub> min or hour Area under the curve = AUC = Dose/VD × K <sub>el</sub> or AUC = AUC <sub>0-t</sub> + C <sub>0</sub> × T <sub>1/2</sub> μg/ml/hour Bioavailability Actual = F × AUC <sub>0-t</sub> / AUC <sub>0-t</sub> Relative = ΔAUC <sub>0-t</sub> = F <sub>rel</sub> × Dose / VD × K <sub>el</sub> Trapezoid rule = (C <sub>0</sub> + C <sub>n</sub> ) / 2 × (T <sub>n</sub> - T <sub>0</sub> )
Clearance = the volume of blood (C <sub>0</sub> ) or plasma (C <sub>t</sub> ) that is cleared of the drug in a certain time (minutes/ hours). This is related to the volume of distribution and the elimination rate constant an increase in VD or K <sub>el</sub> will increase Cl. Cl = VD × K <sub>el</sub>	Glomerular filtration = is the filtration of the blood at the glomeruli. The speed at which this occurs is known as the glomerular filtration rate (GFR). This is essential for clearance. Kidney damage can cause GFR to lower this then lowers clearance GFR = Urine concentration × volume / plasma concentration. In the case of GFR it is the creatinine concentration that is measured not drug concentration
Half life = this is the time taken for the plasma concentration to decrease by half T <sub>1/2</sub> = 0.693 / K <sub>el</sub> . This is affected directly by clearance and volume of distribution. An increase in VD causes an increase in half life. Half life is also increased by the decrease of clearance. (Table 3-1 birkett)	Zero orders this is where the process is independent of drug concentration [ie slow release preparation such as tablet or patch or slow intravenous infusion] (page 34 (ark). Can be used to describe absorption or elimination dA/dt = -K <sub>0</sub>

- Students can check progress with interactive tests, provided to complement each topic area:

Parameters of Linear kinetics (I.V)		Answer to 2 decimal places
Question		Answer
The half life of a drug is 6 hours. What is the elimination rate constant? (per hour)		
The kel of a drug is 0.56/ hour, what is the half life? (in hours)		
If we know the Kel and Cl of a drug, which parameter can we deduce?		
The dose of a drug is 2.5mg, at time zero 40ng/ml reaches the plasma. What is the Vd? (in L)		
The Vd of a drug is 80L and the Cl is 13 L/hour. What is the kel? (per hour)		
Using the kel value from above. What is the half life of the drug? (in hours)		
100mg of a drug was given the Vd is 50L and the Kel is 0.56. What is the AUC (μg/ml/hour)?		
True or False (answer T or F)		Answer
The half life is the time taken for the drug to be eliminated from the body?		
The higher the Kel the shorter the half life?		
The volume of distribution is the distribution of a drug in the body at time zero?		
The Clearance is directly influenced by the kel and the area under the curve?		
The C <sub>0</sub> is the plasma concentration at any time?		
The area under the curve tells us how much drug has reached the plasma concentration over a time period?		
Increasing the Clearance decreases the Half life?		
Increasing the Volume of distribution decreases the Half life?		

- Currently available through University classroom PC access, work is underway to launch it through MyAberdeen.
- One of the original aims was to provide workbooks for students and the simplicity of the design means selected sections can be provided as a hard copy exercises as required.

## Conclusion

- Feedback from the level 3 cohort given access suggest this is an invaluable resource.
- Overall, these interactive, student designed resources provide flexible, effective and independent support for pharmacokinetic students.