

ETHICS AND DRUG RESISTANCE

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ABSTRACT

This paper reviews the dynamics behind, and ethical issues associated with, the phenomenon of drug resistance. Drug resistance is an important ethical issue partly because of the severe consequences likely to result from the increase in drug resistant pathogens if more is not done to control them. Drug resistance is also an ethical issue because, rather than being a mere quirk of nature, the problem is largely a product of drug distribution. Drug resistance results from the over-consumption of antibiotics by the wealthy; and it, ironically, results from the under-consumption of antibiotics, usually by the poor or otherwise marginalized. In both kinds of cases the phenomenon of drug resistance illustrates why health (care) – at least in the context of infectious disease – should be treated as a (global) public good. The point is that drug resistance involves ‘externalities’ affecting third parties. When one patient develops a resistant strain of disease because of her over- or under-consumption of medication, this more dangerous malady poses increased risk to others. The propriety of free-market distribution of goods subject to externalities is famously dubious – given that the ‘efficiency’ rationale behind markets assumes an absence of externalities. Market failure in the context of drug resistance is partly revealed by the fact that no new classes of antibiotics have been developed since 1970. I conclude by arguing that the case of drug resistance reveals additional reasons – to those traditionally appealed to by bioethicists – for treating health care as something special when making policy decisions about its distribution.

INTRODUCTION

Though not a new phenomenon, the problem of drug resistance is increasingly being recognized as a serious, growing threat to global public health.

Because of the potential global consequences of drug resistance, and because the emergence and spread of drug-resistant disease is largely a product of drug distribution, drug resistance should be recognized as an important ethical issue – and a matter

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of international justice. After (1) placing the issue of drug resistance in historic and economic context, this article (2) reviews the dynamics of drug resistance, (3) explains why the emergence and spread of drug-resistant disease is the result of both the over-consumption and under-consumption of drugs, and (4) argues that the phenomenon of drug resistance reveals that health, in the context of infectious disease at least, should be treated as a (global) public good. The point with regard to (4) is that the emergence and spread of drug-resistant disease, in economic terms, involves negative externalities. This provides additional reasons, to egalitarian considerations traditionally appealed to by bioethicists, for treating health care as something special when making policy decisions about its distribution. There is no good justification for thinking that free-market mechanisms provide an efficient route to freedom from infectious disease. That the opposite is true is revealed by the current status quo.

STORIES OF SUCCESS AND OPTIMISM

The discovery and development of antibiotics – along with improvements in sanitation and hygiene,¹ and the discovery and development of vaccines – was one of the great successes of medical science. While previous generations lived in constant fear of infliction with deadly infectious diseases, the cures availed by antimicrobials have made more recent generations, in wealthy developed countries at least, relatively invulnerable to previously perilous scourges. With the advent of antimicrobial drugs came tremendous optimism in medicine. It was even believed that infectious disease would be defeated through medical progress.

Penicillin was accidentally discovered in 1928 by the British scientist Alexander Fleming, who noticed that mold killed bacteria growing in a discarded petri dish. Once Howard Florey developed a means of its mass production, penicillin became publicly available in 1944 and was immediately hailed as a ‘wonder drug’ and ‘miracle cure’. In the meantime,

¹ N. Tomes. 1998. *The Gospel of Germs*. Cambridge, MA: Harvard University Press.

the search for additional antibiotics in soil was underway and achieving additional breakthroughs. In 1943, for example, Selman Waksman discovered streptomycin, which proved effective in treating numerous infections including, most importantly, tuberculosis:²

Other ‘wonder drugs’ followed . . . and many dreaded infections became treatable; people were saved from death and from prolonged periods of disability. Tuberculosis sanatoriums closed . . . people with burns over large areas of their bodies, who would have died in earlier years, survived; childhood meningitis (infections of membranes around the brain or spinal cord), formerly a death sentence, was treatable; prolonged, dangerous, and only-sometimes-effective treatments for syphilis and gonorrhoea were replaced by injection or ingestion of an antibiotic . . . the median lifespan [increased] by eight years, from 62 to 70 years, between 1935 and 1955.³

So successful were these and other achievements – including the Salk polio vaccine and the discovery of DDT⁴ – that, as early as 1948, ‘US Secretary George C. Marshall declared . . . that the conquest of all infectious diseases was imminent.’⁵ In 1967, by which time ‘more than 25,000 different antibiotic products had been developed’,⁶ Surgeon General William H. Stewart famously concluded that ‘it was time to close the book on infectious diseases and shift all national attention (and dollars) to what he termed ‘the New Dimensions’ of health: chronic diseases’.⁷

TRAGEDY

Medicine did subsequently shift focus away from bacteriology and parasitology to chronic illnesses such as heart disease and cancer – or what

² S.B. Levy. 1992. *The Antibiotic Paradox*. New York: Plenum Press.

³ US Congress, Office of Technology Assessment. 1995. *Impacts of Antibiotic-Resistant Bacteria*, OTA-H-629. Washington, DC. Government Printing Office: 39.

⁴ Which would be used to fight mosquitoes and thus malaria.

⁵ L. Garrett. 1994. *The Coming Plague: Newly Emerging Diseases in a World Out of Balance*. New York: Penguin: 30–31.

⁶ *Ibid*: 36.

⁷ *Ibid*: 33.

McKeown calls ‘diseases of affluence’.⁸ The pharmaceutical industry, furthermore, has increasingly been busy with hugely profitable ‘blockbuster’ drugs for allergies and depression – and lifestyle drugs for things like baldness and impotence. The focus of industry research and development at present can largely be explained by the fact that the market for vaccines and antibiotics is relatively small. According to Peter N. Goodfellow of GlaxoSmithKline Pharmaceuticals, ‘all revenues for all vaccines combined are less than one year’s sales, in the USA, for [the antidepressant] PAXIL® . . . Antibacterials capture only 8% of the pharmaceutical market, and soon there will be no antibacterials in the top 20 selling drugs.’⁹ A lack of economic incentive has led to decreased antibiotic and vaccine research and development. In 2000, the World Health Organization (WHO) claimed that ‘[s]ince 1970 no new classes of antibacterials have been developed to combat infectious diseases.’ While ‘[o]n average, research and development of anti-infective drugs takes 10 to 20 years’, at a cost in the neighborhood of US \$500 million, ‘there are no new drugs or vaccines ready to emerge from the research and development pipeline’.¹⁰

In the meantime, of course, infectious diseases did not disappear as planned. On the contrary, new microbial scourges such as AIDS and numerous others have emerged in recent decades;¹¹ and old enemies such as tuberculosis are on the rebound. In each of the past few years, AIDS killed 3 million people, and 5 million people were newly infected with HIV. Approximately 40 million people are currently living with HIV worldwide.¹² Adult HIV prevalence rates reach, and exceed, 30% in numerous parts of sub-Saharan Africa. Significant breakthroughs in the way of antiviral AIDS treatments

have, admittedly, been made since the 1980s; but AIDS drugs are (in 2006) accessible to only 24% of those who need them (up from 5% just a few years ago). Little in the way of promising new AIDS medications,¹³ in any case, is currently being developed. Though usually entirely curable, tuberculosis was declared a global health emergency by WHO in 1993 and currently kills 1.7 million each year.¹⁴ In 2002, WHO estimated ‘that between [then] and 2020, approximately 1000 million people will be newly infected, over 150 million people will get sick, and 36 million will die of TB – if control is not further strengthened.’¹⁵ Malaria meanwhile claims over 1 million lives a year. Infectious diseases such as these, and others including measles, diarrhoeal diseases, and acute respiratory infections – such as pneumonia which killed 3.5 million people worldwide in 1998¹⁶ – are currently the world’s largest ‘killer[s] of children and young adults . . . account[ing] for more than 13 million deaths a year – one in two deaths in developing countries’.¹⁷

Both the continued toll of infectious diseases and the lack of new antibiotic development reflect the fact that the vast majority of those afflicted are poor people in developing countries. The problem is that the poor are both more likely to become infected – because of malnutrition and numerous other complex factors¹⁸ – and less likely to be able to pay for the medicines they need. Reduced medical industry focus on antimicrobials is by no means the result of the disappearance of infectious diseases. Nor is it due to a lack of need for new drug development. It is a result of the fact that the medical industry

⁸ T. McKeown. 1988. *The Origins of Human Disease*. Cambridge, MA: Blackwell.

⁹ P.N. Goodfellow. The Barriers to the Production of New Antibiotics. Presentation at the 3rd EMBL/EMBO joint Conference on Science and Society – Infectious Diseases: Challenges, Threats and Responsibilities. Heidelberg, Germany, 2002.

¹⁰ World Health Organization. 2000. *Report on Infectious Diseases 2000 – Overcoming Antimicrobial Resistance*. Available at <http://www.who.int/infectious-disease-report/2000/> [Accessed 30 August 2006].

¹¹ See Garrett, *op. cit.* note 5; and J. Lederberg, R. Shope and S.C. Oaks (eds.). 1992. *Emerging Infections: Microbial Threats to Health in the United States*. Washington DC: National Academy Press.

¹² See www.unaids.org [Accessed 30 August 2006].

¹³ Which will be needed, for example, to fight resistant strains of HIV.

¹⁴ World Health Organization. 2006. Fact Sheet No 104. Tuberculosis. Available at <http://www.who.int/mediacentre/factsheets/fs104/en/> [Accessed 22 November 2006]. See also L.B. Reichman and J.H. Tanne. 2002. *Timebomb: The Global Epidemic of Multi-Drug-Resistant Tuberculosis*. New York: McGraw Hill: x–xi; P. Farmer. 1999. *Infections and Inequalities: The Modern Plagues*. Berkeley, CA: University of California Press.

¹⁵ World Health Organization. 2002. Fact Sheet No 104. Tuberculosis. Available at <http://www.who.int/mediacentre/factsheets/fs104/en/print.html> [Accessed June 2004].

¹⁶ WHO, *op. cit.* note 10.

¹⁷ World Health Organization. 1999. *Report on Infectious Diseases*, Chapter 16, Removing Obstacles to Healthy Development, available at <http://www.who.int/infectious-disease-report/pages/textonly.html>, p. 2 [Accessed 30 August 2006].

¹⁸ See M.J. Selgelid. Ethics, Economics, and AIDS in Africa. *Developing World Bioeth* 2004; 4: 96–105.

largely aims at profits rather than meeting the world's most urgent medical needs. The distribution of medical research resources involves a '10/90 divide' – whereby 10% of medical research funds focus on diseases accounting for 90% of the global burden of disease, and 90% of medical research funds focus on diseases accounting for 10% of the global burden of disease.¹⁹ The majority of medical research focuses on the wants of a minority of the world's population: those who are relatively wealthy.²⁰

RESISTANCE

The lack of new antimicrobial and vaccine development, in the meanwhile, may come back to haunt us all – rich and poor alike. The worry is that the emergence and spread of drug-resistant microbes may reverse previous medical progress. The US Congress Office of Technology Assessment in *Impacts of Antibiotic-Resistant Bacteria* (1995) reports that:

Currently, few bacteria are resistant to all antibiotics, but many more are resistant to all but one or all but a few antibiotics, and the expectation is that resistant bacteria will continue to emerge and spread. The fear is that many bacteria will become resistant to all antibiotics, plunging humanity back into the conditions that existed in the pre-antibiotic age.²¹

More recently the World Health Organization's *Report on Infectious Diseases 2000 – Overcoming Antimicrobial Resistance* claims that

Drug resistance is the most telling sign that we have failed to take the threat of infectious diseases seriously. It suggests that we have mishandled our precious arsenal of disease-fighting drugs, both by overusing them in developed nations and, paradoxically, both misusing and underusing them in

developing nations. In all cases, half-hearted use of powerful antibiotics now will eventually result in less effective drugs later . . . [O]nce life-saving medicines are increasingly having as little effect as a sugar pill. Microbial resistance to treatment could bring the world back to a pre-antibiotic age . . . The potential of drug resistance to catapult us all back into a world of premature death and chronic illness is all too real.²²

WHO currently considers 'antimicrobial resistance to be one of the top three issues in global health.'²³ In the opinion of Karl Ekdahl, Strategic Advisor to the Director of the European Centre for Disease Prevention and Control (ECDC), 'drug resistance is the greatest threat to health over the next 25 years'; and he agrees that 'the antibiotic era may soon be a thing of the past'.²⁴ The potential threat of drug resistance is thus taken very seriously by authoritative, reputable individuals and organizations.

The future extent and impact of drug resistance, of course, remains to be seen; and drug resistance may be containable through appropriate policy implementation.²⁵ Given (1) the magnitude of the threat here described and (2) the fact that drug resistance is largely (as described below) a function of drug distribution, however, drug resistance is clearly an important ethical issue. It is thus astonishing that the topic has more-or-less escaped the attention of bioethics literature.²⁶ I elsewhere explain why the discipline of bioethics has paid relatively little attention to the topic of infectious disease in

²² WHO, *op. cit.* note 10.

²³ S.L. Knobler, S.M. Lemon, M. Najafi, and T. Burroughs (eds.). 2003. *The Resistance Phenomenon in Microbes and Infectious Disease Vectors: Implications for Human Health and Strategies for Containment*. Institute of Medicine, Workshop Summary. Washington DC: National Academies Press: 20.

²⁴ Karl Ekdahl, Ethical Issues from the ECDC Perspective. Presentation at the Bioethical Implications of Globalisation Processes (BIG) workshop on Globalization and New Epidemics: Ethics, Security and Policy Making. The European Commission, Brussels, Belgium, 22 May 2006. (Note that he was not here expressing official ECDC position on this matter; this is his personal view.)

²⁵ WHO, *op. cit.* note 10.

²⁶ It has recently been touched on, however, by C.B. Smith et al. Are there Characteristics of Infectious Diseases That Raise Special Ethical Issues? *Developing World Bioeth* 2004; 4, 1: 1–16; and P. Farmer and N. Gastineau Campos. Rethinking Medical Ethics: A View from Below. *Developing World Bioeth* 2004, 1; 4: 17–41.

¹⁹ Global Forum for Health Research. 2002. *The 10/90 Report on Health Research 2001–2002*. Geneva. Global Forum for Health Research.

²⁰ For social/political/economic explanation of the 10/90 divide, see D.B. Resnik. The Distribution of Biomedical Research Resources and International Justice. *Developing World Bioeth* 2004; 4, 1: 42–57.

²¹ US Congress, Office of Technology Assessment, *op. cit.* note 3.

general.²⁷ Bioethics' neglect of the topic of drug resistance, to date anyway, is at least partly forgivable given that this topic has generally been underappreciated by medical, economic, and policy analysis disciplines.²⁸

DYNAMICS

Resistance occurs when genetic mutations, through various mechanisms, make microbes less vulnerable, or invulnerable, to drugs that otherwise would have destroyed them.²⁹ A previously effective treatment then loses its power to cure. An important facet of bacterial biology is the fact that bacteria are often, through numerous processes, able to exchange genetic material with one another.³⁰ A mutation providing resistance to an individual bacterium may thus be passed on to others of the same or different species. At one level, then, the emergence and spread of drug resistance is merely a biological phenomenon.

The emergence and spread of drug resistant bacteria in human populations, on the other hand, is a social, political, and economic phenomenon as well. The emergence and spread of resistant bacteria is driven by antibiotic usage, because antibiotics themselves select for resistant strains of disease. When one takes antibiotics, the antibiotics kill bacteria that are vulnerable, thus allowing those with genes for resistance to flourish in the absence of microbial competitors. The more a person takes antibiotics, therefore, the greater the chance that antibiotic resistant bacteria will establish themselves in her body. The result is increased frequency of resistance genes in bacterial populations – and increased danger that resistance genes will be passed on to

other, potentially pathogenic,³¹ bacteria. Resistant bacteria, pathogenic or otherwise, can of course be transmitted from person to person. The extent of the emergence and spread of drug resistant pathogenic bacteria in human populations, therefore, reflects the extent of human consumption of antibiotics.

OVER-CONSUMPTION

Part of the problem is thus the widespread overuse of antibiotics. It is estimated that antibiotics are overprescribed by 50% by physicians in Canada and the US, and that 41% to 91% of prescriptions in teaching hospitals worldwide are inappropriate.³² Explanations for this are numerous. Antibiotics,³³ for example, 'are often prescribed for viral infections, for which they have no value, and for self-limited infections that would have cleared up whether or not an antibiotic had been prescribed'.³⁴ In the United States, 40% of primary care physicians prescribe antibiotics when patients present with sore throats and ear aches, without first seeking laboratory confirmation that this is called for. This is largely because of the time required for diagnostic confirmation that the pathogen is sensitive to the drug being prescribed.³⁵ It is also partly due to patient demand for immediate treatment.

Difficult cases arise when there is a small but non-negligible chance that antibiotic treatment would be to the patient's benefit. This may arise, for example, in cases of diagnostic uncertainty – or cases, such as otitis media (ear infection) where the slight expectation of improvement in prognosis via antibiotic treatment might not justify drug costs and risks of side effects. In cases like this, physicians may be pressured to prescribe through fear of litigation – i.e. being sued for not providing something that just might have worked.³⁶ Or they may sometimes conclude that prescription is, perhaps ever-so-slightly, more likely than not to benefit the patient, without

²⁷ M.J. Selgelid. Ethics and Infectious Disease. *Bioethics* 2005; 19, 3: 272–289.

²⁸ P.F. Harrison and J. Lederberg (eds.). 1998. *Antimicrobial Resistance: Issues and Options*. Institute of Medicine, Workshop Summary. Washington DC. National Academies Press; and J. Coast, R.D. Smith and M.R. Millar. An Economic Perspective on Policy to Reduce Antimicrobial Resistance. *Soc Sci Med* 1998; 46: 29.

²⁹ For an accessible review of the mechanisms of drug resistance, see Levy, *op. cit.* note 2.

³⁰ One example is plasmid exchange during a sex-like process called conjugation. See Levy, *op. cit.* note 2, for more on the mechanisms of resistance transference.

³¹ i.e. disease-causing.

³² WHO, *op. cit.* note 10, Chapter 3.

³³ Antibiotics are effective against bacteria – not viruses.

³⁴ US Congress, Office of Technology Assessment, *op. cit.* note 3, p. 11.

³⁵ *Ibid*: 13.

³⁶ *Ibid*: 11.

considering, or giving much weight to, the fact that a practice of prescribing under the circumstances may conflict with public health. Risk-benefit optimization for individual patients need not always coincide with that for society as a whole.

Charles Smith and colleagues point out that another cause of 'excessive use has been an increasing aggressive commercial advertising campaign by many drug companies to promote the use of the newest, most expensive, and most profitable patented antimicrobials'.³⁷ Such advertising is increasingly targeted at patients as well as physicians. The effect of direct-to-consumer advertising on patient demand, and the effect this has on physician prescription practices, has been the subject of empirical study:

In the United States, 95% of physicians surveyed had seen an average of seven patients in the previous six months who had requested specific drugs as a result of advertising. Of physicians questioned, 70% admitted that patient pressure forced them to prescribe drugs they might otherwise have avoided.³⁸

ABUSE

Another cause of drug resistance is the fact that patients often fail to complete treatment regimens prescribed. While this itself promotes resistance, matters are made worse when leftover pills are saved, as they so often are, for 'self-medication' later.³⁹ The fact that antibiotics are poorly understood by the lay public comes into play both in the case of self-medication and when patients demand inappropriate prescriptions from willing physicians. A recent Harris poll found that 39% of US adults 'believe that antibiotics can be used to treat viruses' and that 40% 'believe that antibiotics are at least somewhat effective in treating colds and flus'.⁴⁰

Abuse is further facilitated in developing countries where it is often possible for poorly educated people to buy antibiotics over-the-counter, sometimes one pill at a time, from poorly qualified pharmacists. Additional trouble results from market presence of counterfeit drugs that may be old, poorly absorbed, and/or contain reduced doses of active ingredients.

FARMING PRACTICE

Given that drug resistance increases with antibiotic use, it is disturbing that vast amounts of antibiotics are used in agriculture and aquaculture for prophylaxis, treatment, and growth promotion. 50% (by weight) of antibiotics are used for such purposes. Of particular concern is the common practice of adding 'subtherapeutic' levels of antibiotics to the food of healthy animals in order to promote their growth. In the United States, 'the amount of this subtherapeutic usage is four or five times greater [by weight] than the amount used for treatment of animal diseases'.⁴¹ Long-term, low level exposure like this creates especially favorable circumstances for the promotion of drug resistant bacteria.⁴² While the threat to human health from such a practice is difficult to estimate and study, the worry is that resulting resistant bacteria in animals will be passed on to humans – or that resistant genes in animal bacteria will jump to bacteria which inhabit human hosts. A growing body of evidence indicates that the dangers are real.⁴³ While feeding animals with subtherapeutic doses of antimicrobials used for humans has been banned in Europe and Canada, regulations are lacking in the US and elsewhere. Given the agricultural industry's interests in growth promotion, this issue has unsurprisingly been highly politicized.

⁴¹ Levy, *op. cit.* note 2, p. 137.

⁴² *Ibid.*

⁴³ Vanomycin-resistant bacteria in food, and cases of human infection with drug-resistant *Salmonella typhimurium* and multi drug-resistant campylobacteriosis, for example, have all been traced to farm animals. WHO, *op. cit.* note 10. See also World Health Organization. 2001. *WHO Global Strategy for Containment of Antimicrobial Resistance*, available at www.who.org [Accessed 30 August 2006].

³⁷ Smith et al., *op. cit.* note 26, p. 12.

³⁸ WHO, *op. cit.* note 10, Chapt. 3.

³⁹ Levy, *op. cit.* note 2.

⁴⁰ Harris Interactive. 2002. Harris Interactive Data Show Most Are Reasonably Well Informed on the Use and Abuse of Antibiotics, available at <http://www.harrisinteractive.com/news/printerfriend/index.asp?NewsID=421> [Accessed 19 June 2004].

UNDER-CONSUMPTION⁴⁴

As indicated above, the failure to complete a proper course of antibiotic treatment is one of the things that can promote the emergence of drug resistant pathogens. If treatment is prematurely terminated, then disease-causing mutant bacteria, which would have been killed off if treatment had been completed, may survive and become more strongly established in the absence of microbial competitors. Treatment with the very same drugs may then be less effective. Hence the instructions of physicians to 'be sure you complete the treatment and take all the pills' – and hence the (partial) blaming of 'noncompliant patients' for the problem of drug resistance.

The failure to complete a full course of treatment, however, is by no means always the fault of the patient. 'Noncompliance', according to Paul Farmer, is usually a matter of ability rather than agency. 'Throughout the world', according to Farmer, 'those least likely to comply are those least able to comply'.⁴⁵ As stated before, the poor are most likely to get sick and least likely to afford medical care when they do. They are also most likely to be unable to complete medical treatment once they start it. Poor people in developing countries, quite simply, often cannot afford to complete treatment – especially given the high drug prices set by pharmaceutical companies. In addition to drug costs, difficulty affording time off work and the cost of (often difficult) transportation to (often faraway) clinics pose further barriers to the completion of antibiotic therapy. Sometimes, according to Farmer, it is simply a matter of not having the money to rent a donkey.⁴⁶

Additional barriers are posed by infrastructural constraints of medical systems in poor countries where drug stockouts are frequent. This is well illustrated by the prison situation in the former Soviet Union. Increased crime and incarceration came with the collapse of the Soviet Union. At present,

'[a]lmost 1% of the population of Russia is imprisoned, a higher percentage than any other nation in the world'.⁴⁷ Of the 300,000 prisoners released every year – often with amnesty because prisons are overflowing and space is required for 300,000 new prisoners each year – 10% have active tuberculosis and more than 80% 'have been infected with latent TB. Each of the latter has a 10% chance of developing active TB later in life'.⁴⁸ Of prisoners (and those being released) with active TB, about a third have multi-drug-resistant TB.⁴⁹ These astounding rates of tuberculosis infection and multi-drug resistance owe much to overcrowded, poorly ventilated, damp, dark prison conditions – and the fact that underfunded prisons are unable to maintain a steady supply of the full range of drugs needed for the long-term treatment of TB. The sporadic partial treatment that inevitably results selects directly for multi-drug resistance. Those released are unlikely to receive much better care from the wider health care system – and so the health of their families and communities is subsequently threatened, as is global public health in general.⁵⁰ Tuberculosis is spread in the air. Both in this case and others it must be remembered that (1) infectious diseases (drug-resistant or otherwise) have no respect for national boundaries and (2) their spread is facilitated by increased international travel and trade.

Ordinary tuberculosis can be treated with a six month course of treatment costing \$10. While drug-resistant tuberculosis treatment takes two years and costs 100 times as much, '[e]ven then a cure is not guaranteed'. It is thus widely acknowledged that new TB drug development is needed, as there are now '300,000 new cases per year of MDR-TB worldwide'. In the meanwhile it is unfortunate that, according to the WHO, there has been 'a 40 year standstill in TB drug development'.⁵¹

⁴⁴ By 'under-consumption' I refer to insufficient consumption rather than non-consumption.

⁴⁵ Farmer, *op. cit.* note 14, p. 255. See also P. Farmer. 2003. *Pathologies of Power: Health, Human Rights, and the New War on the Poor*. Berkeley, CA: University of California Press.

⁴⁶ P. Farmer. 2003. *Pathologies of Power: Health, Human Rights, and the New War on the Poor*. Berkeley, CA. University of California Press.

⁴⁷ Reichman et al., *op. cit.* note 14, p. 90.

⁴⁸ Ibid: 53.

⁴⁹ Ibid: 90.

⁵⁰ For more on tuberculosis in the former Soviet Union, see Farmer, *op. cit.* note 46; Farmer et al., *op. cit.* note 26; and L. Garrett. 2000. *Betrayal of Trust: The Collapse of Global Public Health*. New York: Hyperion.

⁵¹ World Health Organization. 2004. Drug Resistant Tuberculosis Levels Ten Times Higher in Eastern Europe and Central Asia. Press Release, available at: <http://www.who.int/mediacentre/releases/2004/pr117/en/print.html> [Accessed 17 March 2004].

SOLUTIONS

Numerous measures for curtailing the problem of drug resistance have been recommended. Increased education of health providers and the public, control of prescription practices, improvement of infection control in hospitals, and reduction of antibiotic use in farming, for example, are important parts of the solution. Given that under-consumption of drugs by the poor is a driver of resistance, increasing access to medications through price reduction or social provision is also needed. Things like increased global surveillance and impact assessment⁵² and improvements in diagnostic technology⁵³ are also essential. Of paramount importance, in any case, are the development of new drugs and vaccines. New antibiotics are needed because the power of our existing supply has increasingly declined, while there has been a dearth of new drug development for decades. Vaccines are important because they prevent infection and the need for antibiotics to begin with.⁵⁴

ECONOMICS AND PUBLIC GOODS

As indicated earlier, however, the medical industry has backed away from new antibiotic and vaccine development largely because of a lack of market incentive. It is too often simply more profitable for pharmaceutical companies to research, develop, manufacture, and market other medical products. Disincentives regarding vaccine production additionally pertain to concerns over liability.⁵⁵ The lack of needed new drugs and vaccines reflects the fact that research and development, and other

business decisions of pharmaceutical companies, aim at profits rather than solutions to the world's most important medical problems. A plausible conclusion is that the commercialization of medicine has resulted in grossly inefficient outcomes. Apparent gross inefficiency (or disutility) is well illustrated by the 10/90 divide, and the fact that AIDS medications are, in 2006, unavailable – because unaffordable – to 76% (down from 95% just a few years ago) of the *millions* of people who need them worldwide. If these two phenomena are not illustrations of inefficiency, then it is hard to imagine what would be.

In the context of infectious disease, and drug resistance in particular, it should be unsurprising if free-market mechanisms have failed to realize efficient outcomes. We here enter the realm of public goods; and, the ability of free markets to provide such goods is notoriously dubious.

Moral justification for free-market economic systems is generally based on the idea that (1) they promote liberty, insofar as individuals are provided with freedom to make their own decisions about what transactions to enter into, and (2) they promote efficiency or aggregate utility.⁵⁶ The first justification is limited insofar as it is negative liberty, i.e. freedom from interference, in particular, that is likely promoted by free-market systems. Since free markets by no means guarantee 'positive liberties' to everyone, there is no reason to believe that everyone will have her most basic needs met under free-market conditions.⁵⁷

Questions about the ability of markets to promote efficiency or utility, on the other hand, are quite complicated. One problem relates to the number of notions of 'efficiency' that come into play.⁵⁸ Another problem relates to empirical difficulties with measuring and comparing – and justifying causal claims about – the 'utility' outcomes of

⁵² Surveillance and impact assessment are important for tracking and appreciating the problem of drug resistance.

⁵³ Improved diagnostics would contribute to surveillance and drug sensitivity testing. The latter would facilitate the making of timely, appropriate prescription decisions.

⁵⁴ US Congress, Office of Technology Assessment, *op. cit.* note 3.

⁵⁵ Corporate reluctance to enter the vaccine market due to liability concerns is well illustrated by the Swine Flu fiasco of 1976 and, more recently, US government difficulty procuring anthrax vaccine. See, respectively, Garrett, *op. cit.* note 5; and J. Miller, S. Engelberg, and W. Broad. 2001. *Germ: The Ultimate Weapon*. London: Simon and Schuster.

⁵⁶ A. Sen. 1999. *Development as Freedom*. New York. Anchor Books.

⁵⁷ Even if (1) negative liberty and (2) efficiency/utility were maximally promoted by free markets, ethical questions about how the promotion of these should be balanced against potentially conflicting legitimate social aims to promote (3) equality and (4) positive liberty remain.

⁵⁸ 'Efficiency' may be used to refer to overall utility, for example. This is how I have been using the term except where otherwise specified. 'Efficiency' may alternatively be used to refer to pareto-optimality, which is further explained below, and which is often (and sometimes mistakenly) used as a proxy for overall utility.

different socio-economic systems. These include, among other things, the difficulty of performing controlled studies of social systems.⁵⁹

The strongest efficiency-based theoretical justification of free markets holds that they *would* promote efficiency in the way of ‘pareto optimality’ assuming ideal conditions were met. A pareto optimal outcome is one where it would be impossible to make any one person better off without making another worse off. In a three party system we imagine the outcome of a series of mutually beneficial voluntary exchanges between parties. Assuming, among other things, that the parties are rational and have full information – and that there are no negative externalities – a pareto optimal outcome can, theoretically anyway, be expected to result via a series of such exchanges via free-market mechanisms.⁶⁰

Externalities are (positive or negative) effects of transactions on third parties. In circumstances where negative externalities occur, the pareto efficiency based theoretical arguments in favor of free markets lose their force. ‘An example of a negative externality is a chemical producer’s discharge of noxious gases into the air: the cost of breathing bad air is not taken into account in the bargain that is struck between the chemical producer and the customer who buys his product.’⁶¹ Externalities relate to ‘public goods’: things available for everyone’s benefit.⁶² Freedom from pollution, and things like clean air, are prototypical examples of public goods. The propriety of free-market distribution of public goods is famously dubious – given that the ‘effi-

ciency’ rationale⁶³ behind markets assumes an absence of externalities.

I have quickly brushed over these basic economic issues to illustrate (1) that the emergence and spread of drug resistant disease involves negative externalities, and (2) that freedom from infectious disease should be recognized as a public good. When a given patient develops a resistant strain of disease because of her over- or under-consumption of medication, the emergence of this more dangerous (more difficult to cure or more expensive to cure) illness poses increased risks/harms to other individuals and (global) society at large. The associated costs to other individuals and (global) society are not taken into account by the prices reached in market exchanges between consumers and drug providers; and so there is no reason to expect efficient outcomes to result from a market in medicine.

It should by now be obvious that the emergence and spread of drug resistant disease involves externalities. That freedom from infectious disease should be recognized as a public good is, in any case, well-illustrated by the facts that (1) clean air is one of the clearest examples of a public good and (2) infectious diseases are often airborne. It is thus reassuring that infectious disease surveillance and drug resistance are finally beginning, in some circles anyway, to be conceptualized in terms of externalities and public goods (and bads).⁶⁴ Although a more detailed technical discussion of public goods is beyond the scope of this paper, suffice it to say for now that the ability of markets to provide for public goods in the absence of governmental intervention is widely acknowledged to be highly problematic from an economic standpoint. In addition to the fact that the costs of externalities are not taken into account

⁵⁹ A. Buchanan. 1985. *Ethics, Efficiency, and the Market*. Totowa, NJ: Rowman & Littlefield.

⁶⁰ *Ibid*: 14–15, for more on assumptions.

⁶¹ *Ibid*: 15.

⁶² Public goods are also standardly defined as goods which are non-excludable and non-rivalrous – ‘once they are provided, no one can readily be excluded from their consumption, and one person’s consumption does not prevent anyone else from consuming them’. R.D. Smith et al. Preface, in *Global Public Goods for Health: Health Economic and Public Health Perspectives*, R. Smith, R. Beaglehole, D. Woodward, and N. Drager eds. New York: Oxford University Press: ix. Though my argument will focus on the issue of externalities – because this is crucial to challenging the standard argument that free markets lead to pareto optimal outcomes – it should be recognized that freedom from infectious disease and freedom from drug resistant disease – just like clean air – meet both of these criteria.

⁶³ Except for the fact that pareto optimality might sometimes serve as a useful proxy for aggregate utility, there is no good argument that free markets would maximize efficiency qua utility even when ideal market conditions are met.

⁶⁴ Harrison and Lederberg, *op. cit.* note 28; Coast et al., *op. cit.* note 28; I. Kaul, I. Grunberg, and M.A. Stern (eds.). 1999. *Global Public Goods: International Cooperation in the 21st Century*. Published for The United Nations Development Programme. New York: Oxford University Press; I. Kaul et al. (eds.). 2003. *Providing Global Public Goods: Managing Globalization*. Published for the United Nations Development Programme. New York: Oxford University Press; and R. Smith, R. Beaglehole, D. Woodward, and N. Drager (eds.). 2003. *Global Public Goods for Health: Health Economic and Public Health Perspectives*. New York: Oxford University Press.

in the bargains struck in market transactions, another reason for doubting the efficiency of markets in the promotion of public goods relates to 'free rider' problems – i.e. since everyone benefits from public goods, there will often be no free-market incentive for private enterprise to invest in their production.

ETHICS AND ECONOMICS: ACCESS TO MEDICINE

We have thus arrived at additional reasons, to those traditionally appealed to by bioethicists, for treating health care as something special when making policy decisions about its distribution. To date, perhaps the best developed account of why health care should not be left to free-market distribution is that provided by Norman Daniels in *Just Health Care*.⁶⁵ We should recognize a right to health care, and guarantee equal access to health care, according to Daniels, because health care is needed to restore species typical functioning which is needed for equality of opportunity which is a requirement of justice; distribution of medical resources should not, then, be left to the whims of the market – justice requires that everyone have access to at least a basic minimum of health care whether or not they are wealthy. This is a good argument. Daniels, however, only captures part of the case for releasing medicine from free-market mechanisms. An additional ethical reason for treating health care as something special when making policy decisions about its distribution is the fact that freedom from infectious disease should be seen as a (global) public good – and there is no good reason to think that free markets provide reliable means for providing such goods. History and the status quo indicate that they do not. There *are*, as Daniels suggests, egalitarian reasons for removing medicine from free-market distribution – but there are utilitarian and (from the standpoint of the wealthy) self-interested reasons as well.

The potential global consequences of drug resistance should reveal that drug resistance – assuming

that something can be done to reduce the problem – is a matter of ethical urgency. The return to a 'pre-antibiotic era', feared by WHO, would be catastrophic. In the meanwhile the costs of treating drug resistant infections are already estimated to be \$7 billion per year in the United States alone.⁶⁶ Understanding of the dynamics behind drug resistance, however, reveals that worst case scenarios are not inevitable. Because resistance results from the way that drugs are distributed, the issue is a matter of distributive justice. A central cause of drug resistance is that drugs are sold at prices that are not sustainably affordable to poor people in developing countries. The fact that drug resistance threatens global health – i.e. everyone – should thus be added to whatever other ethical reasons exist for making antibiotics more readily available to impoverished populations. It is in everyone's interest that poor people are able to finish antimicrobial therapy once they start it. While egalitarian and human rights arguments may provide good reasons for increasing access to medication, a stronger cumulative case can be made through appeal to utilitarian reasons as well.

Insofar as the economic rationale behind a market in medicine is based on the idea that markets promote utility, the legitimacy of a market in antibiotics falls away as argued above. The current global threat of drug resistance reveals that utilitarian aims would most likely be reached if the poor had better access to drugs than they do at present (i.e. largely via markets). On the one hand, the utilitarian rationale for improving access to medication for the poor, via resource redistribution, is quite straightforward: \$10 worth of tuberculosis medication will generally have a far greater payoff in terms of quality of life improvement for an infected poor person than the same \$10 could normally have, by paying for a movie ticket or restaurant meal, for someone who is relatively well off and healthy. On the other hand, however, the utilitarian rationale for improving access to medication for the poor is more profound: When a poor person cannot afford to finish her course of treatment, the resistant strain of

⁶⁵ N. Daniels. 1985. *Just Health Care*. New York: Cambridge University Press.

⁶⁶ R.D. Smith & J. Coast. Antimicrobial Drug Resistance, in *Global Public Goods for Health: Health Economic and Public Health Perspectives*, R. Smith et al. eds. New York: Oxford University Press: 76.

disease that results may threaten everyone. Because this social cost (i.e. externality) of drug resistance is never factored into the market costs of medicines, we here have market failure.

When the public nature of drug resistance is taken into account, utilitarianism would favor increasing access to medicine for the poor over markets *if* the wider social consequences of drug resistance are sufficiently serious, assuming a more efficient system of distribution can be found. Assuming the consequences of drug resistance *are* sufficiently serious – which seems highly plausible, given the concerns of the WHO – then one can argue that equality and utility both favor improving access to antimicrobials for those who need them.

The remaining justification, if any, for a market in antimicrobials would be the libertarian idea that individuals have a right to engage in free-market transactions without coercive taxation for redistributive purposes. Assuming that utility would in fact be promoted by more socialized distribution of antimicrobials, the ethical question would then be: Do not equality and utility *together* outweigh the importance of free-market liberty, in the limited context of anti-infectives at least? Why should anyone think that liberty in the exchange of drugs is more important than these other two goods combined?⁶⁷ The idea that negative liberty should be given priority over both equality and utility regardless of the degree to which these latter two are threatened is implausibly extreme.⁶⁸ Key points to remember are that (1) ethically speaking, the usual justification for markets is the idea that they generally promote *both* utility and (negative) liberty, (2) there is no good (theoretical or empirical) reason to believe that markets promote utility in the context of antimicrobials – in virtue of public goods problems, and (3) the consequences of drug resistance may be disastrous, as opposed to merely suboptimal, from a utilitarian standpoint.

⁶⁷ A third reason in favor of increasing access to medicine is the idea that this would promote positive (if not negative) liberty as well. A fourth reason is that the Universal Declaration of Human Rights recognizes a human right to health. A fifth reason is that the poor are often victims of past injustices warranting reparation.

⁶⁸ The idea that 'side constraints' might be violated in order to avoid 'catastrophic moral horror' is suggested (though perhaps not fully admitted) even by Robert Nozick. R. Nozick. 1974. *Anarchy, State, and Utopia*. New York: Basic Books: 30n.

ETHICS AND ECONOMICS: AVAILABILITY OF MEDICINE, AND PATENTS REVISITED

The public nature of drug resistance applies to ethical debate over intellectual property rights and the distribution of medical research resources as well as to debates about the distribution of existing medications. Patents, ironically, are themselves supposed to address a public goods problem. Knowledge is a prototypical example of a public good.⁶⁹ Insofar as knowledge is (usually anyway) available to everyone, there is a lack of economic incentive to produce it. If the knowledge about how to make a drug could be freely used by all, then there would be a lack of incentive for private industry or private individuals to invest in its development. The resulting incentive problem is meant to be addressed by intellectual property right protection via patents. Inventors are given monopoly powers over their inventions so that they can reap a return (which would not be possible if the knowledge they produced could be used by anyone) on their research and development investment. Without patents, others could 'free ride' on the research and development of inventors – in which case invention would not be viable from an economic perspective. The justificatory purpose of patents is thus that they will motivate important knowledge production that would not otherwise be realized.

Recall, however, that development of (knowledge regarding) new antibacterials (and also new vaccines and diagnostic technologies) is widely recognized as crucial to the solution of the problem of drug resistance. Since existing antimicrobials are increasingly becoming less effective, new ones are needed. In the meanwhile, however, no new classes of antibacterials have been developed for decades. The lack of new antimicrobial and vaccine development – and the 10/90 divide in general – reveals that patents have not in fact provided the incentives that they are supposed to.⁷⁰ Though the motivation behind patents in pharmaceuticals is the idea that without them there would be insufficient incentive for

⁶⁹ Smith et al., *op cit.* note 66.

⁷⁰ S. Sterckx. Patents and Access to Drugs in Developing Countries: An Ethical Analysis. *Developing World Bioeth* 2004; 4, 1: 58–75.

industry to produce the medications needed to address urgent health problems, the reality is that even with patents many of the world's most urgent health problems remain largely neglected. The problem is that medical invention is left very much in the hands of profit driven enterprise – and that pursuit of wealth rather than medical need is what ultimately drives most medical research and development. Patents only provide incentive for research and development of medicines that will make (the most) money – and these are not necessarily coextensive with those that are most important from a global health perspective.⁷¹

CONCLUSION

Drug resistance thus relates to ethical debate over distribution of resources on two important levels. First, we saw that the phenomenon of drug resistance is relevant to debate over distribution of – i.e. access to – existing drugs. An important point here was that drug resistance reveals that, in the context of antimicrobials anyway, there is no good reason to believe that markets do one of the main things they are supposed to do – i.e. promote utility. Second, we saw how drug resistance is relevant to debate over distribution of research resources. Here we saw that, in the context of antimicrobials anyway, patents fail to do one of the main things they are supposed to do

⁷¹ For proposals regarding alternative incentive schemes see M. Kremer and R. Glennerster. 2004. *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*. Princeton, NJ: Princeton University Press; and T. Pogge. Human Rights and Global Health: A Research Program. *Metaphilosophy* 2005; 36, 1/2: 182–209.

– i.e. provide incentives for development of the knowledge (embodied in medicines) necessary for addressing the world's most important medical problems. If the threat of drug resistance is as serious as it appears to be, we apparently cannot rely on market mechanisms and the patent incentive system for solutions.

As with most public goods problems, solutions will require governmental intervention/funding. The fact that the problem of drug resistance is global in scope, while there is no global government, however, is troubling.⁷² The case that globalization should include a global socialization of antimicrobials is, in any case, strengthened by reflection on the dynamics of drug resistance. We leave global provision of treatment for infectious diseases in the hands of profit-oriented commercial enterprise, patent incentives, and market mechanisms at our own peril. If globalization requires the universalization of sensible systems of economic distribution, then free markets may be appropriate for very many ordinary commodities; but we must recognize that different systems of economic distribution are appropriate for different kinds of goods. Public goods warrant special treatment.

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⁷² Smith et al., *op cit.* note 66.