Tuberculosis and antibiotic resistance

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Recently, several Indian newspapers have carried stories on the impact of '*Bt*-cotton gene on tuberculosis (TB)' alleged by Greenpeace, because of the presence of the antibiotic marker gene in these crops. Here, I analyse this risk issue from the use of genetically modified cotton, based on the published literature.

Bt-cotton is a genetically enhanced cotton variety that provides protection against damage by Lepidopteran insect pests of cotton. Doreen Stabinsky, a scientific advisor to Greenpeace International recently claimed (*Times of India*, 2 Nov. 2001) that products (fibre, animal feed, cotton-seed oil) from *Bt*-cotton plants can lead to an increase in the occurrence of antibiotic-resistant bacteria, including those that cause TB and gonorrhoea. She implied that the antibiotic resistance gene (*aad*) present in the *Bt*-cotton genome could be transferred to pathogenic bacteria that cause these diseases, making them resistant to drug therapy.

However, critical scientific review of the facts makes it clear that there is no evidence that such a transfer could occur. Furthermore, there are many studies demonstrating that resistance to the specific antibiotics is relatively common in these disease-causing bacteria. Therefore, there is no additional risk associated with growing or using *Bt*-cotton or products of these plants. Additionally, there are many environmental and safety benefits associated with the use of *Bt*-cotton compared to traditional cotton, like higher yields, reduction in use of chemical pesticides and safety to non-target organisms, that include beneficial insects, birds, fish and mammals, including humans.

General studies by academic scientists and regulatory advisory groups have been undertaken to estimate the potential risks and determine whether the antibiotic resistance genes encoded by DNA from genetically engineered plants could transfer to any species of bacteria in the field, or in the animals or humans that might eat the plant products. There are two mechanisms by which antibiotic resistance genes can be transferred into strains of bacteria that do not already contain these genes.

The first is by direct DNA transfer from a different but related bacterium that is resistant through either conjugation, a kind of mating of bacteria, or by specific infection of the bacteria by bacteria-specific viruses that can transfer DNA between bacteria. Such methods are efficient but restricted to certain kinds of bacteria, including many pathogens. The second is by general uptake of free DNA from the environment. This method is inefficient compared to the first one and rarely occurs in bacteria outside the laboratory. The second method is the only one by which resistance could be transferred from plants to bacteria, and as studied by many scientists, is very unlikely to occur. Such a transfer would be much less frequent than transfers of DNA between bacteria[1–4]. An important consideration is the availability of intact genes (DNA) in proximity to the bacteria. The bacteria that cause TB and gonorrhea only grow in humans, in some animals or in the laboratory. Since the DNA in cotton is severely degraded and removed by washing and processing in making the various cotton products (oil, cotton fibre and especially products used for feminine hygiene or surgical dressings), it is extremely unlikely that these bacteria would be in contact with the DNA in *Bt*-cotton. Therefore it is even less likely that these bacteria could become resistant to antibiotics because of the presence of these genes in the cotton plants.

Different advisory groups in the World Health Organization[5] and the Food and Agricultural Organization of the United Nations reviewed available data in 1993 and in 2000 and determined that there is no evidence that such a transfer is scientifically likely to occur and pose a risk to consumers or the environment. The opinion of the European Commission's Scientific Committee on Plants[6] was clear that the possibility of transferring either the *nptII* gene (kanamycin resistance) or the *aad* gene (streptomycin resistance) from *Bt*-cotton to bacteria is extremely small. Furthermore, in the unlikely event that such a transfer may occur, no additional risk would be involved, as many bacteria are already resistant to these antibiotics[3,7].

TB is a serious, common disease caused by an infection of *Mycobacterium tuberculosis*, and is usually focused in the lungs. It is estimated that there are more than 8 million new infections every year, worldwide. The bacteria causing the infections are frequently resistant to antibiotics because they carry genes for multiple drug resistance, making the disease very difficult or impossible to treat.

Results of hundreds of studies have been published about the antibiotic resistance of the TB bacterium, including many in India. While the number of cases of antibiotic-resistant TB is increasing, it was noted in the 1980s and 1990s that resistance was common in India. Doctors in Chennai studied more than 3000 TB patients over six months of antibiotic treatment in 1989 and found that 31% of the survivors still had active infections, with 65% resistant to the antibiotic isoniazid, 12% to rifampicin and 19% to streptomycin[8]. Testing for antibiotic resistance in 150 strains of *M. tuberculosis* isolated from TB patients in east Delhi demonstrated that many patients had bacteria resistant to one or more antibiotics, including streptomycin[9].

Drug resistance is higher in those who have received antibiotic therapy and the specific pattern of resistance does vary with time and medical practice. A study of patients in Mumbai, with recoverable tuberculin-type bacteria in sputum samples, indicated that 53% were infected with TB resistant to streptomycin and 25% resistant to kanamycin, as well as variable resistance to other antibiotics[10]. Similar results were obtained by Varaiya and Gogate[11] at another hospital in Mumbai, and by Mathur *et al.*[12], in the Jodhpur district. International health-care studies have demonstrated that in many TB patients, bacteria that are resistant to one drug are resistant to three or four antibiotics and that the incidence of multi-drug-resistant tuberculosis is increasing due to ineffective treatment, often because the patient does not take the full course of the prescribed dose of antibiotics during the first months of treatment[13].

It is clear that the common finding of streptomycin and kanamycin-resistant *M. tuberculosis* in TB patients in the late 1980s and early 1990s occurred long before any genetically engineered crops were grown anywhere in the world.

While most strains of bacteria that cause gonorrhoea (*Neisseria gonorrhoea*), an important sexually transmitted disease, are susceptible to streptomycin or kanamycin, resistant strains have been reported[14–16]. Since the DNA in cotton-fibre products that would likely be in contact with the bacteria has either been damaged or removed by washing and processing of the fibre, the probability of transferring resistance from the plant to the bacteria is remote. Further, genes that cause antibiotic resistance to streptomycin and kanamycin are present in many other species of bacteria in the environment. Therefore the bacteria causing either TB or gonorrhoea are much more likely to become resistant through contact with those bacteria.

The information that is available from a large number of important studies, demonstrates that growing *Bt*-cotton in India or anywhere else in the world and using products derived from this crop will be safe and will not have any effect on the incidence of antibiotic resistant-bacteria that cause either TB or gonorrhoea.

In summary, *Bt*-cotton has been grown commercially in the US and Australia since 1996, Mexico and South Africa since 1997, and China and Argentina since 1998. There have been no reports of increased incidence of antibiotic-resistant bacteria that cause either TB or gonorrhoea, which can be attributed to the production of *Bt*-cotton in these countries. Also, several agricultural and environmental benefits have been realized by commercial use of *Bt*-cotton varieties that include reduced chemical insecticide treatments for target pests, highly effective pest control, increased yields and increased population of beneficial organisms in cotton[17,18].

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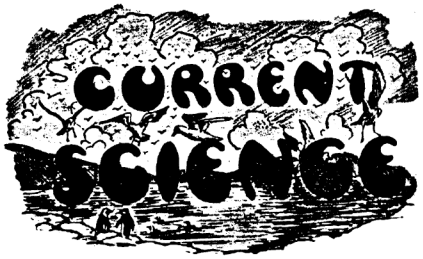

Vol. V] DECEMBER 1936 [No. 6

Public benefactions and science

Lord Nuffield's munificent gifts to the University of Oxford are worthy of admiration and imitation. They must have a strong appeal to the more enlightened and wealthy communities in India, and hopes might be entertained that the Indian Universities and other research institutes would likewise benefit by the philanthropic and patriotic instincts of the rich landed proprietors and industrial magnates in this country. The conservative temperament of the Indian mind has not understood the full significance of the somewhat cryptic saying, 'cast thy bread upon the waters,' for generally it fears, that instead of finding it after many days, it may be totally lost. The sage's assurance that it would return in increasing abundance ought to inspire public confidence. No thoughts of personal gain underlie public benefactions, which are made solely with the objects of assisting the work of self-dedicated scientists, whose labours result in the benefit of our own generation and the generations yet unborn. Practically in every instance, material prosperity is absolutely dependent upon the patient researches of those who seek for no personal reward, and whose work at the time was thought by men of affairs to be of no consequence. It must not be forgotten that the foundations of our greatest present-day advances were laid by scientists, and the increasing returns, which men of business reap, have originated in work inspired by no thought of personal gain. Of all the human activities, perhaps the one thing that cannot be overproduced is scientific