Reproducing classical research on the computer is easy

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Reproducing classical studies and obtaining similar results is usually a difficult and time-consuming task. If, however, the study was done solely by a computer, it may not be quite so tough as ordinary laboratory investigations. We recently undertook to reproduce a classical study by Price [1,2] and found that it is indeed an easy matter to do so.

Methods

Using equations and basic data given in the original articles, we set up a small computer program on a regular personal computer. The original articles acknowledge the computer center of the university but do not mention how the actual calculation was made. We may presume from the computer technology at that time that it was done on a large computer in the FORTRAN language. It was quite likely that the figures presented were drawn by hand using numerical data thus obtained. The current program was written in the BASIC language (Quick Basic for MS-DOS: English version 4.5, Microsoft) for calculating and numerically solving the differential equations (solved as simple difference equations at 1-msec intervals). The numerical data were stored in a file, then transferred to graphic software (Microsoft Excel97). The graph thus produced was further transferred to drawing software (Microsoft Paint in the Windows95) to add the final touches. The original

data were slightly modified to make them easier to use (Table 1).

The names of the compartments do not agree each other in the graph and the table in the original article. We assumed that Viscera in the graph indicates the sum of the CNS, myocardium, portal, and renal compartments of the table, and that Lean indicates the muscle.

Results

The use of values from the original article yielded a graph quite similar to that appearing in the original article (Fig. 1). The time involved in this reproduction was slightly more than a day.

Discussion and conclusions

The reason why we attempted this is that we wanted to reproduce the graph originally published. Contrary to current practice, in earlier times the copyright was not transferred to the publisher but was kept by the authors themselves. We therefore attempted to reach the author to obtain permission, and failed. Rather than struggling to reach the author, we decided to draw our own version of similar graphs.

In the original article, the model and the parameters were given in sufficient detail that there were no difficulties in reconstructing it. Furthermore, the model used is relatively simple and common in the fields of anesthesia and of pharmacokinetics. Whether this applies to all types of studies is questionable. There are many computer models that are quite elaborate and/or esoteric and cannot be described in full detail. In such cases, one may have to struggle to reorganize information before attempting to reconstruct them.

Table 1. Basic model and parameters

Area	Blood flow (ml·min^{-1})[a]	Weight (kg)	Tissue/blood solubility ratio	Volume of distribution (l)[b]
Blood	5400	1.5	1.0	1.50
CNS	800	1.3	1.4	1.82
Myocardium	250	0.3	1.2	0.36
Portal	1700	2.5	1.9	4.75
Renal	1000	0.3	2.0	0.60
Muscle	1400	55	1.5	82.5
Fat	250	10	11.0	110.0

[a] Blood flow of blood compartment of 5400 ml equals cardiac output, whereas 1.5 kg equals the volume of blood with which the drug is mixed before it begins to be delivered to various tissues
[b] The original paper does not list the last column, Volume of Distribution. This is obtained as weight multiplied by tissue/blood solubility ratio, assuming the density to be close to unity
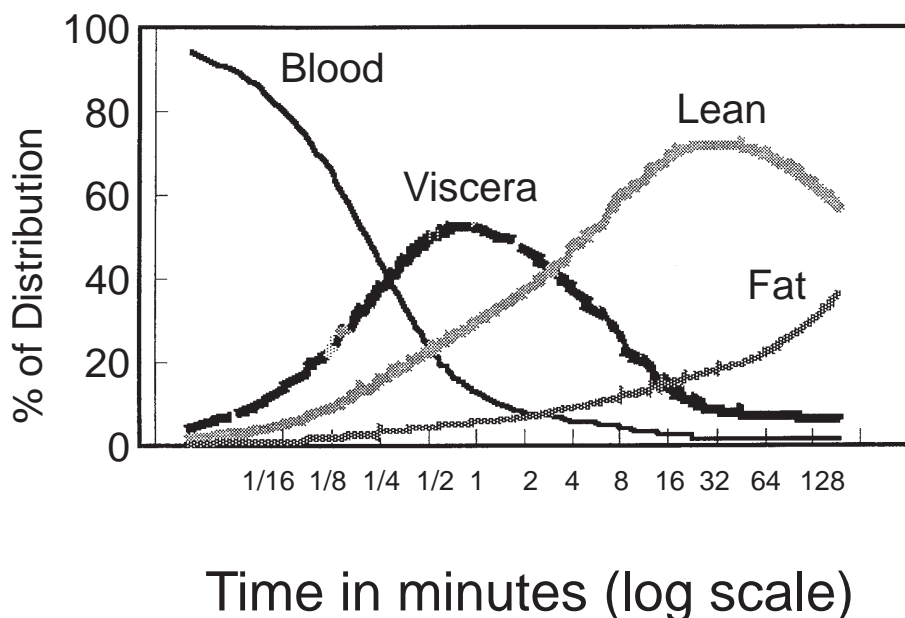

Fig. 1. Reproduced graph showing thiopental distribution. Abscissa: time in minutes after administration in logarithmic scale. Ordinate: percent of the total amount of thiopental administered accumulating in various compartments of the body. The original article stresses that patients wake up from thiopental not because it shifts from brain to fat, but because it shifts to muscle (Lean in the graph)

We may tentatively conclude, therefore, that a computer study is relatively easy to reproduce when the original model is simple and is described in full detail. As a corollary, we should try to describe the model in full detail in reporting this type of study.

References

1. Price HL (1960) A dynamic concept of the distribution of thiopental in the human body. Anesthesiology 21:40–45
2. Price HL, Kovnat PJ, Safer JN, Conner EH, Price ML (1960) Uptake of thiopental by body tissue and its relation to duration of narcosis. Clin Pharmacol Ther 1:16–22