OMA
ONTARIO MEDICAL ASSOCIATION

POLICY PAPER

When Antibiotics Stop Working

ANTIBIOTIC RESISTANCE[i] IS AN UNDER-RECOGNIZED PROBLEM IN ONTARIO AND THE REST OF CANADA. ANTIBIOTIC RESISTANCE REFERS TO THE ABILITY OF BACTERIAL INFECTIONS TO WITHSTAND ANTIBIOTICS THAT HAVE BEEN SUCCESSFULLY USED TO TREAT THEM IN THE PAST. SOME RESISTANT BACTERIA THAT OFTEN MAKE NEWS HEADLINES ARE METHYCILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) AND VANCOMYCIN-RESISTANT ENTEROCOCCUS (VRE), BUT THERE ARE MANY OTHERS THAT DO NOT GET THE SAME AMOUNT OF ATTENTION. RESISTANCE TO ANTIBIOTICS IS GROWING AMONG A MULTITUDE OF BACTERIA, WITH INCREASINGLY HARMFUL EFFECTS ON HUMAN HEALTH.

The increase of antibiotic resistance represents the need for a change in thinking. Long ago, bacterial infections were very urgent, untreatable, fatal problems. More recently, infections have become low-risk medical events, treatable with antibiotics. Several generations of clinicians have been trained in the philosophy that antibiotics will treat and prevent infections with few downside health risks, and several generations of people hold the same expectations when we get sick. Now, medical practice is changing, and broader society must change with it. We must recognize that some antibiotics have stopped working, some infections are self-clearing and do not require therapy, and there are negative effects of antibiotic use on human health.

Bacteria have been gaining resistance to antibiotics since they were first discovered, but the health impact of this has only recently begun to be felt. Dr. Alexander Fleming found that bacteria could become resistant soon after he discovered penicillin in the 1940s, but until recently this has not had a noticeable effect on patients' health; physicians have had alternative antibiotics at the ready to use against bacteria when one antibiotic stopped working.[1] Only now are we beginning to see bacteria with multiple or total resistances to antibiotics.

The impact on patients has reached a dangerous level. For example, there are cases of urinary tract infections with extended-spectrum beta lactamase (ESBL)-producing bacteria. ESBLs make the bacteria that produce them resistant to all beta-lactams, a commonly used class of antibiotics. These urinary tract infections, normally treated with a course of pills, require intense intravenous treatment with rarely used (and therefore less familiar) antibiotics.

Another example is pneumococcal bacteria, which cause pneumonia, and which have become increasingly resistant to a class of antibiotics called macrolides. In a recent instance, a patient who had pneumonia was prescribed macrolides and was reasonably expected to get better at home, but became seriously ill and was discovered unconscious by a family member. The presence of resistant bacteria required hospitalization and an intense round of treatment with more powerful (and more toxic) antibiotics.[ii]

In other cases, the attempted treatment of one infection has lead to serious illness with another kind of infection.

For example, one patient who had Escherichia Coli (E. Coli) growing in her urine but had no symptoms (a condition called asymptomatic bacteriuria) was given antibiotics. The patient began to suffer from diarrhea 10 days later. The treatment of the E. Coli, which was unnecessary, led to a resistant infection with Clostridium Difficile (C. Diff). The patient spent a total of four months in the hospital recovering from the C. Diff infection.

All the various antibiotics used in human and animal medicine fall into "families" or classes, which are large groups of antibiotics that have a similar chemical backbone. Such families include penicillins, cephalosporins, aminoglycosides, and others. This can be understood by imagining families of animals, like mammals, reptiles, fish, and others. Within each family many things are similar, but a few things will make one species in the mammal family — horses — very different from another species in the same family — zebras. When experts talk about families of antibiotics, we could imagine that ampicillin and amoxicillin are like horses and zebras; both in the family penicillin, but slightly different from each other. When we say in this paper that bacteria are becoming resistant to an entire family of antibiotics, we mean that all of the antibiotics that have that same chemical backbone are becoming ineffective, despite other differences.

Additionally, these families of antibiotics have been broken into "lines," with the first line being the most important to human health. These first-line antibiotics are the first choice when a patient gets sick, because they are most effective, least harmful to the patient, and easiest to administer. Through the second line and third line of antibiotics, the drugs become less effective, more harmful, and more difficult to administer. This might mean that instead of getting a pill for three days with few side-effects, a patient with a resistant infection will be hooked up to an IV for five days and have more side-effects.

While some bacteria only have resistance to second-line or third-line antibiotics right now, which may make it seem like they are less of a problem than bacteria with resistance to first-line antibiotics, antibiotics on different lines can be in the same families. Resistance to second-line or third-line antibiotics is an important warning sign that bacteria could already be, or quickly become, resistant to their first-line relatives, and cause serious problems for human health.

Three of the most obvious results of antibiotic resistance are beginning to be experienced by physicians in Ontario: the need to use unfamiliar antibiotics to treat patients, the need to use more toxic antibiotics to treat patients, and the longer duration of illnesses in patients. Physicians will have to resort to medications that have not been used in many years because they are now the only effective treatments, and these will have a greater negative impact on the patient's body and overall health. Patients will also have to spend more time in hospitals or battling infections in the community. The fourth result of antibiotic resistance is a greater risk and higher rate of death. Patients are now dying from infections that physicians have been successfully treating for decades.

Community practices are changing in response to the burden of illness. Physicians are rethinking the antibiotics they select, and they are adopting guidelines of non-prescription for the most common infective complaints that are sometimes due to viruses or resolve without therapy (e.g., ear infection, sinus infection, and upper respiratory tract infections). In the coming months and years, rapid changes may be required in community, emergency, hospital, and nursing home settings.

While some antibiotic resistance is directly and exclusively related to human medicine, other antibiotic resistance has its source in veterinary medicine and agriculture. In Ontario, there is little control over which antibiotics in what quantities are given to food animals, and a lack of surveillance over the ability of animal owners to purchase locally or import antibiotics as they see fit.

The federal and provincial governments regulate which antibiotics can be used in animals. These regulations restrict the use of first-line human antibiotics for animal medicine, but this is simplistic and has not been effective to prevent antibiotic resistance since human and animal antibiotics are related.

Currently, the United States Food and Drug Administration (FDA) is gradually implementing bans on the extra-label use (i.e., the use of antibiotics in a way not indicated on their label) of classes of antibiotics in animal husbandry which are also used in human medicine. Certain antibiotics are indicated for use as prophylactics (illness preventers) or growth promoters, while others are not indicated for these uses but are still given to large groups of animals to achieve these results. The use of antibiotics for prophylaxis or growth promotion, whether indicated or extra-label, seriously compromises preserving the effectiveness of antibiotics. Effective April 5, 2012, cephalosporins are banned by the FDA from extra-label application to groups of animals in the United States.

The FDA is taking these steps because it believes there is sufficient evidence that this application leads to antibiotic resistance and risks human health. At the same time, in Canada, it is still legal to administer cephalosporins extra-label to groups of animals (e.g., in poultry production).

Summary Of Recommendations

1. The Government of Ontario must develop a system for farm industry surveillance to keep track of the identities and quantities of antibiotics being purchased, and those being moved into or out of Ontario. Currently, surveillance of antibiotic movement does not exist in the province.

2. Surveillance should be established in areas where it does not exist (agriculture) and strengthened in areas where it does exist (medicine) in order to collect data and gain a firmer understanding about antibiotic resistance in both humans and animals.

3. Electronic health records should be utilized to allow physicians to compare patients' past prescriptions and diagnoses. This would reduce variability and allow physicians in the community, hospital, emergency department, or long-term care facility to make optimal decisions about which antibiotics to prescribe to patients.

4. An independent institution should be established in conjunction with one of Ontario's medical schools to use currently available data to develop and maintain optimal antibiotic use guidelines that physicians in Ontario can use to guide their practice, particularly when dealing with resistant bacteria and unfamiliar antibiotics.

5. Ontario should ban the prophylactic or growth-promoting use of antibiotics, whether extra-label or indicated, in animal husbandry. This step is fundamental to preserving the effectiveness of antibiotics.

6. A veterinary prescription-only standard of access to antibiotics for animals must be instituted. The province should require a veterinary prescription and/or supervision of the use of all antibiotics on farms. The current practice allows for unsupervised, unscientific, and ultimately dangerous application of important medications.

7. Amendments to Ontario's Livestock Medicines Act must be made to close the "own use" loophole created by the Food and Drugs Act and its Regulations, to ensure that large volumes of antibiotics cannot be freely imported into the province and be applied to animals en masse without surveillance or regulation.

8. The federal government must engage in antibiotic conservation and amend the Food and Drugs Act and its Regulations to close the "own use" loophole. People importing antibiotics for any reason should all be held to the same standards, and surveillance should be established to allow the collection of data about which drugs are entering our country and what their intended use is.

9. The federal government should provide funding for research, strengthened surveillance, and educational campaigns focused on antibiotic resistance. There is a dearth of community-based surveillance of organisms and resistance patterns, and this must be rectified.

10. Everyone who has access to antibiotics must act responsibly and prudently with them. Patients must work alongside physicians to modify the expectations of receiving antibiotics for certain infections, even if patients have received antibiotics in the past for similar complaints. Physicians, patients, allied health-care professionals, and dispensing parties (pharmacists), need to be aware of the importance of this issue and incorporate that knowledge into their own practice and use.

A challenge facing government regulators and the agricultural, veterinary, and medical communities is that it is very difficult to predict precisely when a negative health effect will arise out of the use of antibiotics in humans or in animals, or how severe the effect will be. Motivation to preserve the effectiveness of antibiotics comes from the fact that we can never tell when the evolution of resistance is going to happen or begin to cause complications for humans, animals, or both. It has been demonstrated in other Canadian provinces, Europe, and the U.S., and in both humans and animals, that limiting the use of certain antibiotics will lower the rates of resistance in bacteria. Evidence suggests that resistance trends can be reversed and the effectiveness of antibiotics protected, thus Ontario is urged to join other jurisdictions in taking action to limit the use of antibiotics.

Effects Of Antibiotic Resistance On Patients

The effect of antibiotic resistance on patients is of the utmost concern to physicians. At the individual level, patients are getting sicker than they used to from bacterial infections that have been treatable for many decades. There are many physician experiences that demonstrate this trend. For example, a decade ago, antibiotics could have effectively treated a child suffering from strep throat (caused by a Streptococcus infection). It is becoming more common for a child to have repeated strep throat infections, and for these to develop into more serious consequences that have not been common for many years, such as scarlet fever.

Infections like MRSA are becoming discouragingly common and difficult to treat. MRSA infections can happen in the community or in a hospital to healthy and sick people alike, though people who are already ill and whose immune systems are busy fighting other illnesses are especially vulnerable. Currently, a few antibiotics are still effective at treating these infections, though there are cases of healthy individuals having recurrent MRSA infections for many months. Similar challenges are presented by C. Diff and VRE in hospitals or long-term care facilities.

Patients who contract an infection with resistant bacteria spend more days in hospital on average than those who have an infection with bacteria susceptible to antibiotics. Health Canada found that people with infections resistant to antibiotics were more likely to be hospitalized than those with susceptible infections, even after the patients' different underlying illnesses were taken into account. Like the above-mentioned case of the patient who spent four months in hospital with C. Diff, these patients tended to be sick longer and hospitalized longer.[2]

Penicillin and Pneumococcal Infections

Ampicillin and amoxicillin are two beta-lactam penicillins which have been effective at treating formerly deadly infections for decades. However, some bacteria, such as Streptococcus Pneumoniae serotype 19A, which causes bacterial pneumonia, sepsis, and meningitis, have acquired new cell wall proteins that confer resistance to this family of antibiotics. Penicillin and amoxicillin were the long-time antibiotics of choice to treat pneumonia, but their ability to treat this illness is now less certain. Other less-familiar antibiotics with higher potential toxicity are needed to treat meningitis when penicillin fails.

Another study conducted in the United States confirmed the Health Canada findings: hospitalized patients who became infected with VRE had a 6% higher rate of death and a six-day longer hospital stay than a similar group of uninfected hospitalized patients.[3] When Enterobacter species were studied, infected patients endured a five-fold risk of dying, and an average of nine days in hospital.[3] Patients infected with ESBL-producing E. Coli spent an average of four days longer in hospital than similar uninfected patients.

In addition to these groups of patients with resistant infections, there have been individual cases in which patients become untreatable because there are no more antibiotics available to combat the bacterial infection they have. For example, a Dutch woman died in 2010 after getting an E. Coli infection. She developed a bacterial infection of the bloodstream (urosepsis) from a urinary tract infection caused by multi-drug resistant E. Coli bacteria.[4] These bacteria were able to produce ESBL, making them almost totally resistant to antibiotics.

In both hospital-acquired and community-based cases of bacterial infections in the U.S., the death rate attributable to resistant bacterial strains was higher than the rate attributable to susceptible strains. The highest death rate was observed with multi-resistant strains.[2]

At the level of individual patients, infections with resistant bacteria are becoming more frequent, more difficult to treat, and more deadly. Patients are suffering longer with infections that often would have been quickly treated five or 10 years ago, at a greater cost to the health of the patients and to the health-care system as a whole. There are many cases of patients dealing with such resistant infections, and these are going to become more common in the near future as bac-

terial infections that are resistant to antibiotics affect more patients in Ontario.

Effects Of Antibiotic Resistance On The Health-Care System

There are health-care system-wide effects of antibiotic resistance among bacteria. The costs associated with specific outbreaks and high levels of antibiotic resistant infections in Canada are growing quickly. A study that examined the costs of MRSA infections at Sunnybrook Health Sciences Centre in Toronto found that the total direct cost over a two-year period was $525,108.[5] This study was published in 2001, when Canadian rates of having this strain of bacteria (either being infected or being "colonized" — having the bacteria in the body but not having a clinical infection) were 4.2 cases per 1,000 hospital admissions. At the time, the rate of MRSA across Canada was estimated to cost approximately $50 million.

By 2007, rates of MRSA among the Canadian population had doubled to 8.5 cases per 1,000 hospital admissions.[6] In 2010, the National Collaborating Centre for Infectious Diseases (NCCID) estimated that direct health-care costs associated with MRSA and resistant enteric bacteria in Canada would reach between $104 million and $187 million annually[7] — this is $64 million to $102 million more than such infections would cost if the bacteria were susceptible to antibiotics. The trend of increasing costs to the health-care system will continue in proportion to the growing number of resistant infections.

The Process By Which Bacteria Gain Antibiotic Resistance

We each have many billions of bacteria in our bodies at all times. It's important to note that billions of good bacteria, as well as small amounts of bad bacteria, are ever present in healthy individuals. These bacteria divide and duplicate (copy themselves) every 30 minutes or less. In very virulent infections, bacteria duplication may happen every three or four minutes. These duplications in both good and bad bacteria do not occur perfectly, which is the essence of how mutation and change happen; there is always a little genetic difference for each duplication.

An effect of these minor changes is that bacteria can gain the genetic ability to resist antibiotics. One such change that gives bacteria resistance is a change in a bacterial protein that prevents the binding of fluoroquinolones (for instance, ciprofloxacin or levofloxacin) to the bacteria, making the bacteria resistant. These bacteria can be exposed to large amounts of fluoroquinolones without any effect because the antibiotic no longer works to prevent bacterial growth and duplication. This DNA adaptation-giving resistance will be passed on to the offspring of all these bacteria.

In such a case, if a patient contracts a bacterial infection with this kind of bacteria, a small number of the bacteria will have undergone this genetic change and be resistant to fluoroquinolones. If this patient is treated with a fluoroquinolone antibiotic like ciprofloxacin, then the group of infection-causing bacteria that do not have a modified protein will die, but those that do produce it will survive the exposure to the antibiotic. As a result, the conditions will have unknowingly been created for the survival of bacteria that are more resistant to certain antibiotics than other bacteria of the same species.

The resistant bacteria will start to multiply, and will get passed from the patient to someone else through a variety of means. Whereas the resistant bacteria were initially the minority for the first patient, the next time a patient falls ill with an infection with these bacteria, the resistant ones might make up the majority of the infection in the patient's body. That might not cause complete resistance for this patient — it simply might be more difficult to make the patient well again, and different antibiotics might need to be used — but with more duplication of the surviving bacteria and perhaps a few more mutations, the bacteria will gain complete resistance.

This process occurs in the body of patients without them or their physicians knowing. As in all cases of resistance, these are evolutionary biological processes; resistance mutations are random and unpredictable, and we have no idea when they will occur.

Once resistance in bacteria "A" takes place, DNA transfer is a second way for them to propagate this resistance among other bacteria. Bacteria can trade DNA with other bacteria, and they do not have to be the same kind of bacteria to do this, though some bacteria are better at trading DNA than others. If bacteria A are ESBL-producing, and meet other bacteria, "B," of a different species, some of A and B can actually join cell membranes and trade DNA. Bacteria B leaves with A's DNA, and now will have the same ESBL production ability that bacteria A have, even if bacteria B have never been exposed to antibiotics before. Bacteria B will also pass this resistance on to their offspring, and so whenever bacteria B do come into contact with an antibiotic, they will be able to withstand it.

Additionally, bacteria that are resistant to one kind of antibiotic may also have the ability to resist other related antibiotics. For example, if bacteria produce ESBL and a patient becomes infected with these bacteria, a physician who

prescribes ampicillin will see that this antibiotic is no longer effective. To help the patient, the physician may decide to give the patient something more powerful — and also more toxic. The physician might think that this second antibiotic will treat the infection quickly, but in this case the bacteria's ESBL production works against many antibiotics in a specific class (all beta-lactam antibiotics). Since the first and second antibiotics the physician tried are from the same family, neither will treat the infection. ESBL production is powerful against a class of antibiotics that are very important to human health. Bacteria that have this resistance tool, and those with which they exchange DNA, are very dangerous as a result.

Finally, it is important to note that bacteria can gain resistance to antibiotics even when they are not the cause of disease in a sick patient or the target of the treatment. A downside to using antibiotics against one bacterial infection is the exposure of all of the other bacteria in the patient's body to that antibiotic. In the case of pneumonia caused by pneumococcus for example, the E. Coli and all the other bacteria in a patient's body are gaining resistance to the antibiotic that is treating the pneumonia. A number of studies of resistant Salmonella and E. Coli, and more recently Campylobacter, infections in humans have shown that patients who had prior antibiotic treatment for a different illness, before the onset of these infections, were at increased risk of having an infection due to resistant bacteria.[2]

Bacteria are highly adaptive organisms that have a number of different routes through which they can gain resistance to antibiotics. It is important to remember how adaptive they are when thinking about the use of antibiotics in medicine and in agriculture, as evidence is mounting that the use of antibiotics anywhere in the living environment can create the selection pressure needed to bring about the evolution of resistance. It is also important to remember that any time a person is given antibiotics as treatment, the risk of having a resistant infection in the immediate future increases.

The Challenges Around Antibiotics In Medical Settings

The cycle of resistance among bacteria has implications for patients in community, emergency, hospital, and nursing-home settings. Both inpatient (hospital and nursing home) and outpatient (community and emergency) settings have advantages and disadvantages when it comes to maintaining the efficacy of antibiotics.

In inpatient settings, the patient's environment is controlled and the use of antibiotics is supervised. The opportunity for appropriate and responsible use of antibiotics is more available in this setting than among outpatients. However, in such a setting, there is also a higher percentage of people who need antibiotics focused in a smaller space, so there is a high concentration of antibiotic activity. This means that selection for resistance among bacteria is concentrated in one physical location and occurs frequently, and that resistant bacteria will have fertile ground to grow and pass DNA to other non-resistant bacteria. Further, in hospitals, all patients with similar medical conditions are grouped together. These people will have, or be susceptible to, similar kinds of bacterial infections. This provides a reservoir where resistance can happen to the advantage of bacteria and the disadvantage of patients.

In the outpatient setting, patients are physically separated from each other, so there is not a concentrated number of infected patients grouped together as there are in a hospital. Outpatients are also in better general health; on average, they are not as severely ill as inpatients. These conditions benefit outpatient treatment, and are disadvantageous to the spread of resistance among bacteria. However, there are other liabilities with outpatient treatment that do promote resistance.

First, the chance of someone improperly taking their course of antibiotics is high. Second, many outpatients who are prescribed antibiotics would get better without taking them because they have infections that are self-limiting. If the patient starts to feel better, they will assume it is the result of the antibiotic, but it may not be. There is sometimes no way to know if there was a problem with the chosen antibiotic in outpatient settings; it may have worked, or a resistant infection may have simply cleared up on its own. The antibiotic resistance is essentially invisible to physicians in these cases.

Another disadvantage is that outpatients often have expectations that a physician will give them antibiotics, even when they are not likely going to be effective. When a physician believes that a patient has a viral infection and does not offer antibiotics for the reason that they are not effective against viruses, the patient may ask for antibiotics because this is what he or she has had in the past, or the patient does not want to take a chance. There are many forms that this conversation can take, and culture plays a role in the patient's expectations regarding medical care. In this way, the patient and physician become the agents for administering an unnecessary antibiotic if the physician does not resist as strongly as may be warranted. If the patient takes antibiotics and happens to have — as most people do — a low level of bad bacteria in their body unrelated to the present illness, these bacteria are suddenly subjected to the selection process for resistance.

Further, when physicians know that a viral epidemic, such

as the flu, is happening in their community, they know that it is not treatable with antibiotics. However, if, for example, a physician has two patients come in with the flu and does not prescribe them antibiotics, and one gets better but one returns a week later with a bacterial illness that took over opportunistically from the virus and does need antibiotics, the physician might feel responsible for the patient's worsening condition. This patient may not understand why the physician did not prescribe antibiotics in the first place.

It can be confusing to patients that a viral infection can lead to the presentation of a bacterial infection, for example, when a person with the flu ends up suffering from pneumonia. This physician may start to think that he or she should be more aggressive with prescribing, to make sure that patients do not have to come back to the clinic, or that he or she should bend prescribing rules for particular patients. As a result, the physician may make the decision to prescribe antibiotics more often and, unfortunately, unnecessary courses of antibiotics may be prescribed. In this way, unwarranted use of antibiotics may contribute to the development of resistant bacteria.

There is now good evidence to suggest that anytime a physician prescribes an antibiotic, when the patient comes back at a later date with a different infection, it is more likely to be resistant. If the initial antibiotic was necessary, there is no means to protect the patient from resistance in this second infection. However, if the first antibiotic prescription could have been avoided, resistance in the second infection may not have occurred.

Physicians are beginning to change the way they prescribe antibiotics for ear, sinus, throat, and urinary tract infections because many of these are self-limiting, and will get better without antibiotics. Even in these cases, patients who are sick most often prefer to come away from a visit to their physician with something that they believe will help them, especially for the relief of their symptoms. For sinus infections, a steroid nasal spray will make a patient feel a lot better, whereas an antibiotic will not. Such non-antibiotic treatment of symptoms for self-limiting infections like those mentioned above can do much more to help patients while preserving antibiotics for the cases in which they are effective and warranted.

Viruses, Bacteria, And Antibiotics

Unlike resistance in zoonotic enteric bacteria (E. Coli, Salmonella, etc.) which can pass between animals and humans, human infections with non-enteric resistant bacteria, such as pneumonia, are almost entirely the result of antibiotic use in humans. Resistant non-enteric infections, including pneumonia and sexually transmitted infections, are major human health problems in Canada and abroad.[2] In the United States, approximately 40% of prescriptions for antibiotics are given for the treatment of common acute respiratory tract complaints: ear infections (otitis media), sinus infections (sinusitis), sore throat (pharyngitis), and bronchitis.[12] These conditions are predominantly caused by viruses, and treating them with antibiotics does not improve the condition which brought the patient to the physician.[2] Antibiotic prescriptions for colds and upper respiratory tract infections account for a large portion of the human contribution to the "unnecessary" use of antibiotics, and physicians are beginning to adopt modern guidelines of non-prescription for these ailments.

The Role Of Patients

Patients have an important role in preventing the development of resistance as well. When a patient and physician begin a discussion with a similar outlook on the need for the prudent use of antibiotics, an appropriate outcome that most benefits the patient is likely.

It is important for patients to understand that not every infection should be treated with an antibiotic. The expectation that a certain complaint (e.g., a phlegmy cough) should always have an antibiotic can lead to an unnecessary prescription, as mentioned above. It may be that with the same phlegmy cough in the past, a patient has been prescribed antibiotics and has felt better. As we now understand though, this patient would have gotten better without those antibiotics, as a phlegmy cough such as is caused by bronchitis is one of the top complaints for which antibiotics are prescribed but not needed. It is important that a conversation take place between a physician and a patient about why antibiotics are needed or not. It should be remembered that sometimes having no antibiotic is much better for a patient's overall health.

Antibiotics need to be taken carefully and as prescribed. Keeping a log of the time the antibiotic was taken, and at what dose, fits with standard medical practice in inpatient settings and should be used by all patients as well. Placing a pen and paper beside the medicine bottle and setting an alarm for the next dose can ensure regularity and efficacy of the antibiotic.

Crucially, patients should never share prescriptions with anyone else. This is more common than one might think. Patients must remember that sharing antibiotics has a very slim chance of doing good and a very high likelihood of doing harm to the other person. Prescriptions are tailored to each person, in terms of dose and frequency, as well as the kind of antibiotic chosen and personal medical history. Sharing left-over antibiotics cannot provide the same benefit as receiving a full, individually prepared prescription for an infection, and only enhances the resistance of bacteria.

Finally, there is only one safe way to dispose of antibiotics. All left-over medications should be taken back to the pharmacist. This is true for antibiotics, but also any other kind of prescription drug. Due to new sudden illnesses, death, or certain treatment regimes, people may find themselves with extra antibiotics that are not needed or have become outdated. Putting these into the toilet or garbage will expose billions of bacteria to these antibiotics, and these bacteria will gain resistance. Pharmacists have safe methods of disposal, and all medications should be taken to them when no longer needed.

Decreasing Resistance Through Prudent Use Of Antibiotics

Given the nature of the biologic world, there is nothing that science or medicine can do to completely prevent resistance among bacteria. Even the most responsible use of antibiotics can eventually result in resistance. However, with conscientious and prudent use, the incidence of resistance, and the rate at which it occurs, rapidly decrease. Such a decrease in resistance among bacteria has been seen in jurisdictions where physicians have reduced the numbers of prescriptions of particular antibiotics they prescribe, and in jurisdictions that have banned certain classes of antibiotics from being used in agriculture, as will be discussed in greater detail below. Measures such as these prolong the effectiveness of antibiotics.

Due to the vital importance of antibiotics to human (and animal) medicine, it is essential that we do not overuse them. Only 75 years ago, in the pre-antibiotic days, bacterial infections claimed many lives very quickly. At that time, if a healthy individual in Ontario developed pneumonia in both lungs, death would occur within two or three days. Thirty years ago, if an individual got the same kind of infection, the family physician would prescribe penicillin. The patient might feel sick for two or three days, but would return to health very quickly. Currently, if a healthy person develops pneumonia, the physician might prescribe a macrolide, but this patient might get worse, and a week later the physician would try a second-line antibiotic. The patient may then get better in a number of days with the course of a more toxic and less familiar antibiotic, but suffer unpleasant side-effects, such as a drug rash or a yeast infection. These days, patients sometimes get much sicker before getting better. We are heading full-circle, to a post-antibiotic time.

The Link Between Antibiotic Use In Animal Husbandry And Human Health

Beginning with the 1969 Swann Report in the United Kingdom,[8] many studies on the topic of antibiotic resistance in food animals have been conducted, the results of which demonstrate that researchers and governments have been aware of antibiotic resistance in bacteria for many years. In 1988, multi-drug resistant Salmonella Typhimurium was found in cattle in England and Wales. This strain of resistant bacteria subsequently became common in humans, poultry, sheep, and pigs.[9] In 1995, the U.S. approved the use of fluoroquinolones in poultry, and two years later 14% of chicken samples contained bacteria called Campylobacter Jejuni (C. Jejuni) that was resistant. The number of antibiotic resistant C. Jejuni infections in people increased in the same time period from 1.3% in 1992 to 10.2% in 1998.[9] In 2004, 82% of Salmonella isolates gathered from retail meats in the U.S. and China were found to be resistant to many antibiotics related to those used for human medicine.[10] In 2009, in the Netherlands, Dutch researchers found that one in three human isolates of E. Coli carried the same gene as that found in retail chicken.[4] They also found that the proportion of urine samples and blood cultures with E. Coli resistant to cephalosporin antibiotics had risen from 2.7% in urine and 3.6% in blood in 2008, to 3.4% in urine and 5.6% in blood in the first half of 2010. These seemingly small increases represent a significant impact on patients.

As mentioned above, in the U.S., an increase of C. Jejuni infections in humans was linked to the licensing of fluoroquinolones for use in poultry production. The investigators conducting the study detected a high prevalence of quinolone-resistant C. Jejuni in retail chicken products produced domestically. They documented DNA fingerprints in this resistant C. Jejuni from domestically produced poultry that were identical to those in the resistant C. Jejuni from infections in humans.[4] Patients infected with C. Jejuni who were treated with fluoroquinolones had a longer duration of diarrhea if they had resistant C. Jejuni than if they had non-resistant C. Jejuni infections (an average of 10 days versus seven days).

A 2007 study of pig farms in Ontario and British Columbia found that E. Coli bacteria had 24% resistance to tetracycline, 17% resistance to sulfamethoxazole, and 16% resistance to ampicillin.[11] These important antibiotics are all used for non-therapeutic (meaning either illness preventing or growth-promoting) use in pigs in Canada. This study also found a 100% correlation between resistance to antibiotics within the same family.[11] This is an important finding because it demonstrates the fact that bacteria can become resistant to entire groups of related antibiotics which are important to human and animal medicine. The rates of antibiotic resistance among zoonoses (bacteria that are passed between humans and animals) in Ontario are described in the Appendix on page 41.

Unlike bacteria that are unique to humans, resistance among zoonoses (such as Salmonella and C. Jejuni) can be linked to the use of antibiotics in animals. These bacteria are believed to acquire their resistance on farms, since animals are the predominant reservoirs of these organisms, and bacteria spread easily within and between farms.[2] In developed countries, food animals are the principal source of zoonitic infections for humans, and when people do become infected, person-to-person spread is uncommon.[2] As one example, in the case of the previously mentioned Dutch woman who died of an E. Coli blood infection, the strain of E. Coli she was infected with was found to be identical to a strain found in chickens sold for food. The *Dutch Journal of Medicine* reported that 87% of retail poultry meat contained E. Coli bacteria that produce ESBL, and are therefore resistant to modern antibiotics.[4] As evidence mounts that the use of antibiotics in animals has negative impacts on humans, and the effectiveness of antibiotics to treat human infections, the urgency of modifying the use of antibiotics is becoming clear.

The Case Of Salmonella Heidelberg In St-Hyacinthe, Quebec[25]

Where antibiotics are widely applied at low doses, high rates of antibiotic resistance among bacteria are likely to be found. High rates of resistance among bacteria in turn lead to lower levels of effectiveness among antibiotics typically used against them. This relationship has been demonstrated a number of times, but there is an illustrative example from Quebec that shows this link clearly.

It's a common practice in Canadian egg farming to inject eggs or day-old hatchlings with Ceftiofur, a cephalosporin antibiotic. These extra-label injections are done to prevent infections in eggs and chicks. This represents a massive application of cephalosporins to poultry across the country, and an enormous selection pressure on bacteria to adapt to its presence. Salmonella Heidelberg (S. Heidelberg) has done just that, and antibiotic resistant S. Heidelberg is common in both Canadians and Canadian poultry.

The egg farmers of Quebec lobbied the government to support a voluntary ban on the use of Ceftiofur for eggs and hatchlings in response to data from the 2003 CIPARS report, and were successful. In an analysis of farms around St-Hyacinthe, researchers found that when Ceftiofur was in use, resistant S. Heidelberg was high in humans and poultry. After the voluntary cessation of injections with Ceftiofur, resistance plummeted among samples of S. Heidelberg, demonstrating that there was a clear link between the extra-label application of Ceftiofur and resistance among S. Heidelberg.[26] When some farmers broke from the voluntary ban and began to reintroduce Ceftiofur injections into eggs and hatchlings, the rate of resistance in S. Heidelberg began to rise again as well.

This is a stark example of the connection between resistance in bacteria and broad extra-label applications of antibiotics, and also how we can preserve antibiotic effectiveness. When resistance among bacteria trends upward, the effectiveness of antibiotics in treating infections with them will trend downward. Currently, most species of troublesome enteric bacteria are trending toward resistance to antibiotics, and so the effectiveness of those antibiotics to treat sick people is lessening. As mentioned previously, the FDA has just banned the extra-label application of Ceftiofur to poultry, based on the risk it poses to human health and the effectiveness of antibiotics. Reducing or stopping the extra-label use of antibiotics for mass application to food animals is one important way to reduce the selection pressure on bacteria, and thereby lower the rates of resistance to antibiotics. This case from St-Hyacinthe is unique because the farmers voluntarily gave up the use of Ceftiofur; however, it may be that to make real headway against resistance and to prevent the kind of regression that took place when some farmers broke the agreement, enforceable regulations are called for.

The Volume Of Antibiotic Use In Food Animals

Currently in Ontario, farmers are permitted to use certain antibiotics listed within the Livestock Medicines Act to prevent illness among their animals. Indicated and approved antibiotics are sometimes applied at non-therapeutic doses to prevent disease or promote growth, though these two functions are related. Some non-indicated and unapproved antibiotics are used in a similar fashion, which is called "extra-label" use, since the antibiotics are not being used as indicated. The long-term administration of low doses of antibiotics prevents certain illnesses among herds of pigs and cattle, flocks of sheep and goats, and flocks of chickens, particularly among large numbers of animals held in close quarters. However, this long-term dosing of animals provides a good environment for the selection of resistance because it encourages "survival of the fittest." Infrequent and short high-dose antibiotic treatments pose a lower risk for resistance.[13] Farms are important reservoirs of bacterial resistance because of the high number of zoonotic bacteria in farm animals, the frequent contact between animals and humans at all stages of development and food production, and the current heavy use of antibiotics in farming.

It is crucial to human health that the use of animal medicines that are in the same family as human medicines be very prudent. As mentioned above, bacteria become resistant to entire families of antibiotics because they evolve to resist the way the antibiotic works. This means that antibiotics approved for use in livestock which are in the same family as antibiotics only used for humans will contribute to the resistance of bacteria to human antibiotics.

Information regarding the quantities of antibiotic use in animal husbandry is limited, but available data show that in places where antibiotics are approved for prophylactic or growth-promoting use in farming, many thousands more kilograms of antibiotics are used per year for animals than for humans.[14] For example, in Denmark in 1994 — the year that the Danish ban on extra-label antibiotic use in farm animals was introduced — 24 kg of the antibiotic vancomycin was used for human treatment, while 1,000 times more of the related antibiotic, avoparcin, was used in animal feed.[15] Concurrent rates of VRE began to rise in farm animals in Europe, fueling European bans on antibiotics in agriculture. By 2009, Denmark's total volume of antibiotic use for farm animals was reduced to 65 times the total volume of antibiotics used for humans.[16]

After the European ban on extra-label antibiotic use in animals was implemented, the estimated total consumption of antibiotics across the European Union (EU) and Switzerland was 5,093 tonnes shared between therapeutic use in all food animals and non-therapeutic use in poultry and livestock in 1997.[17] In the same year, approximately the same volume of antibiotics was used for humans, bringing human use of antibiotics slightly above the rate of use for animals, at 52% of the total EU use that year. This nearly 1:1 ratio is much closer to the ideal rate of antibiotic use. Unfortunately, data of this kind is unavailable in Ontario (and Canada), so we are unable to determine if the use of antibiotics in animals is 10, 100, or even 1,000 times the use of antibiotics in humans in this province.

The use of antibiotics in animals that are closely related to those antibiotics used for humans risks the long-term effectiveness of these drugs. As mentioned above, once antibiotic resistance that originates in animal sources has been established in bacterial populations, human health can be adversely affected directly and indirectly. Direct effects include infections resulting from resistant bacteria transmitted from animals to humans. Indirect effects include the transfer of resistance genes from bacteria in animals to bacteria that uniquely affect humans through DNA exchange.[2]

The History Of Bans On The Use Of Antibiotics In Animal Husbandry

Sweden and Denmark were the first countries to introduce progressive bans on the use of antibiotics as growth promoters in food animals in 1986 and 1995, respectively. The European Union was close behind Denmark banning the use of five antibiotics for growth promotion in 1999.[29] In response to calls from public health experts in 2010, the government of the Netherlands ordered a 50% reduction in the use of antibiotics in farm animals by 2014.

The experiences of Sweden and Denmark have been that the initial rates of illness in animal herds (often with diarrhea) were higher after banning certain antibiotic growth promoters, but that after some time (one year in the case of Denmark) illness rates returned to pre-ban levels.[13,18] A frequently used argument against banning antibiotic growth promoters in farm animals in the U.S. and Canada is that Sweden, Denmark, and other European nations suffered farming industry losses as a result of bans, and that they have yet to recover.[18,19,20] However, though there were initial increases in animal illness, various modifications to farming techniques lessened the frequency and impact of infections. Industry representatives from Denmark stated that with changes in animal husbandry — such as giving animals more space, giving piglets longer weaning times, and modifying diets — the farming industry not only recovered, but

has continued to grow at a steady pace since the bans.[13, 21]

That same year, the U.S. Food and Drug Administration prohibited the extra-label use of fluoroquinolones, based on findings that the extra-label use of these antibiotics in food-producing animals presents a risk to human health.[22] After various attempts to limit other antibiotics, in January 2012, the FDA approved a ban on the extra-label use of cephalosporins for disease prevention in groups of animals, mainly eggs or day-old chicks.[23] Cephalosporins are a class of antibiotics that are crucial to the treatment of human diseases. The FDA's ban prohibits the use of cephalosporins at unapproved dose levels, frequencies, durations, or routes of administration, and for disease prevention. Through the ban, certain agricultural applications in the U.S., such as injecting cephalosporin drugs into eggs, which is also common practice in Canada, will be prohibited. The FDA defended the ban by stating that the preservation of the effectiveness of this class of drugs is critical to human health.[23]

In Canada, the federal government and provinces share responsibility for the regulation of antibiotic use in agriculture, with provinces having the ability to add more stringent regulations to federal laws. Ontario is far behind all of the above-mentioned jurisdictions in its approach to the use of antibiotics in animal husbandry. While the FDA continues to make small steps toward limiting the non-therapeutic use of antibiotics in agriculture in the U.S., and many European countries have long-standing bans on such use of some or all antibiotics used for human treatment (e.g., Sweden in 1986, Denmark in 1994, and the European Union in 1999), Ontario does not even have a surveillance system in place to collect information about the volume of use of antibiotics among food animals in the province.

Through a clause in the federal Food and Drugs Act and its Regulations governing an animal owner's "own use" of antibiotics, people engaged in animal husbandry may bring unlimited quantities of antibiotics across Canada's borders from the U.S. and other countries.[24] The clause states that as long as an antibiotic is being transported for a person's private application to an animal that they own (and not for re-sale), they may move antibiotics across the border into (or out of) Canada. While "own use" may sound like a home remedy, it is anything but. This clause allows large amounts of antibiotics into Canada without any surveillance of quantity or guarantees of quality, and also means that agricultural industries can use antibiotics on a large scale in the mass production of food animals. The amounts of antibiotics given to animals are unknown, and veterinarians are rarely consulted in this practice. While this clause in the Food and Drugs Act is important to owners of animals that require antibiotics for therapeutic use, it allows producers of food animals to purchase and apply unknown quantities of antibiotics for non-therapeutic and extra-label use, without surveillance. In this way, the use of antibiotics in farm animals is unscientific and unregulated. The import and export of antibiotics is legal under present regulations, but unsupervised and unaccounted for, and this should be corrected.

Ontario would benefit from the establishment and implementation of a surveillance system for the import of all antibiotics for animal use. Such systems have been in place in many other countries for decades, and it is surprising that neither the province nor the federal government have implemented such a system here. Ontario's food animal industries might be well served by re-evaluating the current standards for the extra-label administration of antibiotics in animal feed, since the province's comparatively lower standards not only jeopardize human health, but also trade relations with other jurisdictions with stricter standards, such as Europe and the U.S.

When Antibiotics Stop Working

When antibiotics became available in the 1940s and 1950s, they were miraculous. For years, penicillin was a great and powerful cure for many infections. After a few decades, penicillinase-producing staphylococcus bacteria, which are resistant to penicillins, evolved. Penicillins no longer worked to treat patients with such infections; instead, physicians had to use methicillin. Methicillin was wonderful in the 1970s; within 24 hours a physician could see improvements in a patient's condition. After another 25 years, MRSA evolved, which is resistant to methicillin and all other penicillins and cephalosporins. At present, there are a few effective antibiotics to use against MRSA, but these bacteria have multiple resistances, and the drugs have higher toxicities.

Though the evolution of resistance among bacteria has always been a possibility and a threat to the effectiveness of antibiotics, recently, resistance has reached levels in humans that are significant enough to create concern among medical experts, public health officials and government bodies. There are three important results of the proliferation of antibiotic resistant bacteria for human health.[2,13,27] These are:

1. Higher incidence, longer duration, and greater severity of illnesses. More people will get sick for longer periods of time, and they will be more seriously ill than they would have previously been with an infection of the same bacteria.
2. Higher rates of mortality from treatable bacterial infections. More people who get sick with bacterial infections that have

been easy to treat for many decades will end up dying from them as resistance to our available antibiotics increases.

3. Longer stays in hospital and more aggressive treatments, sometimes involving drugs with higher toxicity. Resistant bacterial infections are more difficult and expensive to treat than susceptible infections. As people become sick with resistant bacteria, older, less familiar, and more dangerous antibiotics will be applied to try to save their lives.

Antibiotic resistance is a challenge to medicine both because the resistance may be invisible to physicians due to the nature of an infection with resistant bacteria, and because, in some cases, resistance creates very difficult challenges for physicians struggling to help the patient. If a patient has a bladder infection caused by bacteria and it is treated with a drug that the bacteria are resistant to, the treatment will fail. However, because bladder infections, though uncomfortable, are often self-limiting, the physician who prescribed the antibiotic that failed may not see the patient again or find out that the antibiotic was ineffective. The patient will get better on his or her own. On the other hand, if a patient has an infection and continues to get worse after the first prescription fails, physicians find themselves up against medical uncertainty with regard to which available antibiotics might still be able to treat this infection, and what the outcome of using these on the patient might be.

As bacteria develop resistance to the antibiotics we currently use, treating infections from these bacteria becomes much more difficult. A daunting set of complications caused by antibiotic resistance contribute to a greater risk of serious illness and death for patients: the decreased effectiveness and/or higher toxicity of antibiotics that are still effective for treatment of antibiotic resistant bacteria; the delays in treatment with an effective antibiotic, when physicians notice that their first choice is ineffective and they need to find an alternative; the total absence of an effective antibiotic in some circumstances; and the increased need for surgery or other procedures as a result of resistant bacterial infections that antibiotics are not effectively treating.[3]

Concluding Recommendations

Hitherto, the onus has been on public health professionals to prove the link between antibiotic use and antibiotic resistance among bacteria. The evidence is now pointing directly to the rise of antibiotic resistance and our overuse of antibiotics in various contexts. We know that resistance may happen even with the most prudent use, so our challenge is to reduce antibiotic use in all the places that we are able to in order to stem the tide of resistance as antibiotics become less effective. We are jeopardizing a valuable resource in Ontario, and antibiotic stewardship is a commitment not just for physicians and farmers, but for everyone, including veterinarians, pharmacists, nurses, patients, pet owners, and parents.

It is crucial that the Government of Ontario address the use of antibiotics and the development of resistance. The province should develop a system for food industry surveillance to keep track of the identities and quantities of antibiotics being purchased, sold, and moved into or out of Ontario. Surveillance should be established in areas where it does not exist (such as import/export of agricultural antibiotics) and strengthened in areas where it does exist (such as human medical settings) in order to collect data and gain a firmer understanding about antibiotic resistance in both humans and animals.

Electronic health records should be engaged to allow physicians encountering patients for the first time, or in tertiary care settings, to compare patients' past prescriptions and diagnoses. This would allow physicians in the community, hospital, emergency department, or long-term care facility to make optimal decisions about which antibiotics to prescribe to patients. An independent provincial institution should be established in conjunction with one of Ontario's medical schools to use currently available data to develop and maintain optimal antibiotic use guidelines that physicians in Ontario can use to guide their practice, particularly when dealing with resistant bacteria and unfamiliar antibiotics.

Additionally, Ontario should ban the prophylactic or growth-promoting use of antibiotics, whether extra-label or indicated, in animal husbandry. Jurisdictions such as Europe and the U.S., which happen to be important trading partners, have already taken these measures. A veterinary prescription-only standard of access to, and application of, antibiotics for animals must be established. These measures would entail amendments to Ontario's Livestock Medicines Act, to close the "own use" loophole created by the Food and Drugs Act and its Regulations, and ensure that large volumes of antibiotics could not be freely imported into the province and be applied to animals en masse without surveillance or regulation.

Finally, the federal government must engage in antibiotic conservation, and amend the Food and Drugs Act and its Regulations to close the "own use" loophole. People importing and exporting antibiotics should be held to the same standards regardless of their reason, and national surveillance should be established to allow the collection of data about which antibiotics are entering our country, and their intended use. The federal government should also provide funding for research and educational campaigns focused on

Appendix

A Quantification Of Antibiotic Resistance

There is a trend toward greater levels of resistance among bacteria in all places where the use of antibiotics is high. Surveillance of antibiotic resistance in food animals is currently performed in Canada. However, a national surveillance mechanism for the development of antibiotic resistance among bacteria specific to humans is non-existent. The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) collects samples of Salmonella strains from humans, and a variety of bacterial species from food animals. Despite the dearth of human surveillance data, the data CIPARS collects from animals are an important indicator of the impact of antibiotic resistance on human health, because the bacterial species that are tracked are all zoonoses, which means that these bacteria pass easily between animals and humans.

Salmonella

CIPARS data from 2009[28] show that among the Salmonella isolates collected from humans in Ontario, two of the most common strains (Salmonella Heidelberg and Salmonella Typhimurium) are resistant to antibiotics in all three lines (first-line antibiotics are the most important). Other strains of Salmonella have been found to be resistant to second-line and third-line antibiotics. According to CIPARS, however, large variations in rates of resistance among Salmonella over time make it difficult to get a sense of a clear upward or downward trend. It is also difficult for researchers to capture all the various strains from human samples.

CIPARS data is more robust from animal samples in terms of species of bacteria collected and the ability to track resistance trends. Salmonella strains from beef cattle showed over 40% resistance to a number of second-line and third-line antibiotics. In retail chicken meat in Ontario, Salmonella strains were 40% resistant to Ampicillin, Streptomycin and Tetracycline, with over 20% resistance to a variety of first-line and second-line antibiotics. Data show that resistance among Salmonella isolates recovered from chicken is increasing over time in the province. In pigs on farms, Salmonella isolates are 40% resistant to four important antibiotics, and abattoir surveillance found similar levels of resistance. Salmonella resistance in pigs is generally trending upward.

E. Coli

Escherichia Coli (E. Coli) surveillance shows similar increasing trends in resistance. In abattoir surveillance of beef cattle, E. Coli isolates were over 20% resistant to second-line antibiotics. Surveillance of retail beef in Ontario yielded the same results, and resistance is trending upwards in the province. Abattoir surveillance of chickens in Ontario showed that E. Coli isolates were 40% resistant to important first-line and second-line antibiotics. In farm surveillance of pigs, E. Coli isolates were over 75% resistant to Tetracycline (a third-line antibiotic), and 40% resistant to Ampicillin and two other antibiotics. Abattoir surveillance of pigs yielded the same results. Levels of resistance among pigs on farms and in abattoirs are holding steady or slightly increasing. Retail meat surveillance of pigs in Ontario shows that E. Coli is 35% resistant to Tetracycline. E. Coli resistance to antibiotics in retail pig meat in Ontario is increasing for all antibiotics except four, including Tetracycline, which are holding steady.

Campylobacter

Campylobacter species (C. Jejuni and others) have very high levels of resistance to important classes of antibiotics, some of which is due to intrinsic resistance. In abattoir surveillance of beef cattle, Campylobacter isolates were over 80% resistant to a second-line synthetic quinolone (Nalidixic Acid), which is commonly used to treat it, and over 40% resistant to Tetracycline. In retail meat surveillance of chickens in Ontario, Campylobacter isolates were 40% resistant to Tetracycline. Samples of species of Campylobacter except C. Jejuni and E. Coli taken from chicken were 100% resistant to Ciprofloxacin, a first-line antibiotic, and Nalidixic Acid.

Enterococcus

Retail meat surveillance of chicken in Ontario revealed that Enterococcus bacteria are over 50% resistant to second-line antibiotics, and over 80% resistant to some second-line and third-line antibiotics. Specifically, Enterococcus Faecium was 100% resistant to Lincomycin (second-line), and over 60% resistant to at least six other first-line, second-line, and third-line antibiotics. Farm surveillance of pigs showed that Enterococcus is over 60% resistant to second-line antibiotics, and over 80% resistant to Lincomycin and Tetracycline. Levels of resistance in Enterococcus among pigs is holding steady or slightly increasing over time, while Enterococcus resistance among chickens is very high but may be trending downward in Ontario.

antibiotic resistance. There is a dearth of community-based and hospital-based surveillance of organisms and resistance patterns, and this must be rectified.

Everyone who has access to antibiotics must use them in a responsible and prudent manner. Patients must work alongside physicians to modify the expectations of receiving antibiotics for certain infections, even if patients have received antibiotics in the past for similar complaints. Disposing of antibiotics safely, and not sharing antibiotics with anyone else, are both crucial to maintaining the efficacy of antibiotics. All parties, including the expanded number of allied health-care professionals, dispensing parties (pharmacists), physicians, and patients need to become more aware of the importance of this issue and incorporate that knowledge into their own practice and use.

Collectively, we have to do the utmost to preserve the effectiveness of antibiotics at fighting infections. There may be short-term drawbacks, particularly in animal husbandry, but the reduction of unnecessary antibiotic use is in the best interests of humans and animals in the long term. Slowing the evolution of resistant bacteria now is the only way to ensure that our antibiotics will still treat human and animal infections in five or 10 years. Increasing antibiotic resistance is an urgent issue that affects us all, and is within our power to change.

Permission And Citation

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Footnotes

i. Throughout this paper we use the term “antibiotic resistance” to refer to the ability of bacteria to resist treatment by antibiotics and antimicrobials and the term “antibiotic” to refer to both of these, given the close relation of these substances and the popular understanding of the term “antibiotic” outside of medical circles.

ii. Unless otherwise referenced, patient examples are drawn from the experiences of physicians in Ontario.

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