

Bauer A W, Kirby W M M, Sherris J C & Turck M. Antibiotic susceptibility testing by a standardized single disk method. *Amer. J. Clin. Pathol.* 45:493-6, 1966.
[Depts. Microbiology and Medicine, Univ. Washington, Sch. Med., Seattle, WA]

This paper described technical details of a standardized agar diffusion test and gave zone sizes of growth inhibition for over 20 antimicrobial agents that were correlated with minimum inhibitory concentrations and with clinically applicable breakpoints for susceptibility and resistance. It brought together contributions from the separate laboratories of these Seattle investigators for use in the clinical microbiology laboratory. [The SC[®] indicates that this paper has been cited in over 2,220 publications since 1966.]

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As the number of antibiotics increased in the early 1950s, there was an obvious need for an *in vitro* susceptibility test simpler than the broth dilution method. A number of antibiotic disk-diffusion procedures came into use, most of which were unstandardized and employed a variety of media, inocula, disk contents, and end-point criteria. One approach was to determine the presence or absence of growth of the test organism on an agar plate around two or three small paper disks containing different contents of antibiotics. But the characteristics of diffusion through agar did not permit adequate agreement between this procedure and the results of dilution methods. As a result the agar-diffusion method fell into disrepute among critical observers despite its widespread use.

Our contribution was utilization in the clinical laboratory, beginning in 1952, of the principle that there is actually a direct inverse correlation between the size of the

zone of inhibition around a paper disk and the log of the minimal inhibitory concentration (MIC) as determined by a dilution method. This was also recognized by a number of other workers, including Bondi¹ and Anderson² in the US and Ericsson³ in Sweden. Alfred Bauer, who joined me a few years later as a research fellow and subsequently worked with Sherris, was especially industrious in documenting the advantages of the single-disk method and its relationship to dilution test results. Refinements concerning a standardized inoculum size and zone size/MIC relationships for the different antibiotics as well as extending the method to additional gram-negative pathogens were added by Sherris and Turck. There were many requests for information, and the paper cited here was finally published in 1966 to bring together the contributions of the Seattle investigators.

This quite complete description of the single-disk method gradually gained wider acceptance. Eventually, after a long series of meetings and hearings, the Food and Drug Administration (FDA) in 1972 published recommendations in the *Federal Register* that were in essence the same as those described in our widely quoted paper. Ericsson and Sherris also coordinated the efforts of an international study group that published a monograph in 1971 that included recommendations that were similar in principle to those of the FDA.⁴

Thus, our paper has been widely cited because it was a definitive and detailed description, incorporating earlier contributions by us and others, of a simple, efficient, and practical way of measuring clinically applicable susceptibility of bacteria to a number of antimicrobial agents simultaneously. The increasing use of the technique over the last 20 years has provided reliable and reproducible data for clinical and epidemiological use.

1. Bondi A, Spaulding E H, Smith D E & Dietz C C. A routine method for the rapid determination of susceptibility to penicillin and other antibiotics. *Amer. J. Med. Sci.* 213:221-5, 1947.
2. Anderson K N, Kennedy R P, Florde J J, Shulman J A & Petersdorf R G. Effectiveness of ampicillin against Gram negative bacteria. *J. Amer. Med. Assn.* 187:555-61, 1964.
3. Ericsson H & Svartz-Malmberg G. Determination of bacterial sensitivity *in vitro* and its clinical evaluation. *Antibiot. Chemothor.* 6:41-74, 1959.
4. Ericsson H M & Sherris J C. Antibiotic sensitivity testing. Report of an international collaborative study. (Whole issue.) *Acta Pathol. Microbiol. Scand. Sect. B (Suppl. 217)*. 1971. 90 p.