

BETWEEN THE SPECIES

Issue VIII

August 2008

cla.calpoly.edu/bts/

The Social Contract, the Conservative Attitude, and Antibiotics Development

Eli Weber

Colorado State University

Abstract

The prevalence of antibiotic resistant microbes has led to a call for new antibiotics development. Due to the irresponsible practices of the medical community in prescribing antibiotics, much of the demand for new antibiotics is suspect. I argue that the social contract, which properly includes human relationships with laboratory animals, requires a conservative attitude toward new antibiotics development. This attitude places limits on the justificatory role of demand in determining whether a particular research project meets the conditions for morally justified research, as defined by Rollin's utilitarian principle.

Identifying the Scope of the Problem

Antibiotic resistant microbes are a major public health concern, and medical practitioners are currently calling for newer and more potent antibiotics, despite the scientific challenges of developing these products and the low rate of return for pharmaceutical companies. Many factors lead to the existence of antibiotic resistant microbes, and there is significant empirical data suggesting that human prescribing practices are a major contributor to this phenomenon. Laboratory animals endure great suffering and death in order for antibiotic drugs to reach the market, and it seems that the pursuit of new pharmaceutical products without comparable or even greater emphasis on changing dysfunctional human activities is a violation of the social contract with animals. This

contract is apparent in both the companion and husbandry sector of human-nonhuman relationships, and properly belongs in the research arena as well.

In this paper, I will focus on a particular area of pharmaceutical research, the development of new antibiotics. I will first present the theoretical background of the argument that the social contract with companion and agricultural animals also applies to laboratory animals, and that the social contract should include cultivation of a conservative attitude toward using animal products. I will then provide empirical evidence to support the claim that the demand for new pharmaceuticals is artificially high, and that human behavior is a significant cause of the need for new antibiotics. Finally, I will argue that the conservative attitude inherent in the social contract requires us to make an effort to address the human causes of antibiotic resistant diseases, rather than subjecting laboratory animals to painful and stress-inducing procedures in order to meet this artificial demand for new antibiotics.

Pharmaceutical Research and the Utilitarian Principle

Bernard Rollin argues that laboratory animal research should conform to the utilitarian principle, which requires that “the benefit to humans (or humans and animals) clearly outweighs the pain and suffering experienced by the experimental animals.”¹ Rollin states, however, that it is impossible to use the utilitarian principle in evaluating drug research, as there is no way of knowing when a given chemical is likely to be of therapeutic value. In this section, we will consider some implications of the utilitarian principle in light of the statistical realities of antibiotics development and argue that the utilitarian principle, although helpful, is not sufficient for evaluating the moral appropriateness of antibiotic development research.

Despite the outcries of abolitionists, not all animal research is unjustifiable, and some laboratory animal suffering is justified under ideal conditions. Applying the utilitarian principle to pharmaceutical research ought to require that we consider the extent to which demand for new pharmaceuticals is artificially increased by the irresponsible practices of both medical professionals and consumers, as assessing this factor is critical to evaluating the legitimacy of the necessary animal suffering involved in new research projects. This

becomes difficult when evaluating the demand for new antibiotics, in light of the prevalence of infectious diseases, which kill approximately 14 million people per year.² Many infectious diseases are exceedingly uncomfortable and lead to a significant amount of human suffering. In addition, current literature indicates the proliferation of ever stronger strains of microbes, many of which are resistant to all but the newest and strongest antibiotics available. Thus, we are easily influenced by the reality of mass human suffering associated with antibiotic resistant infections.

Although we are compelled to consider dysfunctional human behavior in evaluating antibiotic development, it is not clear that we can do this effectively by applying the utilitarian principle. The utilitarian principle does not allow for secondary considerations such as the source of demand for a product.³ By focusing on the balance between suffering and likely benefit, the utilitarian principle is an effective way to limit research to that which is truly necessary, but it fails to account for the dysfunctional causes of the necessity that it evaluates. For example, the utilitarian principle might allow for development of a new antibiotic to treat tuberculosis, provided that the benefit is likely to exceed the animal suffering associated with the drug's development. However, the utilitarian principle lacks a mechanism for considering that a significant source of need for new antibiotics to treat tuberculosis is human-caused. Many tuberculosis sufferers fail to complete their treatment regimens as directed, leading to the need for a second round of antibiotics that are much stronger. Inadequate exposure in the first treatment cycle allows microbes to develop a resistance to the initial treatment regiment, and an antibiotic resistant microbe is created. The utilitarian principle has no means for taking facts of this sort into consideration.

We might also consider some implications of applying the utilitarian principle to pharmaceutical research. Rollin cites statistics indicating that the ratio of beneficial substances to substances that are tested ranges from one in ten thousand to one in one hundred thousand.⁴ Even a conservative estimate of one in five thousand indicates that numerous instances of animal suffering and death are for no identifiable purpose, other than the exceedingly unlikely possibility that testing will result in a marketable substance. A .02% success rate does not seem to meet the requirements of the utilitarian principle,

even without the additional considerations that we are suggesting. We have some reason to believe that the utilitarian principle does support a significant reduction in development of new antibiotics, simply due to the exceedingly unlikely possibility that the associated suffering will lead to any measurable benefit.

It is noteworthy that a lack of basic understanding of infectious diseases has been cited as a significant contributor to the lack of success in developing new antibiotics.⁵ Most currently used antibiotics were developed in the 1970's, and no new class of antibiotics was discovered during the 1970's, '80s, and '90s. One hypothesis for resolving this issue is that greater knowledge of systems biology would be helpful in improving this abysmal record. Subjecting animals to painful testing procedures is difficult to justify when researchers lack the relevant knowledge of infectious diseases that would make their research more productive. Obtaining such knowledge would likely reduce the number of failed drug trials, resulting in a net reduction in animal suffering and allowing some pharmaceutical research to be justified by the utilitarian principle. Until such knowledge is acquired, however, it is not clear what percentage of antibiotics research projects are justified, regardless of the potential benefit that a particular project might have. It seems that the utilitarian principle is somewhat inadequate in determining the moral appropriateness of a particular research project, which leads to the necessity of the social contract model in evaluating laboratory animal research.

The Social Contract and the Conservative Attitude

The social contract is significant in defining the parameters of appropriate treatment for both companion animals and agricultural animals. It seems that the social contract equally applies to laboratory animals, due to a similarly reciprocal relationship. The social contract requires not only a certain level of treatment and respect for animals, but also a conservative attitude toward use of animal products. In this section, we will consider the feasibility of extending the social contract model to research animals, as well as supporting the importance of the conservative attitude that we are advocating.

The social contract is relevant to human relationships with both companion and agricultural animals. The social contract is essentially an agreement to treat others in a

certain way provided we are treated the same way in return.⁶ Although social contracts between humans and animals are implicit, they remain morally relevant. In the case of companion animals, human beings receive numerous benefits as a direct result of having animals in their lives. Our pets comfort and console us, providing unconditional love that few humans are capable of. The significance of this is well-documented, as companion animals have been utilized in treatment of mental illnesses and credited with improving quality of life for invalids and the elderly. This contribution is in addition to the more conventional benefits that many of us experience as a result of having pets. The social contract entails that because animals have given up their wild natures in order to live with humans and provide benefits to us, we owe them a reciprocal degree of respect and appropriate treatment.

The social contract is even more apparent, and perhaps more directly comparable to laboratory animals, in the institution of animal agriculture. To state the nature of this version of the social contract as basically as possible, “we (humans) take care of the animals, and they take care of us.” This means that the sacrifices associated with providing food, products, and a livelihood for humans necessarily entails a moral obligation to the animals. Agricultural animals uphold their end of the social contract by providing us with nutritious food and useful products. Our end of the social contract is to provide for the well-being and basic interests of agricultural animals, including adequate space, relevant enrichment, and attention to physical and psychological needs.⁷

Both agricultural and companion animal relationships provide a comparable model for the relationship between human beings and laboratory animals. In each of these arenas, animals have equally given up their wild natures and submitted to less than ideal conditions for the benefit of humans. Humans are obligated, by the social contract, to make a concerted effort to meet the interests of the animals to the greatest extent possible. Certain degrees of suffering and mistreatment are not acceptable for any reason under the conditions of this contract. Laboratory animals “take care of us” by providing life-saving and health improving products. In much the same way, companion and agricultural animals provide a measureable benefit to humans. As the social contract model suggests,

by choosing to have these types of relationships with animals, humans have entered into a social contract that requires a certain degree of treatment and care.

The social contract requires that humans exhibit some degree of personal responsibility for their choices. Rollin is highly critical of the current environment of irresponsible behavior toward pet animals and the resulting social institutions, which implicitly support an attitude of indifference toward animal interests. One such example of this institutional support concerns the legislation designed to protect animals. Although strides have been made, companion animals are still viewed primarily as property, and pet owners are granted the discretion to do as they wish with their property. As a result, mutilation procedures like declawing and ear clipping are commonplace, and there are no legal repercussions for morally reprehensible acts like euthanizing a dog rather than paying to board it while the owner is on vacation. These are clear examples of pet owners violating the basic rights of companion animals for their own convenience. This lack of individual responsibility toward companion animals represents a clear violation of the social contract. Humans are failing miserably in upholding their half of the contract, treating animals as mere property and means to our ends without regard for their most basic interests.

The social contract also requires a conservative attitude toward the use of animal products. A conservative attitude is a disposition of respect for animal sacrifices that allow for certain products to be available, and a devaluing of purposeless waste. The historical tendency of Native Americans to use all parts of the buffalo, as well as showing respect for the animal before killing it, is a paradigm example of this attitude (although the historical accuracy of this depiction is somewhat suspect). Rollin's discussion of the importance of personal responsibility in caring for pet animals is another example of the conservative attitude. The conservative attitude is equally present in the social contract with agricultural animals. Throwing away beef that could easily be eaten or wasting eggs on petty acts of vandalism, for example, would not be acceptable to most individuals who recognize the social contract. If an animal suffers in order that we might benefit, it is reasonable to claim that humans have a moral obligation to honor and respect this sacrifice by not wasting animal products.

The conservative attitude toward companion and agricultural animals that we have identified is readily applicable to the social contract with laboratory animals that we are suggesting. Consider the following example. A beef cow is born and raised for the purpose of providing meat for humans. Inevitably, some suffering or discomfort is likely in this animal's life, despite our best effort to minimize such conditions. In addition, this animal will eventually give its life so that we might live. This sacrifice requires humans to be conscientious of our use of meat. It would not be justifiable to increase meat production simply so that humans could waste meat products haphazardly. What reason could we possibly give for facilitating such a practice? Certainly any reason that might be offered would seem superficial and inadequate in light of the requisite animal suffering involved. Analogously, a lab mouse might spend its natural life having new antibiotics tested on it. This animal will also experience suffering despite our best effort to minimize such conditions. Ultimately the animal will die, often at the conclusion of a research project and possibly as a direct result of the products tested upon it. This animal has also made the "ultimate sacrifice" in order to benefit humans. If we would not be justified in increasing meat production to facilitate irresponsible human behavior, it follows that we should not increase pharmaceutical testing in order to facilitate irresponsible behavior. Such actions would equally represent a violation of the social contract with animals, and a failure to embrace the conservative attitude that the social contract requires.

The Problem of Antibiotic Resistant Microbes

Antibiotic resistant microbes are an increasingly significant concern in the medical community, and medical practitioners are calling for newer and more potent antibiotics. A brief review of the problem is therefore necessary if we are to understand the tendency to justify all antibiotic development research as necessary and the challenges associated with rejecting this justification.

Concerns regarding antibiotic resistance emerged in the late 1990s,⁸ and it is typically cited as a major concern for medical practitioners. Current statistics conclude that up to 70% of all infectious bacteria are resistant to at least one commonly prescribed antibiotic,

and resistance is predicted to increase at 4% to 7% per year. This problem is especially significant in the developing world, where it is often difficult to acquire large quantities of newer antibiotics. This is compounded by the exceedingly difficult nature of antibiotic development, and the fact that many pharmaceutical companies do not invest heavily in the development of new antibiotics, due to the low rate of return compared with drugs designed to treat long-term illnesses.

Despite these challenges, many new antibiotics are being developed, with 7 new drugs receiving FDA approval in 2005, out of 81 approvals that same year. In addition, approximately 18 new antibacterials are currently being tested. These numbers seem insignificant until we consider the conservatively estimated success rate of .02% cited earlier. The 7 drug approvals from 2005 are the result of 35,000 substances tested, while the 18 drugs currently in clinical trial might have as many as 90,000 unmarketable substances in their histories. Based on the significant need for better antibiotics, however, many researchers are calling for new drugs to be developed despite these technical challenges.⁹

This cry for help is potentially problematic in light of the necessary animal suffering involved with such development activities and the well-documented correlation between medical practices, patient expectations, and overprescription of antibiotics. An analysis of the irresponsible human practices fueling the need for newer antibiotics indicates that, although the current situation is somewhat supportive of a push for new antibiotics, much of the demand for stronger drugs is artificially enhanced and not morally justifiable.

The Case for Human Behavior as a Cause of Artificial Demand

There is a significant body of research which supports the claim that human practices of antibiotic prescription are excessive and dysfunctional, and that this is a significant contributor to the emergence of antibiotic resistant diseases, as well as a driving force in the call from the medical field for newer and more potent antibiotics. Establishing that the demand for new antibiotics is artificially high requires that we draw a correlation between antibiotic resistance and dysfunctional human behaviors. A majority of research concerning the problem of overprescription centers around the habits and attitudes of

medical practitioners, but a small percentage of this literature also considers the role of patient expectations as a relevant contributor to this issue. We will consider this minority cause before turning to the role of physician behavior as the primary source of artificial demand for antibiotics.

There is much evidence to support the claim that patient expectations are a significant contributor to the overprescription problem. The most common manifestations of this problem are patient pressure exerted on doctors,¹⁰ patient assumptions that new and innovative antibiotics are always better and therefore desirable,¹¹ and patient failure to follow treatment protocols.¹² A 2007 survey of practitioners in Ireland supports the claim that patient behaviors are a contributing factor to overprescription of antibiotics, citing 54.7% of respondents who strongly agreed with the claim that patients often expect a prescription for antibiotics, even when inappropriate. 22.7% of responding physicians reported feeling under pressure to prescribe antibiotics for patients.¹³ This suggests that patients are not only making it clear that they expect to be given antibiotics, but that doctors are somewhat influenced by this expectation.

Additional data also supports the claim that this pressure from patients is having an effect on doctor prescribing patterns. A 2007 article in *Pharmacotherapy* cited data from a survey of British patients with respiratory conditions, 72% of whom reported expecting antibiotic therapy. The physicians who prescribed antibiotics reported that antibiotic therapy was only clinically indicated in 20% of the surveyed patients. Another 20% of prescribing physicians reported writing a prescription in order to get the patient out of the office, rather than out of clinical necessity.¹⁴ It seems that patients seeking medical care have certain expectations for treatment, and physicians are responding in an effort to placate them. Not only is this problematic in light of the emerging problem of antibiotic resistance, it is also a violation of the social contract with laboratory animals that we are advocating. Reckless use of valuable medicines is not consistent with the conservative attitude required by the social contract, and statistical data provided supports the claim that a significant amount of current antibiotics use is frivolous, unnecessary, and responsive to dysfunctional social norms concerning medical care. It would seem difficult to justify the development of new antibiotics without first addressing these

irresponsible social behaviors, and their measurable impact supports our claim that much of the demand for new antibiotics is artificial.

If the problem of overprescription is to be addressed realistically, medical practitioners must also be held accountable for their contribution to this growing concern. To some extent, the previously discussed problem of patient expectations is properly a problem with practitioners as well. As professionals, their own ethic should require them to make responsible decisions, regardless of patient expectations which are often naïve and uninformed. However, in an environment of fee-for-service medical care, it is difficult to remain unreceptive to patient expectations. The line between patient and customer is blurry, making it difficult to separate between doing what is medically- indicated and satisfying the customer.

Economic concerns aside, there are several prominent causes of overprescribing antibiotics that are more directly related to physician protocols. The Journal of the Canadian Medical Association cites four causes of inappropriate prescribing behaviors among physicians. Lack of physician knowledge, lack of experience, training environment that supports overprescribing, and avoidance of time-consuming patient education are all significant contributors to the problem of overprescribing antibiotics.¹⁵ These essentially break down into two categories: ignorance of relevant data, and influence of external factors.

Ignorance-based causes of overprescribing are perhaps the easiest to resolve. Lack of experience with prescribing is something of an unavoidable phenomenon, although the minimal time invested by medical schools to educate their students on responsible treatment protocols is a contributing factor,¹⁶ and adequate supervision of new physicians would likely alleviate most of this problem. The greater concern in this category is the problem of genuine ignorance about proper prescribing protocols among knowledgeable medical professionals. One source of this ignorance is poor judgment of treatment outcomes.¹⁷ Many physicians are not very good at knowing what treatment is likely to succeed, so they err on the side of caution and prescribe antibiotics. Other sources of genuine ignorance among physicians include not understanding what treatment protocols

are appropriate. For example, despite numerous studies supporting the conclusion that antibiotics are not effective in treatment of the common cold, antibiotics are regularly prescribed for cold sufferers.¹⁸ This practice remains dangerously typical despite the obvious common-sense conclusion that antibacterials are not an effective treatment for a viral infection, which common colds tend to be. Improper prescribing behavior of this kind is caused by physician reliance on outdated information, fear of undertreatment, and misguided beliefs.¹⁹ The belief that antibiotics will not hurt but may help is especially problematic, as it clearly represents a lack of understanding of the problem of overprescription, as well as a failure to display the conservative attitude that the social contract requires.

Physicians are not solely responsible for the phenomenon of overprescription, and the irresponsible behavior of physicians is often externally influenced. We have already mentioned the influence of patient expectations and economic considerations. We might also mention one of the cited hypotheses that antibiotics are prescribed in order to avoid time-consuming patient education. This is symptomatic of the nature of our medical system, which focuses on economic goals rather than optimal treatment protocols. Many physicians are evaluated and paid at a piecemeal rate, and their self-interest motivates them to maximize the number of patients seen per day. In addition, patient expectations require that medical practitioners explain complicated medical scenarios to individuals who may not be well equipped to understand, and in a manner that is sufficient to overcome a patient's preconceived notion of what is necessary. Quite simply, it is easier to write a prescription than it is to engage in this trying educational endeavor.

The most significant external influence on physician prescribing behaviors is that of the pharmaceutical industry itself. Due to the challenges of keeping physicians up to date on the latest medical research on pharmaceuticals, many physicians get a large portion of their continuing education directly from pharmaceutical representatives. In addition, the close relationship between the industry and individual physicians can lead to a conflict of interest. Many physicians receive personal benefits from prescribing as many antibiotics as possible, with higher compensation rates for new antibiotics. Finally, the prevalence

of pharmaceutical advertising supports patient attitudes that antibiotic treatment is always preferable, and that unnecessary prescriptions do no harm.

There are many additional issues that contribute to the problem of overprescribing antibiotics. Our intention is simply to illustrate that the demand for new antibiotics is being affected by a wide variety of dysfunctional practices of both physicians and patients, and that the demand for new antibiotics is therefore somewhat artificial. Much like the problems associated with companion animal treatment, many irresponsible individual activities in the medical field are being buttressed by the social institution of overprescription. Just as animal shelters should be utilized conservatively so as to prevent reinforcing dysfunctional attitudes toward companion animals, development of new antibiotics should also be conservatively approached so as to encourage self-correction of these problems and prevent the unjustified suffering of laboratory animals that would be necessary if the artificially high demand for new antibiotics were to be met.

Application of the Formal Argument

We have thus far presented the philosophical background supporting an extension of the social contract to research animals and argued that the social contract necessitates a conservative attitude toward the use of animal products. We have utilized relevant empirical data to support the claim that the demand for new antibiotics is artificially enhanced by irresponsible human behaviors. We now turn to a formalization of our main argument in an effort to clarify its conclusions.

The following represents the argument presented in a basic format:

- 1) The social contract requires a conservative attitude towards use of products that rely on animals, directly or indirectly, for their development.
- 2) Personal and professional responsibility are important features of this conservative attitude, and failure to act as such is a violation of the social contract.

- 3) Demand for a product that is artificially increased by irresponsible human behaviors does not provide sufficient justification for animal suffering.
- 4) The demand for new antibiotics has been artificially increased by irresponsible human behaviors, which manifest in the practice of overprescription.
- 5) From 3 and 4, animal suffering for the purpose of developing new antibiotics is not justified solely by reference to the demand for new antibiotics.
- 6) From 2 and 4, the call for new antibiotics and the practice of overprescription do not reflect the conservative attitude of personal and professional responsibility that is an important feature of the social contract.
- 7) From 1 and 6, the call for new antibiotics and the practice of overprescription are violations of the social contract.

Premise 1 assumes that the social contract applies to laboratory animals and that the conservative attitude is a key component of the social contract, as we argued earlier. Premise 2 is an articulation of what the conservative attitude entails and is based on extending Rollin's claims regarding personal responsibility and companion animals to other areas of human-nonhuman relationships. Premise 3 is perhaps the most controversial, relying on the content of Premises 1 and 2 in order to support the notion that personal responsibility and the social contract do not allow for demand to be haphazardly referenced as justification for certain actions that cause harm. Premise 3 also relies on common-sense notions of how valuable products should and should not be used. Inclusion of the term "sufficient" is significant, and is intended to limit the influence of artificial demand for antibiotics without eliminating the relevance of legitimate demand. The claim is simply that demand alone, if it is artificially enhanced, does not morally justify testing new antibiotics on animals. Premise 4 is based on the empirical data presented which supports the claim that dysfunctional human behavior is increasing the need for new antibiotics. We are left with three relatively uncontroversial conclusions, namely that animal suffering for the purpose of developing new antibiotics is not justified solely by reference to demand, that the call for new antibiotics and the

practice of overprescription are not consistent with the conservative attitude properly associated with the social contract, and that the call for new antibiotics and the practice of overprescription are violations of the social contract with research animals.

We should note that this argument does not lead to the conclusion that no new antibiotics can ever be developed. Our claim is simply that the appropriate conservative attitude toward antibiotic development, as necessitated by the social contract, does not allow us to justify developing new antibiotics solely on the basis of demand, since much of the demand is artificially influenced by irresponsible human behaviors. At an absolute minimum, efforts should be made to address the problem of dysfunctional human behaviors before substantial investment in antibiotic development is undertaken.

Antibiotic development is becoming increasingly difficult from a scientific standpoint, and it is in our interest to curtail the wasteful practices of patients and physicians so that future new antibiotics are not wasted without maximizing the utility of their potential.

Animal interests aside, we have good pragmatic reasons to adopt the conclusions of this argument. We also have good reasons, from the standpoint of animal rights, to adopt the conservative attitude necessitated by the social contract and apply it to evaluating new antibiotics development projects.

Conclusion

In the case of developing new antibiotics, once we incorporate the appropriate conservative attitude required by the social contract, the utilitarian principle does support a reduction in research on new antibiotics, at least until the problems of overprescription are addressed. The challenge of applying the utilitarian principle in this area is that we are tempted to justify a great deal of suffering in order to allow for significant breakthroughs to take place. This is not surprising in light of the prevalent devastation of infectious diseases worldwide. However, based on the empirical data presented, the conservative attitude required by the social contract makes it difficult to justify a good deal of suffering that the utilitarian principle might have allowed us to overlook.

Although the utilitarian principle is an important starting point for evaluating research, we should also consider the source of demand for new antibiotics by applying the

conservative attitude of the social contract. This will result in more stringent criteria for morally justifiable antibiotics development research that utilizes animal testing, protecting laboratory animals from unjustifiable suffering. It will also force both consumers and medical practitioners to be more cautious in their attitudes toward appropriate use of antibiotics. By adopting the conservative attitude, both human and non-human may benefit.

References

- Brehaut, Jamie. "Do physician outcome judgments and judgment biases contribute to inappropriate use of treatments?" *Implementation Science* Vol.2 2007.
- Cadieux, Genevieve, Robyn Tamblyn, Dale Dauphinee, and Michael Libman. "Predictors of inappropriate antibiotic prescribing among primary physicians" *Canadian Medical Association Journal* Oct. 9 2007.
- Cotter, M. and L. Daly. "Antibiotic prescription practices of general practitioners" *Irish Medical Journal*, Vol. 100, Issue 9 2007.
- Ebert, Steven C. "Factors contributing to excessive antimicrobial prescribing" *Pharmacotherapy*, Vol. 27, Issue 10, Part 2 2007.
- Kumble, K.D. "Anti-Bacterial Drug Discovery Using Systems Biology", *Mini-Reviews in Medicinal Chemistry* Vol.6, No.11 2006.
- Liu, J. and H.P. Ren. "Tuberculosis: Current Treatment and New Drug Development" *Anti-Infective Agents in Medicinal Chemistry* Vol. 5, No. 4 2006.
- Rollin, Bernard. *Animal Rights and Human Morality* (Amherst, NY: Prometheus, 2006).
- Rollin, Bernard. *Farm Animal Welfare* (Ames: Iowa State Press, 1995).
- Sharma, Rashmi. "Antibacterial resistance: Current problems and possible solutions" *Indian Journal of Medical Sciences*, Vol. 59, Issue 3 2005.
- Simasek, Madeline and David A. Blanding. "Treatment of the Common Cold" *American Family Physician* Vol. 75, No. 4 2007.

¹ Bernard Rollin, *Animal Rights and Human Morality* (Amherst, NY: Prometheus, 2006) 183.

² K.D. Kumble, "Anti-Bacterial Drug Discovery Using Systems Biology", *Mini-Reviews in Medicinal Chemistry* Vol.6, No.11 2006: 1275.

³ Based on Rollin's discussion of how this principle is applied, from *Animal Rights and Human Morality*.

⁴ Bernard Rollin, *Animal Rights and Human Morality* (Amherst, NY: Prometheus, 2006) 279.

⁵ K.D. Kumble, "Anti-Bacterial Drug Discovery Using Systems Biology" *Mini-Reviews in Medicinal Chemistry* Vol.6, No.11 2006: 1276.

⁶Bernard Rollin, *Animal Rights and Human Morality* (Amherst, NY: Prometheus, 2006) 51.

⁷ See Rollin's *Farm Animal Welfare*.

⁸ Rashmi Sharma, "Antibacterial resistance: Current problems and possible solutions" *Indian Journal of Medical Sciences*, Vol. 59, Issue 3 2005: 120.

⁹ See Sharma 2005, Kumble 2007, Liu and Ren 2006, and Ebert 2007.

¹⁰ M. Cotter and L. Daly "Antibiotic prescription practices of general practitioners" *Irish Medical Journal*, Vol. 100, Issue 9 2007: 598.

¹¹ Steven C. Ebert "Factors contributing to excessive antimicrobial prescribing" *Pharmacotherapy*, Vol. 27, Issue 10, Part 2 2007: 1275.

¹² J. Liu and H.P. Ren "Tuberculosis: Current Treatment and New Drug Development" *Anti-Infective Agents in Medicinal Chemistry* Vol. 5, No. 4 2006: 331.

¹³ M. Cotter and L. Daly "Antibiotic prescription practices of general practitioners" *Irish Medical Journal*, Vol. 100, Issue 9 2007: 598.

¹⁴ Steven C. Ebert "Factors contributing to excessive antimicrobial prescribing" *Pharmacotherapy*, Vol. 27, Issue 10, Part 2 2007: 1275.

¹⁵ Genevieve Cadieux, et al "Predictors of inappropriate antibiotic prescribing among primary physicians" *Canadian Medical Association Journal* Oct. 9 2007: 877.

¹⁶ Steven C. Ebert "Factors contributing to excessive antimicrobial prescribing" *Pharmacotherapy*, Vol. 27, Issue 10, Part 2 2007: 1274.

¹⁷ Jamie Brehaut "Do physician outcome judgments and judgment biases contribute to inappropriate use of treatments?" *Implementation Science* Vol.2 2007: 20.

¹⁸ Madeline Simasek and David A. Blanding "Treatment of the Common Cold" *American Family Physician* Vol. 75, No. 4 2007: 517.

¹⁹ Steven C. Ebert "Factors contributing to excessive antimicrobial prescribing" *Pharmacotherapy*, Vol. 27, Issue 10, Part 2 2007: 1285.