Ethical Issues in Family Practice: Are we prudent when using antimicrobials?

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Introduction

The term 'emerging infectious diseases' generally is used to classify a variety of diseases: [1]

(1) Completely new diseases,
(2) Old diseases occurring in new places and in new populations;
(3) Old diseases with new presentations;
(4) Diseases newly resistant to available drug therapies.

In this article, we focus on the latter, diseases newly resistant to available drug therapy in other words, diseases, the treatment of which is compromised because of drug resistance and argue for the prudential use of antimicrobials.

Discussion

There is a force existing in nature as a survival trait or property. It is so mutable that it can be distributed amongst the foundational ecological building blocks of nature in the genes of microorganisms. Without microorganisms, life as we know it on this planet would not exist. Now, imagine in our contemporary world that all the trillions and trillions of microorganisms living in and on all organic and inorganic life (*e.g.* skin, bark, organs, tissue, leaves, thermal vents, fins, feathers, earth, air and water) were to acquire this property and in an instant become resistant to all antimicrobials. In such a world, no effective medicines would be available for people, animals or plants needing relief from the scourge of infectious diseases and injury. Because of population pressures and continued environmental degradation, we would experience a rise in new, old and emerging infectious diseases. Medicinal drugs would no longer be effective. Pesticides would no longer be functional. Water supplies would be contaminated because chemical purification would no longer be successful. Factors such as these would feed into other life systems in a never-ending circle of misery. We would exist in a world of disease. But this scenario is hypothetical (or is it?). The trait or property of drug resistance *is* the force. Drug-resistant microorganisms *do exist* in nature, the survival trait of drug resistance *is mutable,* things in nature *are united* ecologically and we *continue* to devalue nature. Increasing global resistance to antimicrobial drug therapy is a reality; with increasing momentum, it will destroy the "…stability, integrity and beauty of the biotic community." [2]

Alexander Fleming, the one who discovered penicillin, recognised both the benefits and potential harms of antimicrobials right from the start. He was gravely concerned about their indiscriminate prescription by doctors and that people would be able to purchase them without a doctor's prescription. In 1947, he wrote: [3]

The greatest possibility of evil in self-medication is the use of too-small doses, so that instead of clearing up the infection, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred-out which can be passed on to other individuals and perhaps from there to others until they reach someone who gets a septicaemia or a pneumonia which penicillin cannot save. In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted.

His calls remained unheeded, for this was the beginning of the 'antibiotic age'. Technology would provide all the answers as humans 'fled from reality to an altogether

more soothing world of techno-pastoral dreams'.[4] In the 1940's the drug manufacturing industry was born and the idea of technology as a universal 'fix' was not only unalterably embedded but also mediasised in our consciousness. This resulted in, amongst other things, the creation of a public myth, the myth of technology as omnificent. This perpetuation created false assurances; whatever we might do to our environment, technical means would be found to remedy any ills. For example, the technological 'fix' of antimicrobial therapy told us that infectious disease was an unfortunate condition of the past now remedied by progressive application of our knowledge and wit. For example, the Nobel prize-winning author of a 1962 textbook, the *Natural History of Infectious Disease*, wrote: [5]

At times one feels that to write about infectious disease is almost to write about something that has passed into history.

It is not surprising that the evolution of a global reliance on technology seems to provide a soft cushion on which we rely, blissfully assuming that whatever happens, someone somewhere somehow will provide the technological means to propel us out of the quandary. However, as Vogel points out, technology allows us to affect the natural world in ways both outside and within ourselves in ways that are 'cumulative, irreversible and planetary in scale', so our absolute reliance on it appears to be ill grounded. [6]

Our technological knowledge admittedly is vast and often without thinking, we readily accept new technologies. For example, we seem to have no problems in accepting the overt manufacture of some microorganisms, for example those designed to 'eat' oil resulting from spills. But the equal acceptance of drug-resistant microorganisms is a different matter. The issue of bringing into nature *supra-natural* (those imposed upon nature; those not evolved naturally from nature) entities does not seem to turn on the issue of human contrivance or manufacture. Rather, it seems to turn on the immediate gratification associated with the potential of antimicrobial therapy to alleviate diseases and the potential of oil-eating microorganisms to clean up our environmental oil-spill catastrophes. Many concerns raised in genetic engineering appear to be negated in this perception, in particular the objection based upon the unknown dynamics of genetic modifications becoming transferred to other living entities, then into ecosystems and the biosphere. Relevant to this is a quotation from Capron: [7]

[The real threat] … posed by modern genetics is to the collectivity, by the changes that genetics can bring about in values and the alterations it generates in our perceptions and understandings of the world, not merely because of its ***discoveries*** *(as was true of Copernicus and Darwin) but also because of its* ***ability to modify*** *living things, including human beings.*

The 'ability to modify living things' appears to be downplayed in creating both oil-eating microbes and drug-resistant microorganisms. Only the immediate gratification of undoing either the results of oil spills and disease processes takes precedence.

Concerning oil-spills, the alleged purpose of oil-eating microorganisms is to have a mechanism readily available to avoid the catastrophes done to nature resulting from oil spills. It is well known that the use of one technology often may be applied for other purposes. Thus, oil-eating microbes, for example, could be used as a subtle weapon to threaten the oil production of some countries, a possible secondary and more sinister application. In the former case, we might view it as a good; after all, most people are dismayed when they see sea creatures, birds and other life forms killed or damaged because of oil contamination. As long as they fulfil a human need or desire, manufactured life forms may be both presented to and accepted by the public as a good. Yet if we dig deeper, we may identify that the public does not have the necessary information concerning any possible adverse effects. The point is that as long as our worldview is centred only on human interests we will not be able to see much less understand that our actions and inactions may directly affect nature. Concerning the latter, most people would be shocked to consider such a usage. But we must remember, as Rifkin identifies, "no application of technology has only benign consequences".[8]

Concerning oil-eating microorganisms, the issue about the application of such technology is two-fold: the possibility of genes moving into the broader environment and that their presence might serve to deflect attention from factors involved in oil spills in the first instance. It might be argued that such microorganisms would be constructed genetically without reproductive capacities. But even if that is the case, in their eventual organic breakdown we would have to know how any residual components might potentially interact with other organic life. In some perverse way, the intense research and development associated with the creation of oil-eating microorganisms may send a message that unsound vessels might be accepted just as long as any unfavourable consequences such as shipwreck and any resultant oil spills are controlled.

The same concerns may apply to drug resistance. Living things are already being modified as the drug-resistant trait is acquired. Simultaneously we now seek new antimicrobial therapies based on genetic engineering. If, for example, such therapies are designed not to reproduce or to die after destroying their targets, it still does not answer questions concerning the possibility of such properties escaping into the larger biotic community. Movement in this direction, it may be argued is a good, after all, living in a world full of disease is not a desirable one.

But the seemingly omnipresent reliance on technological fixes, as opposed to us evaluating ways in which we contributed to the problem of emerging infectious diseases and drug resistance in the first place, becomes cast in shadows.

In ordinary life, we tend to seek immediate gratification based on our interests and reliance on technological 'fixes' without considerations of broader consequences. All *supranatural* organisms, here presented as oil-eating microbes and drug-resistant microorganisms, share a certain commonality. Both can change nature. Concerning drug resistant microorganisms, the fabric of nature is changed because the trait of drug resistance is mutable and thus can be accepted readily by other microorganisms. As drug resistance becomes more established in nature, it will necessarily change our world. Our world will be changed because we may no longer have the means by which to change the course of infectious diseases in human, animal and plant life.

In historical perspective, antimicrobial usage represents a little over fifty-five years. The *global* problem of drug resistance is of a more recent vintage. In less than 2 generations, because of gross and imprudent antimicrobial usage, we now have documented reports of increasing numbers and types of drug-resistant microorganisms. [9] As Levy (*ibid*) puts it:

We are presently witnessing a massive, unprecedented evolutionary change in bacteria.

The lesson we learn from the problem of drug resistance is to consider that even seemingly benign applications of technology may carry global consequences. As for drug resistance, it exists in nature and about that, we can do nothing except try to contain the process. To contain the process above all requires a shift in our worldviews. This is because if we only consider human concerns then we miss the point that the additional stress we place on the environment (*e.g.* population pressures, environmental degradation) coupled with the penetration of drug-resistant microorganisms into the environment equals greater chances of drug resistance to spread. It is a circular process.

Can we gain insight on how to manage or control drug resistance? It should be clear that moral responsibility for both lies squarely in human social behaviour (for microorganisms have no moral responsibility). However, it would seem in this complex situation that our personal options in assigning or accepting moral responsibility are not so clear-cut. This is because of the various ways in which antimicrobials are viewed and used (and abused) worldwide. For example, do we tell a doctor in Bangladesh that he is immoral because he follows the cultural practice of his country-selling drugs in lieu of a consultation fee? In countries where antimicrobials are available on the 'open market' or sold without regulation, do we prohibit poor patients from buying one or two capsules of a pharmaceutical product for they can not afford a complete regimen? In other words, how do we convince often itinerant and illiterate tradespersons and hawkers to sell only complete regimens or regulate the selling of antimicrobials worldwide? By what means do we ensure that patients complete their drug regimens in spite of their (at least often claimed) adverse side effects?

Pressuring the animal-food industry to reduce drug use may be possible if there is common knowledge concerning drug resistance and if it is in some way organised. However, the interests of business and politics may impede action in this regard. For example, in 1986, the Fogarty International Center of the United States National Health Institute concluded a three-year project concerning the state of antimicrobial usage and worldwide resistance.[10] This report identified that in 1987, current antimicrobial production was sufficient to meet the needs of citizens globally if all antimicrobials were effective and if resistance was not a factor. However, the distribution and the extent of drug resistance were found grossly unequal. To make the situation more difficult, they identified that in areas where antimicrobials were most needed, drug therapies met with the greatest amount of antimicrobial drug resistance.

Importantly, their study led to other findings such as although enough antimicrobials were being produced, most would not be useful in the face of large-scale resistance (*ibid*: 22). The extent of resistance, they found, varied with the particular drug type used and from country - to - country. Moreover, whilst the frequency of resistance to particular drugs varied with microorganisms overall, distant countries still shared the same kinds of resistant strains (*ibid*: 26). Despite the commitment of the Fogarty Team, the report did not achieve its aim of public awareness. This is because, as Levy asserts: [9]

Political manoeuvrings and actions by pharmaceutical companies convinced U.S. officials and the National Institute of Health, which sponsored the project that the problem was being overstated and that support for the planned meeting and any future attempts should be withdrawn.

Levy (*ibid*) refers to this as a 'sad commentary' on the world in which we live and wonders 'if this *avant-garde* initiative had been allowed to continue whether the global crisis of antibiotic resistance would be as grave as that which we face today'. As in environmental degradation and illnesses linked to environmental factors, the problem of drug resistance must negotiate with the interests of big businesses and political will if it is to be controlled.

Do we rather focus on patients who, because of e.g. adverse side effects, do not complete drug regimens? Or do we develop a grading scale of condemnation assigning greater (or lesser) weight to those

who claim for autonomous or other reasons they cannot complete the course? Prudentially, on one level, educating doctors and other medical practitioners is indicated. Should the focus be on expanding coverage of emerging infectious diseases and drug resistance in medical schools, specifically the ways in which they will increasingly alter the practice of medicine (HIV/AIDS and increasing drug resistance to therapies is a good example)?

Doctors' lack of knowledge is also acknowledged as a great factor in the increase of drug resistance: inadequate diagnosis of diseases, incorrect drug selection for treatment or prophylaxis of infections, and incorrect prescription of doses, duration and routes of antimicrobials.[1,9,11] Other subjects worthy of study might include more quantitative ones, such as why doctors prescribe in response to patient pressures, why fears of litigation override obligations to prescribe correctly, why financial gain pre-empts proper patient care, and the influence of drug promotional pressures on practice. We should address how poor underlying health and high need influence drug choices. Issues inherent in the hazards of self-medication and problems innate in non-compliance should be investigated. Myths such as 'expensive is better' and 'more drugs are better' should be demystified, inappropriate beliefs discarded.

Governments should ensure that national drug and quarantine policies are appropriate and well communicated. Concerning quarantining humans who carry drug-resistant microorganisms, it would be an exercise in futility because of its prevalence in nature. Specific to drug resistance, essential drug lists must be established, updated and most of all communicated. Sales of drugs should be regulated, not left to the informal sector. Infection control strategies for disease control and drug resistance monitoring should become part of public debate. Hospitals should establish infection control committees to oversee their own drug resistance policies, and update and distribute such policies widely as more knowledge becomes available.

But doctors and other health care professionals are not the only people involved. From industrial misuse of antimicrobials as growth promoters to the creation of what are essentially monocultures of animals in which the potential for emerging infectious disease is enhanced, others too are implicated. The pharmaceutical industry is not immune to criticism, for example, in its focus on drug development for mainly developed countries and often-unethical practices of drug promotion. Moreover, the focus on genetically engineered microorganisms and drug therapies may have, we have suggested, untoward costs on the biotic community.

Prudential measures to contain global drug resistance requires at least changes in social, economic and political philosophies, enforcement of global infection controls, political will to sustain sustainable development, and limitations on human population and consumerist practices. These are examples of prudential measures that are aimed at the control of drug-resistant microorganisms. But the reason we arrived at the situation in the first place, is because we considered ourselves to be above all else. We developed antimicrobial therapy for human benefit without considering its broader ramifications. It might be argued that at the time when antimicrobial therapy began we were not aware of possible side effects. Granted some effects we did know, and some we did not anticipate. Yet, that is precisely where the problem lies for our tendency, then and now, is to place absolute faith in technology without consideration of factors other than us. Drug resistance shows that we cannot exclude nature from our lives and from our considerations. What we do or do not has implications beyond us. Since the trait of drug resistance is existent about that, we can do nothing. Our only hope for containment lies in the prudential use of antimicrobials. As the past World Health Organisation's Director-General G. H. Brundtland stated: [12]

Used wisely and widely, the drugs we have today can be used to prevent the infections of today and the antimicrobial-resistant catastrophes of tomorrow. However, if the world fails to mount a more serious effort to fight infectious diseases, antimicrobial resistance will increasingly threaten to send the world back to a pre-antibiotic age. Our grandparents lived during an era without effective antibiotics. We don't want the same situation for our grandchildren.

References

1. Centers for Disease Control and Prevention, USA. Update: Staphylococcus aureus with reduced susceptibility to vancomycin in United States, *Morbidity and Mortality Weekly*, 1997; 6: 813-815.
2. Leopold, A. (1949). *A Sand Country Almanac.* New York: Ballantine Books. 1966: 32.
3. Fleming, A. quoted In: Zimmer, C.. *Evolution-the Triumph of an Idea.* New York: Harper Collins. 2001: 214.
4. Ehrenfeld, D.. *The Arrogance of Humanism. New* York and Oxford: Oxford University Press. 1981: 127.
5. Burnet, F. M. *Natural History of Infectious Disease, 3rd Edition.* Cambridge: Cambridge University Press. 1962: 3.
6. Vogel , L. (ed.). Hans Jonas: Mortality and Morality: A Search for the Good After Auschwitz. Evanston, Illinois : Northwestern University Press. 1996: 6.
7. Capron, A. M. Which ills to bear? Revaluating the 'threat' of modern genetics. In: T. Shannon (ed.). Bioethics. New Jersey: Paulist Press. 1993: 488-516.
8. Rifkin, J. The Biotech Century: Harnessing the Gene and Remaking the World. New York: J. P. Tarcher Publishing. 1999: 7.
9. Levy, S. B.. *The Antibiotic Paradox: How Miracle Drugs are Destroying the Miracle, 2nd Edition.* Boston, Massachusetts: Persus Books. 2002: 114-304.
10. Levy, S. B., J. Burke, E. Wallace (eds.). Antibiotic use and antibiotic resistance worldwide. *Infectious* Disease Review, 8: (Supplement 3). 1987: 22-26.
11. American Society of Microbiology. Report of the ASM task force on antibiotic resistance. Washington, D.C.: The Society's Public and Scientific Affairs Board Press. 1994.
12. Brundtland, G. H. WHO/UATLD Global Project on Anti-Drug resistance Surveillance 1997-2000. WHO Report Number 2.(cited January 2001). Available at: http://www.who/cds/tb/2000.