Letter From the Desk of David Challinor
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In 1900, when my parents were teenagers, they were not only acutely aware of tuberculosis (TB) but undoubtedly exposed to this debilitating and long-lasting disease. In the late 1800's it was commonly known as consumption and was such a part of daily life that its presence permeated the lives of fictional characters, such as Mimi in *La Boheme* and Hans Castrop in Thomas Mann's *The Magic Mountain*, as well as the poet Elizabeth Barrett Browning. My father had TB as a teenager and was sent to a sanitarium in the Adirondacks for the "cure;" my wife's uncle had the disease and was sent to Arizona. My father was lucky because although his lungs were scarred, the Army's physical examination did not detect it and he became a pilot in WWI. My father-in-law, his contemporary, was not so fortunate; he had TB of the hip bone and was immobilized in a body cast for two years. When the unbelievably restrictive cast was removed, his hip had successfully become fused, thereby trapping the TB bacilli and preventing its spread to the rest of his body. The result of his successful battle with TB was a dependence on crutches and a wheelchair for the rest of his life. This month's letter is about tuberculosis, its current resurgence and what is being done to contain its expansion.

TB thrives under crowded conditions and when the industrial revolution lured hordes from the countryside to the crowded tenements of factory towns, the disease became rampant. In my parents' generation, almost every family had lost a child to it. The wan appearance of those afflicted gave it the name "the white plague."

With better housing and sanitation, the incidence of TB dropped markedly in North America, Australia and Scandinavia during the early 20th century. New antibiotics developed after WWII helped speed the decline of the disease, but these new treatments seldom reached southern Africa and east Asia. Today, some 30% of the globe's human population carries TB. Not all develop the disease, but these carriers cause ten million new cases annually, of which 3 million die—more than from AIDS or any other infectious disease. Even in the developed world, TB is ever-present and is frequently the lethal blow to HIV patients with their compromised immune systems. My father ultimately died from TB 60 years after the TB bacilli encapsulated in his lungs, because lung cancer from smoking released the dormant bacilli.

The disease, caused by a bacterium (*Mycobacterium tuberculosis*), was first identified in 1882 by Robert Koch, a German bacteriologist and physician (1843-1910). When magnified, the bacteria appear as slightly curved rods known as bacilli. There are several kinds of this bacteria, one of which (*M. bovis*) is found in cattle and can be transferred to humans through milk. The risk of such infection is now slight because milk is pasteurized for human consumption and virtually all dairy herds in Europe and North America are free of TB. Another group of this bacteria, known as non-tuberculosis

mycobacteria, has proliferated with the increase in HIV-infected people. This strain attacks the lymph nodes and the skin, particularly in children.

Despite the widespread nature of TB, the bacillus itself seems rather benign. Unlike more lethal bacteria, it does not secrete toxins nor release enzymes that kill cells. In cultures it grows significantly slower than other bacteria. Despite these seemingly unthreatening characteristics, the bacillus has one extremely potent quality—it is protected by a special waxy covering from attacks by the host's immune system. The bacillus is so well-armored that it can survive inside microphages—specialized cells in our bodies that engulf and normally destroy other unfriendly bacteria. After being "swallowed" by microphages, the bacteria are trapped in membrane-covered sacs—pouch-like structures in plants and animals—called phagosomes, and it is within these bodies that alien bacteria are destroyed by our protective enzymes. The TB bacilli, however, not only survive and multiply within the microphages, but are spread throughout the entire body as the microphages circulate through the lymphatic system.

At this stage, a battle develops between the bacilli and our immune system, which results in the creation of tubercules or small swellings inside of which are a mixture of immune cells, macrophages, dead cells, etc. Tubercules appear among those body parts that have concentrations of TB bacilli. Tubercule presence is evidence that the body is fighting back, but the struggle proceeds so slowly that the bacteria have time to cause considerable tissue damage. For the TB victim, survival depends on which side triumphs: the bacilli with their slow steady assault, or our immune system's ability to destroy the bacilli or at least curb its spread.

Most TB infections begin in the lungs when the bacilli are inhaled. Mucous membranes normally protect the tops of our lungs against invasive bacteria. When TB bacilli—inside the tiny sprayed droplets coughed up by an infected person—are inhaled by another, the bacilli-laden droplets penetrate to the lungs' perimeters where small air sacs exist in which oxygen is transferred into our system and carbon dioxide is removed as we exhale. These small gas exchange sacs or alveoli are coated not with protective mucous but rather with microphages, the very cells that gobble up bacilli. Thus ingested, the bacilli are carried within microphages to the lymph nodes near the top of the lungs where they thrive in the high oxygen content of freshly inhaled air. In 95% of healthy people the TB will go no farther. This stage is called primary TB, and the only evidence of the bacilli in such people is the shadow often visible in x-rays at the top of the lungs. The infected individual shows no sign of distress as his/her immune system causes the tubercules that are formed to be absorbed; all that remains are small scars on the lungs. In New York City where I grew up, this was called "subway TB" and you went on with your life, often unaware you had been infected at one time.

However, if your body is stressed by malnutrition, AIDS or some other disease, your immune system often fails to protect you, and you may eventually succumb to full-blown TB. The bacilli, once inside, can lie dormant for decades until conditions are right for them to break out and begin their lethal assault, as happened to my father when stricken with lung cancer. A common location for dormant bacilli is in the lungs and, except for AIDS victims, about 85% of people who get TB have pulmonary TB. Untreated TB carriers commonly have a persistent dry cough. In such victims, the bacilli spread and invade blood vessels, which in turn leads to expectorating blood. This stage is accompanied by shortness of breath, fever, weight loss and chest pain, with death generally following.

Fortunately, modern medicine has made impressive advances in treating TB. As is often the case, the earlier the diagnosis, the better the odds of recovery. The surest diagnosis is through a sputum sample, but only about 60% of people with active TB test positive this way so a backup chest x-ray is necessary to locate where to take a tissue sample for analysis. It is crucial to identify the exact strain of TB infecting a patient so that the ideal combination of antibiotics can be administered. Prompt diagnosis is essential because an untreated TB patient can infect up to ten people a year. As drug-resistant strains of TB increase, patients now commonly receive at least four drug combinations. Even with aggressive treatment the cure often takes up to a year. Some drugs have noxious side effects, but an even greater problem for TB control lies with those patients who feel so much better after initial treatment that they cease taking their medicine, ignorant that their body still contains live bacilli. Many people cannot or will not sustain a year's treatment. Not only are such delinquents increasing their own health risk, but they are contributing to the spread of drug-resistance.

All is not hopeless, however, as new drugs that can kill both drug-resistant as well as dormant bacilli are being developed. The genes of TB bacteria have been sequenced and may help scientists learn new ways to attack the bacilli. If the number of patients shrinks steadily, human hosts may become rare enough to prevent the spread of TB in a human population. It is unlikely that we can ever eradicate the TB that infects wild animals, such as the Cape Buffalo in the southern half of Kruger Park in South Africa, or the zoo herds of Bactrian camels that the National Zoo discovered were TB-infected at our Front Royal facility years ago. However, TB can be controlled and perhaps even become as uncommon as it is now in our domestic cattle herds. It would then no longer be the desperate world-wide problem that it is today.

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P.S. Much of the information in this letter came from *The White Plague*, an article by John Lee in New Scientist (9 November 2002).