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This Week's Citation Classic

Weil C S. Tables for convenient calculation of median-effective dose (LD50 or ED50)
and instructions in their use. *Biometrics* **8**:249-63, 1952.
[Mellon Institute, Pittsburgh, PA]

The acute toxicity of chemicals is most accurately expressed as the median-effective dose, LD50, e.g., the dose to kill half the animals. The tables permit easy calculations of this median and its confidence interval, using a minimum number of animals. [The *SCI*® indicates that this paper has been cited over 410 times since 1961.]

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"Prior to the appearance of these tables, the calculation of the median-effective dose, ED50, LD50, LC50, LT50, etc., required approximately 30 to 60 minutes of time, using the only method then available, mechanical calculators, graphing, tables, curve fitting, and goodness of fit calculations. The probit procedure involved attempting to straighten the sigmoid dose-response mortality data and, therefore, calculate its midpoint. However, to prove' the goodness of fit many animals and dosage levels had to be used.

"When the method of moving averages was published, I found it gave almost identical results as the much more complicated probit method, with much less computational time and with no assumption about curve fitting.

However, I found that when the same mortality ratios resulted, e.g., 0 of 5, 1 of 5, 3 of 5, and 5 of 5 (0,1,3,5) the calculation could be made more simple by use of constants, that I then calculated and put in table form. With the use of my tables and a table of logarithms one could determine the LD50 and its 95% confidence limits in 3 to 5 minutes. Now, with electronic calculators or computers, the time is seconds to a minute.

"At the start, I suggested the use of four dosage levels in a geometric series (a constant number of animals per level). We found that, the majority of the time, with a factor of 2 between dosage levels, we had mortality ratios below and above the median with only 2 to 3 dosage levels; e.g., 1 of 5 and 3 of 5 or 0 of 6, 3 of 6, and 5 of 6; (1,3) or (0,3,5). Not only were these sufficient for calculation but they saved animals. The published tables are for 4 levels; if you write me I will send you others to use with 2 or 3 dosage levels.

"We, and many other toxicologists, have used these tables for many years. They have proved valuable in interlaboratory and intralaboratory tests of consistency. We have found, with LD50 assays using only a total of 10 to 15 rats each, that acute LD50s were consistent in our laboratory over a 12-year period, testing the same 26 chemicals each year. We have also run hundreds of joint-toxic estimates using this method, which would have been impractical, more time and energy consuming, and more costly because of the larger number of animals necessary using the probit methods. And, as beforementioned, this non-parametric method should be preferred in these toxicity assays to the parametric, curvefitting methods."