The Individual Impact of Antibiotic Usage

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Nobody discuss about the large benefits for health derived from the use of antibiotics, even though these benefits have never been properly quantified. Nevertheless, only knowing the benefits, the risks associated with a loss of its potency can be calculated. Conversely, everybody discuss about the risks of antibiotic use. In general, the predominant fears about the use of antibiotics are expressed in the following ways: 1) they can select more and more antibiotic resistant organisms, and therefore a point will arrive in which infections could not be cured any more; and 2) there are important toxic effects eventually associated to antibiotic use.

Any intervention trying to regulate the consumption of antibiotics to its appropriate level should be mainly based on changes in the behavior of antibiotic consumers: prescribers and patients. Of course public health authorities may in critical situations take stringent control measures, obliging to follow certain criteria, but in most modern societies this intervention will be only acceptable in quite exceptional cases. If the targets for changes in behavior are both prescribers and patients, they should be fully convinced of the value of taking *personal* attitudes towards antibiotic consumption. And this conviction is necessarily rooted in egoistic or altruistic feelings, or in a variable interaction between both attitudes.

The individual is expected to adopt personal attitudes towards him and his/her family about the use of antibiotics based on the interest in shaping the best own personal future, and much less so because of the collective risk for other people. We, scientists, should provide data to back the desirable change in attitudes, as worrying without data is the most characteristic pre-scientific manipulation of mankind. For such a purpose of measuring individual drug-induced effects, we are obliged to objectively evaluate the balance of risks and benefits, for each type of individual in the population associated to the consumption of antimicrobial agents during life. This knowledge is absolutely needed to create a scientifically-based culture of use of antimicrobials, and educate and convince the patients, the prescribers, the companies and the administration about eventual interventions. At long term, the building-up of such a culture should have a positive impact on the individual consumer's psychology, and certainly will improve public health as a whole.

In the case of the antibiotic prescriber (most frequently a general practitioner working in community medicine), the attitude towards an external recommendation of using antibiotics in a much more selective way may be a complex one. On one hand, the

prescriber may accept that such a practice will be for the benefit of the patient's in general (public health), for instance, by reducing the resistance rates. But he may consider that restricting the use of antimicrobials to the very clear cases in which prescription is fully justified by objectively documented reasons might also increase a number of risks for his individual patient and for himself. A number of patients non-fulfilling objective criteria for therapy may still have benefits from antibiotics. Severe, even deadly infections in preliminary stage (as bacterial meningitis or sepsis) could be aborted; sub-clinical infections (as urinary tract infections in young girls) may be cured; self-limited infections (as upper respiratory tract infections or otitis media) may be shortened in time or relieved in symptomatology. Moreover, if something wrong unexpectedly happens and the patient was non-treated, the prescriber could be confronted with malpractice lawsuits.

We know that individual tobacco smoking is the main component increasing the individual risk for coronary artery disease or lung cancer, and we also accept the existence of a minor component of social behavior in passive smokers. Conversely, in the case of the risk associated with antibiotic individual hyper-consumption, it might be suggested that the main component could be the behavior of others. That seems to be particularly clear in the case of the emergence and acquisition of antibiotic resistant organisms. The emergence and fixation of resistant variants (mutants) during a single short course of antibiotic therapy is probably low, either for the infecting or the commensal organisms. The conventional wisdom suggests that resistant organisms are mainly acquired "from others" and therefore the individual behavior in antibiotic consumption may play a minor role. That is not entirely true. The individual uptake of antibiotics increases the possibility of acquisition of resistant organisms from exogenous sources. On the other hand, if a single course of therapy has low influence in the emergence of resistant variants in the endogenous flora, repeated courses of therapy may efficiently select such variants. Finally, it is essential to understand the real risk for the individuals is *not* the emergence or acquisition of antibiotic resistant bacteria, but the effects that may result at short or long term of hosting such type of organisms. The individual responsibility in shaping individual risks can be easily understood in those adverse effects resulting from the non-antibiotic action of the drug (as acute or chronic toxicity, effects derived from drug-drug interactions, or hypersensibility). The same is true for the antibiotic effects resulting in an alteration of the physiological role of the normal microbiota associate to the individual.

A typical problem in practical chemotherapy is the problem of minimums. Should an antibiotic being prescribed in a situation in which a minimal benefit is expected from such an use, but at the expenses of only a minimal risk? Such small benefits are only detectable using very large series of individuals, and therefore a parameter, the NNTB (number needed to treat for a benefit) is used. For instance, it has been claimed that antibiotics should not be used for acute otitis media, as NNTB is only 15. On the contrary, the use in acute purulent rhinitis has an NNBT of 6-8, and NNBT of 5 was found for acute bronchitis. For streptococcal tonsillitis in developed countries, reduction of 16 h in symptoms (pain, that can be determined in infants by the "last day of crying") occurs for an NNTB of 2-7. Nevertheless, many experts do not recommend the use of antibiotics in any of these circumstances, because modest benefits should be weighted against risks. A strategy of "wait and see" (before prescribing) has been alternatively applied by clinicians, but the group of patients with delayed use of antibiotics in upper respiratory infection (including sore throat) might have more pain and malaise than

those receiving immediate therapy (REF: Spurling GK). The problem is that we dot have an equivalent clear NNTR (number needed to treat for an adverse event), mainly because the adverse events are more for the community (as antibiotic resistance) than for the individual patient. Moreover –how to compare the *importance for the individual* of these risks and benefits? A mild episode of nausea can be tolerated at the expenses of gaining a certain benefit in reduction of night cough in a patient with acute bronchitis? Certainly both the cultural and educational environment might modify the answer to this question.

There is a problem when presumed minimal benefits might become significant ones.
When a number of interventions that are expected to offer only marginal benefits unexpectedly results in a major benefit, we are confronted with this problem. This typically occurs when this major benefit is rarely associated to the intervention usually causing a small effect. Most prophylactic use of antibiotics is useless for the individual patients; nevertheless, if a life-threatening infection is effectively prevented, even in a minimal proportion of these patients, or if such use might serve to reduce the rate of cross-transmission between individuals, the prophylactic indication should be at least considered. Certainly the justification for the use of antibiotic therapy in acute tonsillitis is controversial in developed western societies, but certainly protects (80% protection) from acute rheumatic fever in low and middle income countries, and probably cuts the chain of transmission of *Streptococcus pyogenes*. Occasionally, that might also occur in developed nations. It seems clear that winter lower respiratory infections of presumed viral origin, should not be treated with antibiotics. Nevertheless, some studies have suggested that when community antibiotic prescribing is reduced beyond a certain limit under the aims of progressing in "rationality", mortality associated with community-acquired pneumonia might increase. We might therefore envisage a number of "antibiotic abuses" (use of antibiotics not justified by its small benefit) that might have had a positive effect on human health. Similarly, the broad ("indiscriminate") use of antibiotics in upper-respiratory tract infections might occasionally prevent severe infections, as bacterial meningitis. Very few data are available to document this possibility. If we compare the bacterial meningitis mortality rates in five South-European countries with high antibiotic consumption in the community, with the same data of five North-European countries with low antibiotic consumption, a trend for higher mortality in the North is suggested. Certainly other factors might have modulated this result, that is presented here only as an indication of the need of progressing in the analysis of this type of correlations.