**Supplementary material**

Hahn-Lyons: The half-life of infusion fluids.

**Data analysis**

Studies referred to in the present review do not include patients with severe heart failure or impairment of kidney function. Those patients are always excluded for ethical reasons as volume kinetics requires a bolus infusion of fluid to be studied.

The turnover has occasionally been estimated from the urine excretion alone,35 time to the first void after an infusion23 24 36 or from the visually estimated reduction of the fluid-induced haemodilution.37 However, most of the elimination T1/2 data presented here was derived from the renal clearance, that is, the urinary excretion divided by the area under the plasma dilution-time curve.12 A few studies calculate the fractional elimination rate from the urinary excretion and the plasma volume expansion over time, which is an equivalent procedure.8 9 16

T1/2 can also be obtained mathematically directly from the haemodilution curve.3-7 This model-predicted T1/2 usually correlates well with the urine-based T1/22 3 but in some studies all eliminated fluid cannot be accounted for as urinary excretion (“third-space loss”).12 Moreover, there is a delay of 15-20 min before model-predicted elimination appears as urine (Fig. 2 C).

Several datasets from the author’s research group were re-calculated to present as much material as consistently as possible, which means that results may differ slightly from the original publication.3-7 18 22 32 However, exceptions from the use of urine-based calculations are few.4 19 46

**Assumptions made in the simulations**

Figs. 3-5 were created using a plasma volume of 3 L, an interstitial fluid space of 8 L and baseline fluid losses of 0.5 ml min-1 (700 ml day-1). These are typical starting values for adult males weighing 80 kg. The reason why the baseline volume of the interstitial fluid space is set to a smaller volume than the 16% reported in physiological textbooks is that the entire space cannot be expanded by iso-osmotic fluid (such as intracranial tissues, bone tissue and organs with a tight fibrous capsule).

**Renal clearance**

The most common way to calculate the *elimination half-life* (T1/2) for a crystalloid fluid is by using the renal clearance (*Cl*R). In the *clearance model* of volume kinetics, this is obtained by dividing the excreted urine volume at the end of an experiment with the area under the curve (AUC) for the plasma dilution.

The plasma volume at baseline is given by the symbol *V*c and the expanded volume *v*c, which means that that volume expansion is given by (*v*c – *V*c) and the plasma dilution by (*v*c – *V*c)/ *V*c.

*Cl*R can then be written as:



When using *micro-constants*, the corresponding expression is:



where *V*c is the volume of the central body fluid space at baseline, which infused fluid expands to *v*c.

The elimination T1/2 is then obtained as ln 2 \* *V*c / *Cl*R (clearance model) and ln 2 / k10 (micro-constant model).

The *fractional turnover rate* is given by *V*c / *Cl*R and 1/ k10, but is not used in this Review.

**Haemoglobin-derived plasma dilution**

The plasma dilution [(*v*c–*V*c)/*V*c] and the expansion of the central fluid space (vc–Vc) are obtained via a conversion of serial measurements of the blood haemoglobin (Hb) concentration into the dilution of *V*c, which is written in the following way to become linear with added amounts of fluid:



where Hct is the haematocrit. Symbols without an index represent baseline values and *(t)* those obtained at a later point in time.

A correction for loss of dilution marker should be performed if the sum of blood sampling and surgical blood loss are considered to be important. For details, see *Anesthesiology* 2005; **103**:460-69. Such a correction was performed in all T1/2 reported in the present Review provided that calculations were based on volume kinetics.

**Calculation of Vc and Cld**

With the *clearance model*, the baseline size of the central body fluid space expanded by infused fluid (*V*c) must be calculated to obtain T1/2.Moreover, a curve-fitting procedure is needed to estimate the distribution clearance, *Cl*d.

These parameters are estimated by applying a least-squares regression routine and fitting the solutions to the differential equations describing the kinetic model to the repeatedly measured Hb-derived plasma dilution over time (Matlab 4.2 or 2012, Math Works Inc., Natick, MA), if possible by using *Cl*R as *Cl* (which can only be done if urinary excretion is measured).

The differential equations describing the clearance model are the following:





where *R*o is the infusion rate, *Clo* is the baseline losses of fluid, and *V*t the size of the peripheral fluid space. Hence, *Cl*d is a proportionality factor for the rate of distribution between *v*c and *v*t which is else driven by the difference in dilution between them.

The *micro-constant model* does not require *V*c to be calculated to give T1/2. However, *V*c has to be estimated to obtain a figure for the distribution clearance. The differential equations are:



Here, the *Cl*d is obtained as the product *V*c and *k*12. Similarly, the *renal clearance* is the product of *V*c and *k*10.

More detailed explanations about how to apply the clearance model is given in:

Hahn RG. *Volume kinetics for infusion fluids.* Anesthesiology 2010; 113: 470-481.