The one-compartment model for volume of distribution has utility, but only poorly describes the distribution of a drug in the body. Our next option is to consider the **two-compartment model**. The two-compartment model adds a peripheral compartment to the one-compartment model. The peripheral compartment represents the opportunity for a drug to leave the plasma and enter other tissues. Drug can equilibrate between the two compartments, and elimination (by clearance through the liver and/or kidneys) only occurs from the central compartment.

An example that demonstrates the two-compartment model is the very early time period after an IV bolus is first injected. Remember that blood is not drawn from a patient until around 15 minutes after the dose is administered so that the drug has time to distribute through the entire blood volume and the tissues. This delay is necessary because the early stages of an IV bolus do not fit the one-compartment model. Mathematically, an IV bolus can be more accurately described by the equation below. This equation is little more than our original one-compartment equation for $C_p$ with an extra exponential term.

$$C_p = Ae^{-at} + Be^{-bt}$$

Graphically, the equation gives the $C_p$-time relationship shown below. One term mostly describes the **distribution phase** of the IV bolus while the other covers the **elimination phase**.
The very early data points are dominated by the first term in the equation ($Ae^{-\alpha t}$) and form a line with a slope of $-\alpha$. This line can be extrapolated back to the y-axis to give a two-compartment model $C_p^0$. While any value for $C_p^0$ is hypothetical, the two-compartment model $C_p^0$ is closer to reality than the one-compartment model estimate. While the $Ae^{-\alpha t}$ term dominates early, it quickly approaches a value of 0 as time increases. As $Ae^{-\alpha t}$ approaches zero, the value of two-compartment $C_p$ simplifies to just $Be^{-\beta t}$, just like our one-compartment model. The slope decreases to $-\beta$, and we can extrapolate the line back to our familiar yet inaccurate $C_p^0$.

Drugs are not limited to two compartments. Models can be much more complicated. $C_p$-time plots can have multiple regions dominated by different elimination and distribution processes. Late in the $\ln C_p$-time plot of almost any drug, however, a linear region emerges and continues throughout the rest of the drug's elimination. The slope of this linear region is labeled $-k_{el}$ and is called the terminal elimination rate constant. It is from this terminal elimination rate constant that the pharmacokinetic parameters ($t_{1/2}$, $CL$, and $V_d$) are often based.

Treatment of a drug in this fashion is equivalent to forcing all drugs into a one-compartment model. Drugs are treated this way for the sake of simplicity. If a drug is reported with multiple elimination rate constants, and therefore multiple half-lives, depending on the time that has elapsed from the IV bolus, then confusion will result. Instead, drugs are reported with a single half-life, which corresponds to the slowest elimination process.