Multidimensional Analysis for Interpreting Antibiotic Susceptibility Data

We are rather surprised at the lack of reaction to the article by Hunter et al. (4) published in *Antimicrobial Agents and Chemotherapy* in 1990 which concerns the application of multivariate analysis to antimicrobial susceptibility data by the use of computer software. This concept was first proposed in 1985 (3, 8) and was developed over subsequent years (2, 9, 11).

As pointed out by Hunter et al. (4), the various statistical techniques and parameters used to define bacterial susceptibility to antibiotics in vitro, i.e., the MIC for 50 and 90% of strains tested (MIC_{50} and MIC_{90}), geometric mean, and linear regression, lead to a considerable loss of information. Indeed, in no way do they take into account the heterogeneity of the population under study; all the individuals (i.e., strains) in a given bacterial population are considered identical, whereas a typical species can comprise several groups with regard to antibiotic susceptibility, for example, a sensitive group plus several groups bearing different resistance determinants. Moreover, the norms (breakpoints) proposed by the various national committees are in fact empirical—"conjectures" in mathematical terms.

In contrast, multidimensional analyses are more descriptive and, as such, more relevant to biological systems. In addition, they have implications for decision making and forecasting (5). The new data, derived from multidimensional analyses, can be considered statistical objects that replace the raw data. Thus, classical statistical methods (Student's *t* test, for example) can be applied to these new data in such a way as to obtain numerical results (6, 7). Questions such as validation and the detection of aberrant elements are raised here, just as in classical statistical analysis.

The plus in the proposed analysis is its multidimensional nature. Clusters appearing in two dimensions are not necessarily distinct in each dimension taken separately (10). The individual is never lost; the recognition of patterns is based on differences between the individuals, and the patterns are then interpreted on the basis of the original variables (1, 5).

As pointed out by Hunter et al. (4), these methods are of value for highlighting the structure of a population, the phylogenetic relationships between its individuals, and the links between the variables used. Furthermore, they stress the relationship between the individuals and the variables, in this case the bacterial strains and the activity of the antibiotics.

In this way, using analysis of principal components and hierarchical ascendent classification, a bacterial species was separated into homogeneous classes corresponding to the various susceptibility and resistance phenotypes for β-lactams. Three practical applications have given concrete results (9, 11): (i) a new model for more relevant interpretation of antimicrobial susceptibility test results which is based on these bacteriological classes (validated by pharmacological data and results obtained in vivo) and which can be used by any microbiologist with access to a microcomputer, (ii) numerical estimation of breakpoints with a known risk, and (iii) calibration of a technique relative to a reference method (the same classes have to be obtained).

Potential applications include the detection of strains with new phenotypes and the evaluation of the activity of new compounds in vitro (2, 9, 11).

REFERENCES

1. **Benzecri, J. P.** 1992. Correspondence analysis handbook. Marcel Dekker, Inc., New York.
2. **Chardon, H., T. Fosse, R. Labia, M. H. Nicolas, C. Poyart-Salmeron, M. Veron, J. Sirot, D. Sirot, et le groupe CERIB.** 1992. Multifactorial analysis of the phenotypes for beta-lactams of 1044 *Escherichia coli* strains, abstr. 328-P20, p. 243. Abstr. 12th Annu. Interdisciplin. Meet. Anti-Infect. Chemother. Paris 1992.
3. **Hornstein, M. J., A. M. Jupeau, M. R. Scavizzi, A. M. Philippon, and P. A. D. Grimont.** 1985. In vitro susceptibilities of 126 clinical isolates of *Yersinia enterocolitica* to 21 β-lactam antibiotics. Antimicrob. Agents Chemother. **27**:806–811.
4. **Hunter, P. R., R. C. George, and J. W. Griffiths.** 1990. Mathematical modeling of antimicrobial susceptibility data of *Staphylococcus haemolyticus* for 11 antimicrobial agents, including three experimental glycopeptides and an experimental lipoglycopeptide. Antimicrob. Agents Chemother. **34**:1769–1772.
5. **Jambu, M.** 1991. Exploratory and multivariate data analysis. Academic Press, Ltd., London.
6. **Lebart, L., A. Morineau, and J. P. Fenelon.** 1979. Traitement des données statistiques. Dunod, Paris.
7. **Lebart, L., A. Morineau, and K. Warwick.** 1984. Multivariate descriptive statistical analysis. John Wiley & Sons, Inc., New York.
8. **Notten, F. J. W., F. H. M. Nieman, and F. H. M. Mickx.** 1985. Antibiotypes of *Bacteroides gingivalis* assessed by antimicrobial disks and multivariate analysis. J. Clin. Microbiol. **22**:1020–1024.
9. **Scavizzi, M., and F. Bronner.** 1987. Un modèle statistique d'interprétation de l'antibiogramme. C.R. Acad. Sci. Paris **304**(III):325–329.
10. **Scavizzi, M. R.** 1972. Existence de deux caractères transférables de résistance aux tétracyclines. Ann. Inst. Pasteur (Paris) **122**:3–17.
11. **Scavizzi, M. R., and F. D. Bronner.** 1988. A statistical model for the interpretation of antibiotic susceptibilty tests. Int. J. Exp. Clin. Chemother. **1(2)**:23–42.

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