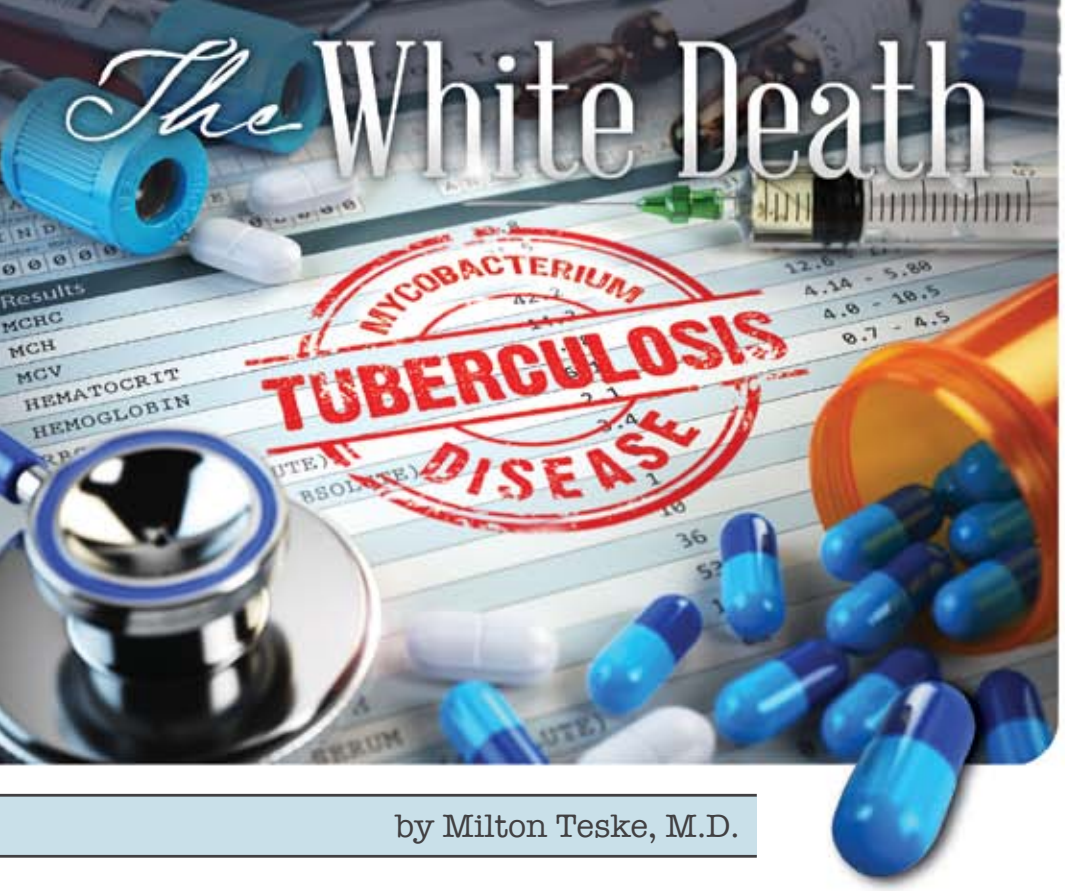
The White Death



by Milton Teske, M.D.

Also know as consumption, phthisis, scrofula, Pott's disease and the graveyard cough, **tuberculosis (TB)** is a slow lingering infectious disease that consumes the victim from the inside, eating away the lungs and other organs, usually over a period of a number of years, before death finally brings relief.

TB has claimed more lives than any other disease in human history.

Today this disease is **preventable** and **curable** with antibiotics. Yet today, in spite of this, it still has the unenviable title as **the number one cause of death** in the world from infectious disease. Not Ebola or HIV-AIDS, or bubonic plague or malaria or influenza or typhoid or cholera or any other plague kills more people. TB is still the number one killer.

Hard to Kill This Bacterium

The *Mycobacterium* responsible for this disease is a very slow growing bacterium. In laboratory testing, most common bacteria can be easily cultured in one to two days. This Mycobacterium can take eight weeks to culture. Most bacteria use sugar or other carbohydrates as their food source, but this Mycobacterium uses fats and cholesterol as its food source. Its physiology is highly aerobic requiring lots of oxygen to grow and probably explains why

2 BILLION
PEOPLE INFECTED WITH TB
(1/3 OF WORLD POPULATION)

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it is primarily a respiratory pathogen although it can infect every organ of the body.

Humans are the only known natural source for TB. And it is only spread by coughing or breathing out fine microscopic droplets containing the TB germs, which can float in the air and be inhaled into another's lungs.

Once inhaled into the little air sacs in the lungs, macrophages there immediately attack it and engulf it. For any other bacteria this would be their end — but not TB. The outside of this bacterium is covered with a thick waxy coating (unlike other bacteria). This way it is protected from being destroyed by the macrophage.

When a bacterium is taken into the macrophage by a process called phagocytosis, it is contained within a small sac (called a phagosome) that quickly merges with a sac containing powerful oxidizing and proteolytic agents (called a lysosome). These lysosomes normally completely destroy the bacteria in the phagosome within minutes.

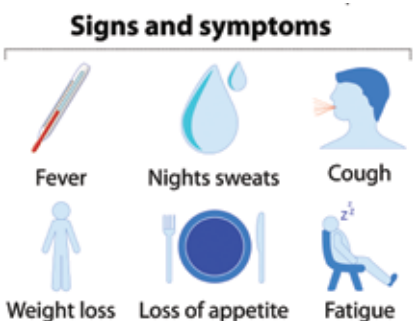
But the waxy coating encasing the TB germs blocks a special bridging protein necessary for the lysosome to merge with the phagosome so the lysosome cannot merge and empty its digestive agents into the phagosome. Thus the TB germs continue to live and grow in this now protected phagosome within the macrophage. And while the bridging proteins necessary for lysosome merger are blocked, it does not block the merger with little sacs containing nutrients necessary for bacterial growth.

There is also a gene in the TB germ that prevents acidification and another one that blocks destruction by powerful reactive nitrogen molecules used to destroy bacteria. And yet another substance (isotuberculosinal) is made that prevents the natural aging and breakdown of the phagosome with the TB germs in it. Thus TB can grow safely in an environment that makes it impossible to eradicate it. And there is also a special gene that makes a special DNA repair enzyme so even if there should be some damage to the TB DNA it can be quickly repaired.

Granuloma Formation

If you can't kill them then at least lock them up in jail so they can't spread and continue their destructive tissue invasion in the lungs or other organs. More macrophages come in to attack the infected macrophages and they fuse together forming giant multinucle-

ated macrophages. Certain cytokines, fibroblasts and proteins go to work to build a protective wall around these giant multinucleated macrophage masses infected with the TB germs and this is called a **granuloma.** Special T-lymphocytes surround them making sure that the granuloma is maintained and TB germs stay safely locked inside. These granulomas can be calcified and can be seen on a chest X-ray. But like a modern day prison, the inmates are kept alive and healthy.



As long as the immune system is healthy, these T-lymphocytes can keep the TB germs locked up in these granulomas for decades. We call this condition a latent TB infection or LTBI. There is no active TB spreading through the lungs or other organs, and the infected person is not contagious or spreading the infection to others.

The problem comes someday when the immune system becomes weakened. Maybe diabetes or cancer or HIV-AIDS or another infection or old age weakens the immune system, or maybe a medication like steroids or chemotherapy or one of the newer biologicals used to treat arthritis or other autoimmune diseases or even severe stress or environmental toxins can do it. Whatever the mechanism when the T-lymphocyte jail-keepers are weakened and cannot do their job, the TB germs can break out and start spreading through the lungs or even other organs in the body. The LTBI has now become active TB.

Active TB

As the TB mycobacteria spread through the lungs the normal lung tissue is destroyed, and large cavities or holes in the lungs develop. These cavities can be filled with necrotic tissue or mucus or purulent sputum that can be coughed up at times. When the infection eats through a blood vessel there can be bleeding into the lung. Coughing up blood-tinged sputum has been considered a death warrant throughout much of history. If a larger artery starts bleeding, the lungs can fill up with blood. Pulmonary hemorrhage was often the cause of death from TB.

The symptoms of active TB besides a bad cough often with some blood-tinge to the sputum are fevers or night sweats, fatigue and weight loss. This was often a slow gradual process taking a number of years. The ongoing weight loss, as the infection consumed one from the inside, led to its common name: **consumption.**

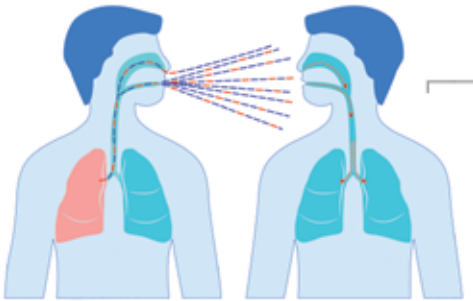
While pulmonary TB is its most common form, it can spread to the brain and spinal cord causing tuberculosis meningitis. It can infect the bones often eating away the spine and is called Pott's disease. In the lymphatic system it can cause enlarged infected lymph nodes often seen in the neck and is called scrofula. These enlarged infected nodes can rupture through the skin and drain at times. It can spread


Scrofula

to the kidneys and other glands. It can become disseminated, spreading through the blood stream to the whole body in a form called miliary TB that soon becomes fatal.

Very Infectious

The coughing of active TB is full of infectious mycobacterium. Even a very few of these mycobacterium is enough to cause an infection when inhaled. A single sneeze can release 40,000 micro droplets — each one capable of causing an infection.


Tuberculosis transmitted from person via droplets from the lungs of people with active TB

Today one third of the world is infected with TB (either LTBI or active TB). In much of Asia and Africa up to 80% are positive for TB infection. About *one and a half million people will die this year* from TB (95% of them in the more poverty stricken developing nations). In the U.S. between 5% and 10% are positive for TB infection.

Trying to get rid of TB

In much of the world a vaccine called BCG is given to try to prevent or at least lessen the severity of the infection. But it is only minimally effective. In the U.S. we do not vaccinate — instead we test and treat positive cases with antibiotics.

We use a TB skin test where a small amount of protein from killed TB germs is injected into the skin of the forearm. If inhaling a TB germ has infected you and your body is fighting it keeping it locked up in a granuloma jail, then your lymphocytes will immediately sense this TB protein injection. Within 48 to 72 hours the spot will become red and swollen hard with all of the lymphocytes swarming to the area and attacking this TB protein. This is a positive TB skin test. We can now confirm it with a blood test called QuantiFERON Gold if there is any uncertainty as to the result.

Treatment

Before the age of antibiotics doctors often prescribed various poisons that often speeded the demise of the unfortunate victims of tuberculosis. But starting in the middle of the 19th century it became popular to try to slow or stop the spread of the

disease in patients infected with TB by sending them to sanitariums. At these sanitariums they received fresh air night and day, pure water, a healthy diet, sunlight and exercise in the open air. They often had some good results.

Now we have antibiotics that can go beyond locking the germs in jail and actually kill them for us. But these mycobacteria are slow-growing and very hard to kill. To kill them in a LTBI it takes 9 months of Isoniazid daily. If one does not have liver problems we can kill them with only 4 months of daily Rifampin.

It is important to treat these LTBIs so they do not progress to active TB at some future date. If you have a positive skin test, getting treated can prevent a future active TB infection as well as protect those around you. By the time active TB is diagnosed and treatment is started, they've often infected many friends, coworkers and family members. Children are especially susceptible to getting infected with TB and often have a more rapid progression of the disease.

Treating Active TB

When one is symptomatic with coughing and there is a positive test, we will collect sputum and look at it under the microscope with special stains to see if we can find any TB germs. We will also culture it for eight weeks to see if we can grow any TB germs. If either one of these is positive, we know that an active TB infection is going on. We will start treatment with at least four different antibiotics at the same time. Treatment can continue for a long time — at least nine months, but sometimes over a year is needed.

The local public health department will send out an investigator, and every family member and coworker that might have been exposed needs to be tested. An infected student can result in hundreds of students needing to be tested. But it is only through work of this kind that we can keep TB under control and hope to someday eliminate it.

The local health officer has the authority to isolate the infected person as long as they are contagious to prevent them from spreading it to others. They also are responsible to see that a full course of treatment is finished to be sure that the infection is stopped. They use DOT (direct observed therapy) where a public health nurse goes out to the house and actually watches them take the pills every day to be sure they are getting all of the doses. (With reliable patients some are doing FaceTime DOT with an iPhone.) It is a lot of pills every day for a long time and we have found that compliance can be low without this ongoing surveillance. These public health nurses can be very creative with various accommodations and bribes to ensure compliance, but if all efforts fail the uncooperative noncompliant patient can be arrested and confined until the course of treatment is completed for the health and safety of the community.

When three sputum tests come back negative for TB the isolation can be lifted and the individual will be given permission to return to work and shopping

because they are no longer infective. But the full course of treatment must be completed. Not only must we be sure that every TB germ in him is dead but also we want to prevent the formation of multi-drug resistant TB germs (MDR-TB). Only partially treating a patient can lead to the formation of MDR-TB. Already MDR-TB is spreading in many parts of the world, and they are now showing up here. These MDR-TBs cannot be killed with our usual anti-TB drugs. They are given four powerful drugs for 18 to 24 months.

Some MDR-TB is becoming even more resistant to some of the stronger drugs used to treat MDR-TB and these are now called **extensively drug resistant TB** or **XDR-TB.** Currently, about 10% of MDR-TB is becoming XDR-TB.

In 2003 for the first time in the world we discovered infections with **totally drug resistant TB** in Italy. These are resistant to *all* of our known anti-TB drugs. They have now been found in Iran and India as well.

End TB Now

End TB Now is a plan by the United Nations and the World Health Organization to try to organize and inspire all the nations of the world to eliminate TB. The prospect of the spread of totally drug resistant TB is an apocalyptic nightmare. Hopefully the nations of the world will dedicate the resources needed toward achieving the elimination of TB before it is too late to prevent this humanitarian disaster.

END TB

"You shall not be afraid ...
of the pestilence ...
A thousand may fall at your side,
And ten thousand at your right hand;
But it shall not come near you.
... Nor shall any plague
come near your dwelling."

—PSALM 91

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