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Broad- and narrow-spectrum antibiotics: an unhelpful categorization

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The expression 'broad-spectrum antibiotic' was used in the mid-1950s, when the bacterial spectrum of chloramphenicol and the first tetracyclines could be strikingly opposed to the narrow spectrum of activities of penicillin G, and streptomycin. In the 1960s, aminopenicillins, then ureidopenicillins, became the broad-spectrum penicillins in comparison with penicillin G. Until then, the quality of being broad spectrum or narrow spectrum was given to an antibiotic only when referring to a comparator. Later, the reference to a comparator was omitted, and broad and narrow lost their relativities and became independent characteristics of a compound, used with different meaning and often improperly.

Never, to my knowledge, was any effort made to define those words. On what segment(s) of the range of bacterial species (Gram-positive cocci and bacilli, Enterobacteriaceae, non-fermentative Gram-negative rods, anaerobes, intracellular pathogens) is the classification as broad- or narrow-spectrum antibiotics to be based? On the narrow side, some compounds are narrower than others (e.g. macrolides versus metronidazole), while on the broad side, many antibiotics are narrower than the very broad ones (e.g. tetracyclines are broader than tazocillin, which is broader than cephalosporins, etc.). I will not attempt now to propose any definition of what is narrow and what is broad. I would like only to draw attention to the overuse of such ambiguous labels for different and even contradictory purposes. In my experience, this consideration justifies ceasing to use them.

Broad spectrum as an expression of greater therapeutic security has mainly been used by the pharmaceutical industry. Most antibiotics are prescribed empirically on a presumptive diagnosis. This implies that several bacterial species are possible causes of the disease. It is correct that a broad-spectrum antibiotic may offer a better chance of covering the causative microorganisms. In the same way, a broad-spectrum agent is indicated in a large number of clinical situations.

Recently, the trend in the pharmaceutical industry has been to replace the concept of broad-spectrum agents by organ- or system-targeted agents. The empirical choice of an antibiotic is determined by the organ or system in which the infection is located. This approach integrates the pharmacokinetic properties and the activity against the more frequent bacteria encountered in the particular location of the infection. Antibiotics suitable for urinary tract infections, respiratory infections, digestive tract infections, etc., have been developed. Progress can be expected from new compounds, and improved clinical approaches for the therapeutic decisions.

The idea of broad-spectrum agents as broad selectors for microbial resistance, although it has a convincing mechanistic simplicity, has never been documented. Bacteria resistant to an antibiotic (naturally or by an acquired mechanism) are normally selected by the agent or by another agent with a similar spectrum or a similar mechanism of resistance. Recent studies indicate that the emergence of resistance genes, their prevalence in one or more species and their spread (clonally, or as genes) are distinct phenomena. These are complex problems in which many factors are involved, such as: the size and the composition of the ecological niche considered; the number of species and the size of their populations; the quantity of the selecting agents (antibiotics and other antimicrobials); the duration of the selection pressure; the pre-existence of low level resistant microorganisms able to survive the concentrations of antibiotics present in the niche; the time of observation; and so on. The ability to select resistant organisms is not related to the breadth of the bacterial spectrum of an antibiotic. It is related to the mechanisms of resistance to that particular antibiotic and to several other factors already mentioned.

The term narrow-spectrum agent is sometimes considered to be a synonym of targeted-microorganism therapy and an indicator of a physician's competence and concern for ecology. As focused a diagnosis of an infection as possible must direct the therapeutic decision to the most appropriate compound(s). The appropriate treatment(s) of an infection are those that have been proven to cure patients with similar infections. The appropriate antibiotic treatment is never defined by its antibacterial spectrum. Who cares about the spectrum when chloramphenicol or ceftriaxone is prescribed to cure enteric fever?

I should like finally to call attention to many guidelines where, without adequate explanation or for

unacceptable reasons, it is suggested that narrow-spectrum antibiotics should be used. It may be asserted that they are less likely to select resistant bacteria. This statement is wrong. There are more naturally resistant species to narrow-spectrum than to broad-spectrum antibiotics and the quickest selection occurs among naturally resistant species. It is true that they are more microorganism-targeted but are they the appropriate treatment? It can be said that they save money, as more so-called broad-spectrum agents have been developed in recent years, and older compounds are cheapest. Moreover, the label of broad or narrow is given arbitrarily; cephalosporins are in fact narrow-spectrum antibiotics (especially when compared with other β-lactams) with a limited activity against staphylococci (no activity against MRSA) or enterococci, no activity against more anaerobes (apart from the cephamycins), no activity against intracellular pathogens, variable activity against non-fermentative organisms.

Many other examples could readily be found to illustrate the misuse of the two adjectives, broad and narrow, applied to the spectrum of antibiotics. It would be advisable to give up such categorization. Perhaps we should base our mental concept of an antibiotic first on its clinical indications and targeted organs and secondly, rather than on its spectrum, on the microorganisms *not* included in its spectrum, and on those which have recently acquired a mechanism of resistance to it.

Jacques Acar
Fondation Hôpital Saint-Joseph,
Laboratoire de Microbiologie Médicale,
185 rue Raymond, Losserand,
75674 Paris Cedex 14, France