When Nature Prefers a Curve

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This work was accomplished with the superb technical assistance of Jean L Brodie while E. Jack Benner and I were fellows in infectious diseases with W.M.M. Kirby at the University of Washington in 1964.

Work began after the simple (and unconceived) idea of my mentor that we needed a better bioassay (comparison of a test sample against a standard preparation) system for antibiotics. The assay in use at that time provided highly variable results and posed a variety of methodologic problems that are detailed in the paper but are too numerous to be fully recounted here.

One major problem derived from the well-recognized curvilinear relationship between the concentration of antibiotic standards and the sizes of the zones of inhibition they produced. Concentrations were determined by a procedure that exploited the natural curvilinear relationship between zone sizes around the filled wells and antibiotic concentrations. Small volumes of serum could then be tested directly and accurately over a wide range of clinically relevant concentrations without dilutions of the samples. [The SCI® indicates that this paper has been cited in more than 840 publications, making it the most-cited paper published in this journal.]

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A specially designed agar punch was used to create multiple small agar wells in specified patterns on a large glass plate containing agar seeded with susceptible test organisms. Concentrations were determined by a procedure that exploited the natural curvilinear relationship between zone sizes around the filled wells and antibiotic concentrations. Small volumes of serum could then be tested directly and accurately over a wide range of clinically relevant concentrations without dilutions of the samples. [The SCI® indicates that this paper has been cited in more than 840 publications, making it the most-cited paper published in this journal.]

Received February 18, 1992

REFERENCES