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How property rights and patents affect antibiotic resistance

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Summary

Antibiotic resistance tends to increase when a patent on an antibiotic expires. Since other companies can now sell the antibiotic, more of the antibiotic is produced and prices fall. Because the benefits of reducing current production go to other firms, pharmaceutical companies will have little concern about future resistance. This 'open-access' problem causes excessive antibiotic use and resistance problems in the future. Extending patents is one solution. However, a pharmaceutical company that has patent protection on a drug that is cross-resistant may have little concern about future resistance. This is because when people use completely different antibiotics which cause bacteria to become resistant to the original antibiotic, then the benefits of reducing current production go to other companies. A single buyer such as national health insurance or private health insurance may also have an incentive to reduce antibiotic resistance since they bear the future cost of future resistance. However, insurance coverage reduces the price that patients pay at the margin and thus the patients are likely to use more antibiotics. National health insurance policies may even set the price of antibiotics so low that resistance problems are created even when the patent is in effect. Copyright © 2004 John Wiley & Sons, Ltd.

How property rights and patents affect antibiotic resistance

Bacterial resistance to antibiotics has prevented humanity's dreams of eliminating several diseases [1]. Antibiotic resistance also causes otherwise easily treatable diseases to become difficult or impossible to suppress. The Forum on Emerging Infections of the US Institute of Health found that 'Antibiotic-resistant bacteria generate a minimum of \$4 billion to \$5 billion in costs to US society and individuals yearly . . . '[2].

Previous authors have pointed out that antibiotic use creates both negative and positive externalities [3–7]. Antibiotic use creates a positive externality because antibiotic use can improve public health by preventing patients from becoming carriers of a disease and thus less likely to infect others ('herd immunity'). Antibiotic use creates a negative externality because antibiotic use by one patient may generate resistant bacteria, that can infect others.

Efficient antibiotic treatment implies that the antibiotic is used until the additional benefit (marginal value of treatment + improved public health) is equal to the additional costs incurred (costs of treatment + increased resistance). If each individual user of the antibiotic were bearing all the costs and receiving all the benefits of their antibiotic use, there would be no external effects, and antibiotic use would be efficient.

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Excessive antibiotic use arises because the user does not bear the cost of increased antibiotic resistance in the future [8]. When antibiotic use creates negative externalities, then (1) regulations, (2) taxation, and (3) tradeable permits can be used to reduce antibiotic use and reduce antibiotic resistance [6,9].

There has been little discussion of how property rights and patents can reduce antibiotic resistance. This article has three purposes. This article explains: (1) how a lack of property rights can cause excessive antibiotic use, (2) how patents create property rights and reduce excessive antibiotic use assuming there is little cross-resistance,[a] and (3) how a monopsonistic buyer can solve the property rights problem and decrease antibiotic resistance (but, in practice often increase resistance).

The negative externality from antibiotic use is analogous to over-fishing in open-access fisheries. Open-access exists where property rights are not well defined and fishermen do not bear the full costs of their fishing efforts. A fisherman who leaves a fish, in the open fishery, to grow larger is unlikely to catch the fish in the future and thus will not receive future benefits from abstinence. An individual who is unable to capture future benefits will keep the fish creating inefficiently large current fishing efforts. Similarly, an individual who is unable to capture future benefits of a non-resistant bacterial strain (susceptible to a specific antibiotic treatment) will in the present use that antibiotic excessively.

A model of antibiotic resistance[b]

Assume that j represents a particular antibiotic such as penicillin or streptomycin. The demand (D) for antibiotic j is represented by $P_t = a - bQ_t$ where P_t is the price of an antibiotic treatment in time period t, a is the maximum price that people are willing to pay for the first antibiotic treatment, b is the slope of the demand curve, and Q_t is the number of antibiotic treatments in time period t.[c,d]

Antibiotic use reduces the risk of infection to other people. For simplicity, we assume the marginal external benefit (MEB_t) is constant. The marginal social benefit is found by vertically adding MEB_t to the demand curve. In other words, the marginal social benefit equals

$P_t^* = a - bQ_t + MEB_t = D + MEB_t$. However, purchasers of the antibiotic are unlikely to benefit from the marginal external benefit to others from using the antibiotic. Since buyers are likely to ignore MEB_t, there is an argument for the use of a public health system or other mechanism that subsidizes antibiotic use.[e] The marginal revenue faced by the supplier of antibiotic j is $MR_t = a - 2bQ_t$. If there exists a public health system or other mechanism to account for the MEB_t, the marginal revenue is $MR_t^* = a - 2bQ_t + MEB_t$.

In Figure 1, the horizontal axis denotes the number of treatments of antibiotic j used to treat bacterial infections and the height of the demand curve (D) shows how much people are willing to pay for one more antibiotic treatment. MC depicts the marginal cost of antibiotic treatment, it includes the marginal cost of producing each additional unit of the antibiotic, the cost of visiting a doctor to get a prescription, and any discomfort from the use of the antibiotic.[f] The MC is assumed to be upward sloping.

If the antibiotic treatment is stopped before all the bacteria are killed, use of the antibiotic in the current period causes more resistant bacteria in the future. $\sum_{n=1}^{\infty} \alpha_n/(1+r)^n \partial R_{t+n}/\partial Q_t$ measures the present value of the additional cost of increased resistance. $\partial R_{t+n}/\partial Q_t$ measures how a marginal increment in current antibiotic use increases the number of resistant bacteria in period $t+n$. t indicates the current time period and n is the number of time periods in the future that the
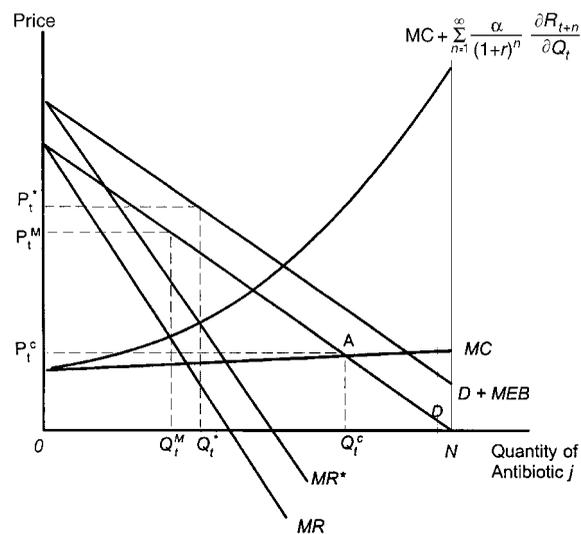

Figure 1. Demand and cost curves for antibiotic j

resistance problem is being measured. Future resistance problems are discounted using the present value formula $1/(1+r)^n$ where r is the interest rate at which future resistance is discounted into current dollars. The higher the interest rate, the less people are concerned about future resistance problems. In other words, the higher the interest rate, the lower the current value of the negative externality caused by future antibiotic resistance.

α_n converts the increase in antibiotic resistance into dollar terms. The larger α_n, the higher the cost of an increase in resistance. An increase in α_n might be caused by the current knowledge that there are few new antibiotics in the pipeline of the drug companies.

Existing evidence indicates that the volume of antibiotic exposure is the key determinate in causing antibiotic resistance [11–13].[g] Resistance to some antibiotics has persisted years after usage has ceased or been substantially reduced. Twenty percent of Enterobacteriaceae were resistant to streptomycin approximately 25 years after streptomycin use was greatly reduced [14]. Likewise, when sulphonamide prescriptions decreased from 320 000 prescriptions per year in 1991 to 7000 in 1999, resistance fell from 46% in 1991 to 40% in 1999 [15].

Cross-resistance is probably one of the main reasons that resistance continues after ceasing or reducing antibiotic use.[h] Chiew et al. [14] found that of their isolates that were resistant to streptomycin, 86% were also cross-resistant to spectinomycin. Enne et al. [15] also conclude that their results suggest that cross-resistance is important.

These results are different from a Finnish study where resistance of group A streptococci which were resistant to erythromycin fell quickly when erythromycin was reduced [16]. This may be because in Finland, erythromycin resistance had emerged recently and the strains were not cross-resistant [15].

When there is cross-resistance, use of antibiotic x creates a negative externality by reducing the effectiveness of antibiotic j. People buy antibiotics to reduce and eliminate bacterial infections. If usage of antibiotic x reduces the effectiveness of antibiotic j, then using antibiotic x reduces the demand for antibiotic j. In other words, when there is cross-resistance between antibiotic x and j, usage of antibiotic x causes a decrease in demand for antibiotic j.

Efficient antibiotic consumption implies that the antibiotic is used until the additional benefit ('cure' + improved public health) is equal to the additional costs incurred (marginal costs of treatment + increased resistance). In Figure 1, the efficient quantity of the antibiotic is Q_t^* where both the external benefit and external cost are taken into account.

Since antibiotic resistance reduces the value of the antibiotic, suppliers of patented antibiotics have an incentive to take into account antibiotic resistance. However, unless there is some mechanism to incorporate external benefits such as subsidies or a public health system, suppliers do not have an incentive to take into account external benefits. To maximize profits, the suppliers will produce where marginal revenue (not including the external benefit) equals the marginal cost (including the external cost). In Figure 1, assuming no public health demand and no cross-resistance, Q_t^M of antibiotic j will be used which is less than the efficient quantity Q_t^*.

Extended patents reduce antibiotic resistance

Ineffective antibiotics are most likely when there is open-access. In the case of antibiotics, open-access occurs when anyone can produce, sell, and use the antibiotic. In other words, no patents or licenses govern the production of the antibiotic and it is sold over the counter. Under these circumstances, producers would be unwilling to incur any cost to enhance the future efficacy of an antibiotic that had no property rights attached to it and thus was subject to open-access. The 14-year delay (1928–1942) between the discovery and the production of penicillin may be attributed to the lack of property rights (patent protection) [1, p. 32–51]. Streptomycin and sulpha drugs got to market much faster partly because Merck and Company and I.G. Farben were secretive until they developed a patentable production process and financially benefitted from their discoveries.

The classic case of open-access is a fishery. Any fisherman leaving a fish in the water to grow larger is unlikely to catch it in the future. This leads fishermen to act as if they were unconcerned about future fish stocks and catch too many immature fish. A prominent reason for open-access in

antibiotics is expired patents. This causes the price of antibiotic j to decrease and the quantity used to increase.

This is depicted in Figure 1. When there is open-access, since producers have no private future benefits to discount, the industry's equilibrium output and price is where $D = MC$. Quantity is now Q_t^c and price is P_t^c. There is no economic profit at Q_t^c because total revenue (TR) equals total costs (TC).[i] With open-access, pharmaceutical companies have less incentive to research and develop new antibiotics.

Antibiotic resistance can be reduced by extending the duration of the patent on antibiotic j. Patents give the owners an incentive to protect the value of antibiotics by curtailing their usage. However, near the end of patent protection, pharmaceutical firms may have an incentive to overuse antibiotics to capture profits which will not be accessible in the future. Another end period problem, is that effectively using old antibiotics may forestall resistance to newer antibiotics. Unfortunately, once a drug goes off patent there is little financial incentive to study new areas of use.

One way to ameliorate this end period problem is to extend the effective life of antibiotic patents.[j] Optimal antibiotic use is achieved by establishing an owner with incentives to consider the effect of contemporary use on future antibiotic resistance. Permanent patents would prevent inefficiently accelerated use of the antibiotic near the termination of the patent. In other words, prolonging the patent period would reduce the incentives to excessively discount future resistance.

A result of an extended patent system is that there will be more infections in the current time period. The cost of this increment in contemporary infections, however, is less than the value of future infections which will be treatable because of fewer resistant bacteria. The pharmaceutical company would establish a reservation price on the antibiotic equal to the discounted expected future value of a future treatment. Only current consumers who value their treatment less than this discounted future price will refrain from purchasing the antibiotic.

Cross-resistance complicates this analysis. Patents on antibiotics do not solve the problem of cross-resistance because using antibiotic x causes bacteria to become resistant to antibiotic j. A solution to cross-resistance problems is to give monopoly patents to an entire antibiotic class.

However, the genetic codes for a bacterium's resistance mechanisms are such that using one antibiotic can cause the bacteria to become resistant to another antibiotic from a completely different class. The prevalence of resistance to penicillin in *Streptococcus pneumoniae* is related to exposure to microlides as well as exposure to penicillin [17]. Thus, the idea of providing pharmaceutical companies with a monopoly for a whole class of antibiotics may not work because of antibiotic resistance caused by the use of antibiotics outside the class they control. Given the large number of companies that manufacture antibiotics, it may not be politically feasible to give monopoly control over classes of antibiotics.

A universal monopoly over all antibiotics would be a solution. This would solve the problem of cross-resistance. However, having a single owner of all antibiotics presents political and economic problems. Another option is having an antibiotic cartel. This would not be legal in the United States. However, government regulations that restrict access to antibiotics, may have similar results to a cartel or monopoly.

Giving companies exclusive rights to sell all the antibiotics in a certain region may be a solution. A problem arises when there is a high price in a region with resistance problems and a low price in a region with less resistance, people would have an incentive to buy where the antibiotic was cheaper and sell where the price was higher.

Using a single buyer to reduce antibiotic resistance

A solution to the antibiotic resistance problem is to have a single buyer who is the residual claimant and has an incentive to take into account future resistance problems. Since the buyer bears the costs of illnesses, it may even take into account the public health effects of antibiotics. In this case, the optimal quantity Q_t^* is used.

Patent protection for the pharmaceutical firm is analogous to the fishery example where the fishery is a privately owned lake. Having a single buyer is like having a fisherman who is the only one who has access to a lake. It does not matter whether there is an owner of the lake or there is a single fisherman, in either case, the owner of the lake or the single fisherman will receive the benefits from

leaving the fish to grow larger. Because of this, either a single owner of the lake or single fisherman are concerned about future fish stocks.[k]

Examples which approximate a single buyer may be national health insurance programs and the coalition for affordable quality healthcare (CAQH) in the United States. The CAQH is a coalition of 24 of America's biggest health plans and insurers. Since health insurance companies are responsible for paying their clients' healthcare bills, the companies have an incentive to take into account future healthcare costs. An insurance company, Aetna, using claims data to identify doctors who over-prescribe antibiotics, sent letters containing center for disease control (CDC) guidelines to the over-prescribing doctors and had a 20% reduction in antibiotic use the next year [19].

However, health insurance and national health insurance systems that subsidize the purchase of antibiotics and subsidize visits to the doctor may also increase antibiotic use above the efficient level.[l] This increased antibiotic use may increase antibiotic resistance.

Equation (1) shows the effect of insurance and national health insurance systems. Assuming no deductible, and the coinsurance rate (the percent paid by the patient) is s, the price paid by the insurer is $(1-s)P_t$. The new demand curve D_I may be written as

$$P_t^{\mathrm{I}} = \frac{a - bQ_t}{1 - s} \qquad (1)$$

where P_t^{I} is the price paid to the supplier of the antibiotic. There are now two demand curves, one by the insurer and one by the patient. If property rights are clear, the seller of the antibiotic will produce where $Q_t^{\mathrm{I}} > Q_t^{\mathrm{M}}$. In other words, with insurance, more than Q_t^{M} is consumed. One experiment found that when people were not charged for medical care, they used 85% more antibiotics than when they paid for part of their medical care [20, p. 169].

Figure 2 shows the effect of insurance. The new demand curve is D_I and the marginal revenue curve is MR_I. If there is full coverage insurance, the coinsurance rate is 0. In Figure 2 the demand curve would be represented by the vertical line at N, i.e. as long as patients perceive any benefit from the antibiotic they would demand it. Patients would not consider the price paid to the suppliers because the price would be zero to the patients. In this case, without some other rationing device, too much of the antibiotic is used.
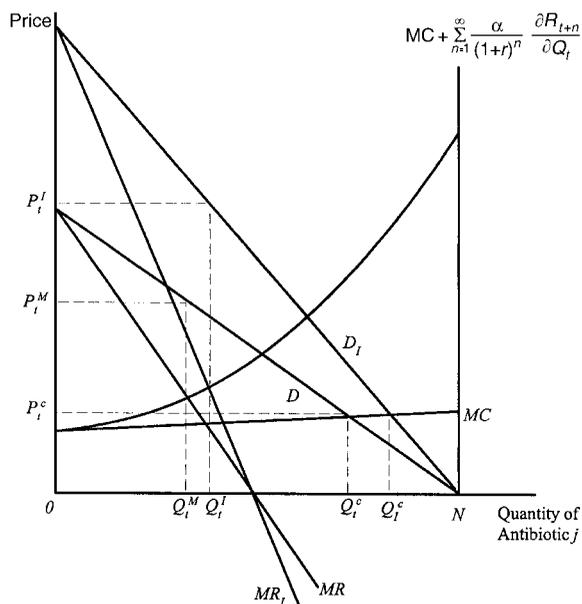

Figure 2. Demand and cost curves for antibiotic j with insurance included

If property rights are not clearly defined or the use of the antibiotic is a common property resource, insurance coverage increases antibiotic use from Q_t^{c} to Q_I^{c}. Instead of moving toward the efficient quantity of the antibiotic, when there is open-access, insurance exacerbates the problem of antibiotic resistance.[m]

National health insurance programs that regulate pharmaceutical prices also may cause excessive antibiotic use. The prices that the national health insurance programs set for antibiotics are equivalent to price ceilings. Suppose that a country sets the price ceiling equal to P_t^{c} in Figure 1. The demand curve becomes P_t^{c} AN and antibiotic use increases to Q_t^{c}, the same quantity as when there is no patent and there is open-access. In other words, national health care plans, when they set the fee schedules equal to the competitive price, create the equivalent of open-access, years before the antibiotic's patent has expired.

An example of this may be Japan where a national fee schedule specifies all procedures and products that can be paid for by health insurance plans and also sets the prices. The fee schedule applies to all Japanese, all insurance plans, and all providers. Since the early 1980s, the Japanese government has sharply reduced the prices that physicians and hospitals can charge for

pharmaceuticals [21]. Ikegami and Campbell argue that '... the major pharmaceutical companies have responded by introducing more drugs that are only marginally 'new' but for which higher prices can be charged. One result is the premature release of third generation antibiotics, leading to rapid increases in bacterial resistance to antibiotics' [21, p. 1298].

Politically motivated single buyers are often the cause of excessive antibiotic use. Doessel [7] pointed out that the Australian Government acts as a monopsonist for legal drug consumers and then subsidizes these already low prices. The effect is to increase antibiotic use and antibiotic resistance.

The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA) has been more successful in reducing antibiotic use.[n] Mölstad and Cars [23] report that STRAMA reduced Swedish outpatient sales of antibiotics by 20% from 1993 to 1997. Children between 1 and 6 years old had the greatest reduction in the use of antibiotics.

There were three parts to the Swedish strategy to reduce antibiotic resistance. First, the national STRAMA group developed guidelines which reduced the use of various antibiotics. They also created a brochure for patients with respiratory tract infections (RTIs) that educated the patients on the relationship between RTIs, antibiotic use, and resistance.

Second, regional STRAMA groups were formed in the counties. Their main objective was to evaluate how antibiotics were being used and the pattern of resistance in their area. After determining the problems, the regional STRAMA group tried to influence health care workers to improve diagnostic procedures and reduce the inappropriate prescribing of antibiotics.

Third, all Swedish microbiology laboratories used the same tests to determine the susceptibility of various bacteria to antibiotics. The results were shared with the national STRAMA group and the regional STRAMA groups.

Since 80% of all antibiotic prescriptions were for out-patients and 60% of the out-patient prescriptions were for RTIs,[o] in most counties, the regional STRAMA educated health-care workers on diagnosing RTIs. They also stressed that antibiotics should not be prescribed in uncomplicated RTIs or acute bronchitis and that national recommendations on RTIs should be followed. Also, to encourage patients to abstain from using antibiotics, most counties offered a free return visit if antibiotics were not prescribed.[p]

This program depends on patients, doctors, and veterinarians following the guidelines. However, in some countries, the threat of malpractice lawsuits may give doctors the incentive to set the therapy longer than required and use antibiotics when they are unwarranted.

Likewise, in some countries, hospitals and doctors receive income from drug sales. In Japan 80% of physicians in private practice and 89% of hospitals dispense their own medicines and these physicians and hospitals derive a substantial portion of their income from dispensing medicines [21]. This creates a principle–agent problem. The agent (the doctor) is benefitted when the principle (the patient) buys more drugs than is optimal.[q] Since in many countries, veterinarians are able to prescribe and dispense, they too may have an incentive to encourage owners of the livestock and pets to buy more antibiotics than is optimal.

Conclusion

Antibiotic resistance tends to increase when a patent on an antibiotic expires. Since new companies can now produce and distribute the antibiotic, more of the antibiotic is produced and prices fall. Because the benefits of reducing current production go to other firms, pharmaceutical companies will have little concern about future resistance. This 'open-access' problem causes excessive antibiotic use and resistance problems in the future.

One solution to this 'open-access' problem is to extend patent protection on the antibiotic. However, if there is cross-resistance between antibiotics, extending patent protection may not work in the long run. Patent protection may not work if people are legally using other completely different antibiotics which cause bacteria to become resistant to the original antibiotic, then the benefits of reducing current production which reduces future resistance go to other companies. The pharmaceutical company that has patent protection on a drug that is cross-resistant may have little concern about future resistance.

This cross-resistance problem could be solved by a monopoly owning all antibiotics. However, whether the monopoly was a quasi-governmental agency or a private company, this solution may not be feasible and there would be serious

concerns about other costs caused by a lack of competition. Likewise, a cartel producer of antibiotics would have similar benefits and similar problems as a monopoly.

Government regulations that restrict access to antibiotics, may have similar results to cartels or monopolies, though the profits may or may not go to the producer. If the profits do not go to pharmaceutical companies, then there are fewer incentive to research and develop new antibiotics. If profits are returned to companies in a cartel, it is unlikely that those profits will go to the specific companies that are the most productive researchers.

A single buyer such as national health insurance or private health insurance may have an incentive to reduce antibiotic resistance since they bear the future cost of future resistance. This is an example of the Coase [1960] Theorem which showed that voluntary bargaining can lead to efficient outcomes even when externalities exist. However, national health insurance and private health insurance are also likely to exacerbate antibiotic resistance problems, ceteris paribus. Insurance coverage reduces the price that patients pay at the margin and thus the patients are likely to use more antibiotics. National health insurance policies may even set the price of antibiotics so low that resistance problems are created even when the patent is in effect.

STRAMA encourages Swedish health-care workers to use guidelines, education, and surveillance to reduce antibiotic use. There are three parts to the Swedish strategy to reduce antibiotic resistance. First, the national STRAMA group developed guidelines and educational materials for patients. Second, regional STRAMA groups evaluate how antibiotics are being used and the pattern of resistance in their area. They then persuade health-care workers to improve diagnostic procedures and reduce the inappropriate prescribing of antibiotics. Third, all Swedish microbiology laboratories use the same test to determine the susceptibility of various bacteria to antibiotics. The results are shared with the national STRAMA group and the regional STRAMA groups. This program would not work if doctors did not go along with the guidelines and patients refused to abstain from antibiotic use.

STRAMA depends on patients, doctors, and veterinarians following the guidelines. However, in some countries, the threat of malpractice lawsuits may give doctors the incentive to set the therapy longer than required and use antibiotics when they are unwarranted and in some countries, hospitals, doctors, and veterinarians receive income from drug sales. This gives them an incentive to prescribe more antibiotics than is optimal.

In analyzing antibiotic resistance, it is crucial to recognize the trade-off that occurs with antibiotic use. More current use implies that the antibiotic will be less effective in the future. While lower current use implies more current infections and/or higher testing costs. Without more widespread and precise data collection and analysis, we are left to guess about the severity of this resistance problem.

This article argues that better data collection and analysis would move us in the direction of better assessment of these trade-offs and that property rights deserve more attention in research and policy. Particularly useful would be (1) data which can reveal what future level of resistance is generated by a current antibiotic treatment and (2) data designed to address what property rights assignments yield the optimal trade-off between suppression of current infections and future antibiotic resistance.

Acknowledgements

Notes

a. Cross-resistance is when use of one antibiotic causes bacteria to become resistant to a different type of antibiotic.
b. This is a negative network externality model.
c. Notice that P_t is the price of an antibiotic treatment not the price for each pill. If the price was for each pill, then patients would be much more likely to stop taking the antibiotic after their symptoms disappeared.
d. This demand curve assumes that patients must buy the full antibiotic treatment. However, in developing countries many poor patients will buy small samples even when it is not legal [10]. Buying small samples makes it much more likely that patients will stop taking the antibiotic when symptoms disappear.

Failure to finish antibiotic treatments creates even more resistant bacteria.

e. Note, however, that pharmaceutical companies do give reduced cost pills to the poor.

f. In some countries a prescription is not required to purchase an antibiotic. In this case, the cost of visiting the doctor can be ignored. Since the price of antibiotic treatment is lower, the MC will be lower, and more antibiotics will be used.

g. The exposure creates an ecological niche for the resistant bacteria by killing the susceptible bacteria. Resistance may also be created by the exchange of genetic material between the same and different species of bacteria.

h. Though the data suggests that cross-resistance is important [15]. The lack of a decline in resistance to sulphonamides may also be caused by one or more of the following additional reasons: (1) the decline has not yet occurred, (2) low fitness cost, and (3) use of sulphonamides in agriculture and aquaculture. Low fitness cost is when, use of an antibiotic is stopped, the resistant bacteria is nearly as efficient as the susceptible bacteria in feeding and reproducing.

i. Q_t^c is the industry equilibrium (where there is no net exodus from, nor net entry into, an industry) because: (1) if $Q > Q_t^c$, then TC > TR, some antibiotic producers would make economic losses and have incentive to exit the industry, thus quantity would drop and (2) if $Q < Q_t^c$ some antibiotic producers would make a supernormal profit, attracting additional producers.

j. Establishing a legal framework (longer patents), which enable the internalization of an externality is a Coasian approach.

k. This is an application of the Coase theorem [18]. If property rights are clear and negotiation is costless, then it does not matter who owns a resource, the efficient solution will be found.

l. If the subsidy is equal to the MEB_t, then, everything else constant, the efficient quantity of antibiotics will be used.

m. In the case of insurance, the efficient quantity will be produced when Q_t^* equals Q_t^I. Everything else constant, the efficient quantity Q_t^* will be sold if property rights are clearly defined and the marginal external benefit equals the coinsurance rate times the marginal cost of antibiotic use.

n. In 1997, Sweden had the third lowest out-patient antibiotic sales in the European Union [22]. The countries with the five lowest out-patient antibiotic sales were Netherlands (8.96 defined daily dose per 1000 inhabitants), Denmark (11.35), Sweden (13.51), Germany (13.58), and Austria (13.80).

o. Twenty-five percent of the remaining out-patient antibiotic prescriptions were for genito-urinary infections.

p. Since 1998 all consultations by children are free of charge.

q. The Japanese spend more per capita for pharmaceuticals than Americans do even though the Japanese prices are lower [21].

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