Patients with moderate to severe infections are given less than maximum empirical antibiotic treatment in order to reduce the rise in resistance. This practice involves two ethical dilemmas: whether the danger to a present patient should be increased (even if by a small degree) to benefit future, unidentified patients; and whether this should be done without the consent of the patient, disregarding the patient’s autonomy. We argue that future patients have a right to come to no harm. Future patients being unidentified, practitioners of medicine have a duty to protect their rights and weigh them against the rights of the present patient. A decision on the collective (guidelines, decision support systems) is a convenient way to do that. Using a temporal discount rate to show that the life of present patients has pre-eminence, to some degree, over future patients does not solve the immediacy of the plight facing a present, identified patient with a very severe infection. We think there are good grounds to take into less account considerations of future resistance for such a patient, or in a formal analysis, to make the ratio of benefits to the present versus future patients dependent on the severity of disease of the present patient. None of these solve the problem of patients’ autonomy. We see no other way but to argue that the right of future patients to come to less harm outweighs the right of the present patient to share in decisions on antibiotic treatment.

Keywords: ethics, antibiotic therapy, rights of unidentified people, professional duties

Introduction

Most antibiotic treatments for moderate to severe bacterial infections are started empirically, without knowledge of the pathogen or its susceptibility. In about two-thirds of patients who are given a full course of antibiotic treatment the microbiological workup is negative and the treatment remains empirical during its entire course. Patients are almost never given empirical antibiotic treatment to cover the entirety of the possible pathogens, even when this is possible (e.g. sepsis of urinary origin). This results in a coverage of about 60%–70% (when compared with the susceptibility of pathogens in microbiologically documented infections). Inappropriate empirical antibiotic treatment is linked to an increase in fatality rate. A strong motive, and it may be the strongest, to restrict antibiotic use, and especially use of broad-spectrum antibiotics, is to slow the rapid rise in resistance. This practice involves two ethical dilemmas: current, identified patients at risk are given less than maximum treatment in order to benefit future, unidentified patients; and the present patient is not informed of the choices and the patient’s consent is not given, although the choice of antibiotics might have grave consequences for the patient’s health and chance of survival. In the present article we intend to explore the balance that should be sought between these two conflicting claims: the expectation of the patient to maximum treatment and shared decisions, and the right of future patients to effective treatment.

Rebuttals based on facts

Several arguments can be presented in trying to deny that the dilemmas are ethical in nature. The first one is to claim that we are indeed aiming at covering all possible pathogens, and failing to do so because of imperfect data or algorithms to use the data. It is easy to show that even in scenarios in which perfect coverage (or very close to it) can be achieved empirically, practitioners do not aim to do so. In many countries and hospitals, carbapenems would achieve an almost perfect empirical coverage for infections that are caused mainly by Gram-negative bacteria (e.g. severe urinary tract infections), yet they are not employed. In countries and hospitals with a low percentage of resistant pathogens (e.g. Denmark or the Netherlands), antibiotic regimens that will achieve almost 100% empirical coverage could be devised for many infections, yet they are not. The concern for future resistance is a consideration.
If the patient is given less than maximum treatment for the patient’s own sake so as to prevent side effects and future infections with resistant pathogens, no ethical dilemma exists. However, the long-term outcome (up to years after infection) of patients given appropriate empirical treatment is better than that of patients given inappropriate treatments.\textsuperscript{5} That is, even taking into account the side effects and future infections, there is an advantage to appropriate empirical treatment. In a formal model, the cost of future resistance to the patient was less by an order of magnitude than the cost to other, future patients.\textsuperscript{1,4} Looking only at the present patient and ignoring the cost of resistance for future patients, we would probably prescribe maximum antibiotic treatment for each patient.

Doctors should avoid antibiotic treatments that are (with a high degree of certainty) not needed: e.g. for obvious viral infections; broad-spectrum antibiotics when the pathogen and its susceptibilities to narrow-spectrum antibiotics are known; excessive length of prophylaxis or therapy. However, even taking these absolute indications to prescribe fewer antibiotic courses and those that have a narrower spectrum into account, most of the antibiotic decisions entail a balance between broadness of coverage and ecological impact.

In many hospitals conditions are far from ideal for containing the spread of resistant pathogens (few single rooms, staff shortages, movement of patients between wards for administrative convenience, poor domestic hygiene, reluctance to close rooms, wards or operating theatres that are the foci of resistant pathogens). The government or hospital management can invest money and efforts into improving these shortages and containing resistance. However, a situation in which these conditions will improve to such a degree that antibiotic selection pressure would not matter is difficult to imagine. Agencies that regulate and control the supply movement of antibiotics can perhaps, in the long run, nullify the threat to future patients, but the supply of new antibiotics is dwindling to almost nothing.\textsuperscript{7} As recognized by Foster and Grundmann,\textsuperscript{6} and by Garau,\textsuperscript{9} the ethical dilemmas exist and cannot be ignored.

### Should we deal with these questions?

Should we as practitioners deal with these questions? Why not leave it to moral philosophers in their ivory towers? Will anything practical emerge from these discussions? If practicalities emerge, might they not take an unwanted direction of a greater emphasis on the autonomy of patients, and a drive towards consumption of antibiotics? We think the answer is in the affirmative; practitioners should be a part of these discussions. We see it as a part of our professional duty to consider these ethical dilemmas (see below). Battin et al.\textsuperscript{12} describe how modern bioethics, with its emphasis on the individual, were shaped in a time when infectious diseases were seen as a problem of the past. Present principles of bioethics are awkward when dealing with the balance between the individual and a group of people. Practitioners should be part of the ethical discussions because the present discourse in bioethics (and, in some countries, the legal discourse) has no upper boundaries to protect unidentified groups of people, while the protection of the individual is paramount to modern bioethics.

We should try and prevent the discussion from drifting in perilous directions. A few examples might clarify this danger. Do we have a firm answer for a septic patient who arrives with an ampuole of meropenem and one of vancomycin (bought outside the hospital) and asks the physician to administer them? What about 100 patients that demand the same? In Israel, the wording of the patient protection law requires informed consent before any medical treatment, and compels the physician (among other duties) to explain to the patient all the available therapy options.\textsuperscript{11} Nothing exempts antibiotic treatment. What if practitioners were asked to conform to the letter of the law and explain antibiotic choices, and obtain consent?

We are already facing simple infections (e.g. cystitis) caused by multiply resistant bacteria\textsuperscript{12} (and probably will encounter more and more in the future). The balance may shift in favour of no empirical treatment for patients at high risk for such infections. We will need firm ethical grounds to do so. Because of our professional duty, because of the rift between bioethics and infectious diseases, and because it leads to practical issues, we should be part of the ethical discourse.

### The rights of unidentified people

The natural instinct of a doctor is to treat the present patient to the best of one’s resources and capabilities. The conflict in antibiotic treatment is between the welfare of the present patient and that of future, unidentified persons. We are convinced (and can show data to support this conviction) that extreme use of antibiotics within months or (a few) years will lead to such an increase in resistance that some patients will face serious infections caused by pathogens resistant to all effective antibiotics. These patients are unidentified people living today, and they have a right to health and preservation of life in the years ahead. Similar arguments can be used to support the rights of future generations.

The ethical justification for the demand to consider future patients’ health interests is based on the idea of justice between generations, which is well known from John Rawls’ discussion of this issue.\textsuperscript{13} However, its origins can be found much further back, in John Locke’s Second Treatise of Government. Locke (1632–1704), who believed that the state of nature is equality, in which persons ‘should also be equal one amongst another’ (p. 269),\textsuperscript{16} dealt with the issue of using natural resources for one’s own welfare, need and property. He insists that natural resources were naturally given ‘to the Children of Men, given to Mankind in common’ (p. 286).\textsuperscript{16} Accordingly, Locke believed that when a person takes something from nature and makes it his own property (by mixing it with his labour), one is allowed to do so only ‘where there is enough, and as good left in common for others’ (p. 288).\textsuperscript{16} This idea is known as Locke’s ‘Proviso’, and is used when we consider the morality of the use of scarce resources. We have to leave the same amount and quality of the scarce resource for others...
who are considered morally equal to us. We can easily think of antibiotics as a scarce resource, and thus cannot make unconstrained use of them if we believe that this might strike at future patients' health or ability to be protected against bacterial infection.

Rights translate into duties: whose duty is it to guard the right of future patients, who are unidentified as yet and cannot speak for themselves? We can argue about the bearers of this duty, but it is quite clear to the authors that doctors are among them. In an often-quoted definition of medical professionalism, the fair distribution of healthcare resources is seen as one of the principles of professionalism, and commitment to just distribution of finite resources as one of its commitments. Other functions of society may bear this duty as well (regulators, for example), but as of today it seems that no one among them is positioned to discharge it.

Another viewpoint from which to examine the duty of doctors is accountability. If, in the near future, many patients will be harmed by resistant pathogens with no available cure, it is quite clear that the doctors who wrote the prescriptions for antibiotics are accountable.

If we can accept these two premises—that future patients have rights, and that it is our professional duty to guard these rights—then the next step is to decide, within our profession, what is the correct ethical model to balance the right of a present patient to maximum treatment and shared decisions against the right of future patients to effective treatment.

Balancing rights

There are two models that will be familiar to many practitioners, and which should be considered in reaching this balance: cost-effectiveness analysis and the Georgetown mantra of bioethics (beneficence, non-maleficence, autonomy, and justice). The inclusion of cost-effectiveness together with the most quoted principles of bioethics looks strange. But we should consider that the cost-effectiveness approach rests solidly on the ethical theory of utilitarianism. It suffers from the many drawbacks of utilitarian theories, but there is nothing in the theory of cost-effectiveness itself that contradicts utilitarianism. It forces the user to reach explicit decisions instead of implicit assumptions that might be biased and unethical.

How does cost-effectiveness deal with the balance between present and future patients? As a basic assumption it sums benefits to different people to reach a maximum aggregate result. The balance between present and future might be solved through a decision based on temporal discounting, i.e. the question of whether we value benefits in the far future less than benefits in the near future. The function to achieve this balance can be non-linear (see below). Cost-effectiveness, but for the technical difficulties in building the model and obtaining the needed data, is a natural tool for the balance we are looking for. However, it has no answer for the question of patients' autonomy.

To feel the urgency embedded in the right to autonomy we should read again Isaiah Berlin's words: 'I wish my life and decisions to depend on myself, not on external forces of whatever kind. I wish to be the instrument of my own, not other men's act of will. I wish to be a subject, not an object; to be moved by reasons, by conscious purposes which are my own, not by causes which affect me, as it were, from outside.'

In Western countries today, when dealing with a single person, the autonomy principle is paramount. We accept the right of a person to make decisions about her or his health, even if these decisions are detrimental to the patient's health. This supremacy is less intuitively clear when decisions affect others.

In the four principles of bioethics, the welfare of future patients is assured by the principle of non-maleficence and by the justice principle. However, there is nothing in the four principles, and little in the bioethical discourse, that might help us balance rights.

We might lessen the difficulty by examining two situations. The first one is writing guidelines, or assembling a detailed decision support system. Although still confronting a group of present patients with future patients, autonomy is out of the equation. Whatever model is used, a committee writing guidelines can aim at the balance that we were seeking. The use of cost-effectiveness or cost–benefit models will attain that by including in the model the damage to future patients caused by resistance.

At this point the introduction of another construct, Rawls's 'veil of ignorance' might be helpful. If we imagine all people behind a veil of ignorance about their status, whether they are current patients or future patients or unaffected by infection, and ask whether the right of future patients to come to no harm because of future resistance should be recognized, the answer would be affirmative. We could well suppose that people behind the veil will also agree to curtail the autonomy of present patients when weighted against the right of future patients to come to less harm. They will probably want decisions to be made beforehand, in the form of guidelines or decision support systems, to be as just as possible, and not left to each patient–doctor encounter (see Weinstein's convincing arguments in favour of collective solutions).

Here we reach the second situation, that of the actual patient–doctor encounter. We have sufficient moral grounds to increase the danger to the present patient (by a small amount) in order to decrease the harm to future patients. We do not think we have a good way to honour the autonomy of patients. We can guess that asking each patient whether they agree to the prescription of less than the maximum antibiotic treatment will not achieve the balance we are seeking. We did not find any empirical research addressing this question to laypeople or patients. However, in a survey of doctors' attitudes, future resistance was the last and the least important factor among the factors that influenced doctors' choices of antibiotic treatment for pneumonia (usually broad-spectrum antibiotics).

To sum up this discussion, the right of future patients to effective antibiotic treatment should be recognized and balanced against the right of present patients. For fairness sake, the decisions should be made in a collective way as much as possible (guidelines, decision support systems). We see no good way of respecting patients' right to autonomy, and believe there are moral grounds to waive it in favour of the future patients' right to come to minimum harm. The infringement of autonomy can be mitigated, but not nullified, by making public, as much as possible, the considerations of antibiotic policy, and perhaps even by widening the circle of people that make decisions on policy.
Arithmetic of rights

What principle should we use to balance the different rights to effective treatment? We said before that the rights of future patients can be balanced against those of present patients in a cost-effectiveness or cost–benefit model. We can use a temporal discount rate (a discount rate based on economic principles will probably vary from 1% to 5%) to show that we put more weight on the present patients’ plight, and also that there is a chance that new antibiotics will enter clinical use.

We feel uneasy doing only that. We feel that the very sick present patient (e.g. the patient in septic shock) is an exception, and that future resistance should be a lesser argument when choosing antibiotic treatment for this patient. This feeling was termed the ‘rule of rescue’ by Jonsen:20 the urgency people feel to rescue identifiable persons from preventable death, even at the cost of enormous, unusual amounts of effort and money.

Rawls was convinced that behind the veil of ignorance people will choose a function that will minimize the worst outcomes rather than a function to maximize an aggregate good (or minimize an aggregate evil).13 Here the worst outcome is the one of an untreated present patient with a severe infection. Again we reach the conclusion that special consideration should be given to these patients.

This consideration can be incorporated into a formal cost-effectiveness or cost–benefit model. The dominant factor in such a model would be the balance between present and future patients. We can use for that a non-linear function that will assign a higher value to the life of a present patient at high risk. In other words, when regarding a patient with severe sepsis, the model will assign less importance to the rise in future resistance, and actually more importance to the present patient.

Similar instances

We have described a situation in which the rights, and then outcomes, of present patients are weighted against those of future patients, and could not envisage a solution that will fully guard the autonomy of patients. The arguments used here might work as well for similar situations. Isolation of patients colonized or infected with multidrug-resistant bacteria involves discomfort and possibly some danger to the patient, to the benefit of other patients. The treatment of patients by doctors in training, and especially the performance of invasive procedures, even if supervised, to accomplish training, and thus benefit future patients, puts present patients at some risk, as the procedure might be safer if performed by an experienced surgeon.

An important question when considering whether to waive the right to autonomy is where to draw the line. The antibiotics example can help us: it is about treatment, not research. Research should be discussed in another frame, where autonomy is paramount. Waiving autonomy in antibiotic treatment achieves clear, measurable (and not potential) gains in health and survival for some people. It involves a very small risk to the present patient, and the maximum is done to reduce this risk. The safety of the present patient is given priority (but not absolute supremacy), and the sicker the patient is, the more that patient’s needs precede others. It can be mitigated by decisions on the collective.

Conclusions

Patients with moderate to severe infections are given less than maximum empirical antibiotic treatment in order to reduce the rise in resistance. This practice involves two ethical dilemmas: whether the danger to a present patient should be increased, even if by a small degree, to benefit future, unidentified patients; and whether this should be done without the consent of the present patient, thus disregarding the patient’s autonomy. We argue that future patients have a right to come to minimal harm. Future patients being unidentified, practitioners of medicine have a duty to protect their rights and weigh them against the rights of the present patient. A decision on the collective (guidelines, decision support systems) is a convenient way to do this. Using a temporal discount rate to show that the life of present patients has pre-eminence, to some degree, over future patients does not solve the immediacy of the plight facing a present, identified patient with a very severe infection. We think there are good grounds to take into less account considerations of future resistance for such a patient, or in a formal analysis, to make the ratio of the present versus future patients dependent on the severity of disease of the present patient.

None of these solve the problem of patients’ autonomy. We see no other way but to argue that the right of future patients to come to less harm outweighs the right of the present patient to share in decisions on antibiotic treatment.

Transparency declarations

None to declare.

References


