The Hygiene Hypothesis. . .

New Health Tip: "Go Play in the Dirt"

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Dr. Crowe's previous research projects have included plasmid replication in *B. anthracis*, functional genomics of *Agrobacterium tumefaciens*, and the manipulation of the immune response in the lung by influenza A virus.

Are you a "germaphobe?" Do you always keep a bottle of hand sanitizer and a container of disinfecting wipes nearby? While you may be saving yourself from catching a cold, scientists have reason to believe it may be bad for your health! The microorganisms that we try so hard to keep at bay may play key roles in preventing us from developing allergies or autoimmune diseases. **Some suggest that bacteria can even make us smarter!**

It is true that over the past century, human life expectancy in industrialized nations has increased dramatically, due in large part to advances in hygiene and public health. Development of clean water systems, tight regulation of food production, vaccine development, and the usage of antibiotics have helped to drastically reduce the number of deaths due to infectious diseases.

Our society's war on germs is ever expanding. In the United States today, the market for hand sanitizers exceeds $70 million, and disinfecting wipes are likewise becoming ubiquitous. But while the shift towards more hygienic lifestyles has undoubtedly decreased the morbidity and mortality rates due to infectious diseases, there are signs that suggest there is a price to pay for our cleanliness.

Many scientists now believe that exposure to microorganisms plays a major role in fine tuning our immune system.

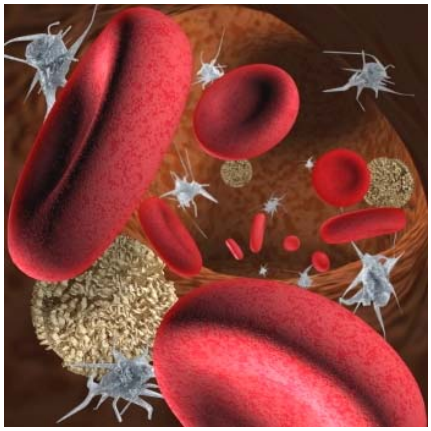


Figure 1: ***Artist's rendition of white blood cells, amongst red cells and platelets. For optimal health, the subgroups of T helper cells must be in a state of balance.***

The "Hygiene Hypothesis" was first proposed in 1989 by David Strachan in an article in the British Medical Journal. This hypothesis was an attempt to explain the observation that hay fever and other allergic diseases were more common among children raised in single-child households. The belief was that these children would have been exposed to fewer germs from siblings while they were growing up. Others have extended these observations to show that children who are cared for at home- as opposed to spending time in day care- have a higher risk of hay fever, asthma, and eczema.

Figure 2: ***Children raised in an environment with an abundance of various microorganisms have been found to have a lower incidence of allergic diseases.***

It has even been claimed that children who grow up on a farm have lower rates of allergic disease than those who grow up in the city.

Taking this idea even further, the reported rates of allergic diseases are much lower in developing nations - countries that might not even have water treatment facilities, let alone hand sanitizers and disinfecting wipes - than in industrialized countries.

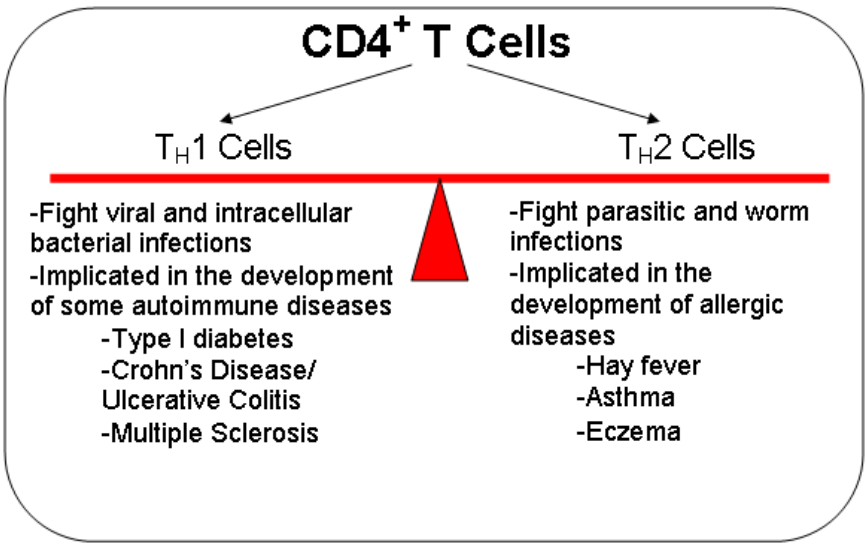
It isn't just allergies and asthma that may be prevented by exposure to germs. Autoimmune diseases such as type I diabetes, multiple sclerosis, and inflammatory bowel disease (IBD, including Crohn's disease and ulcerative colitis) are also much more prevalent in industrialized nations than they are in developing nations. Many believe that parasitic infections and worm infections might protect people from developing autoimmune diseases. In fact, if you look at a map of which nations have the highest prevalence of autoimmune diseases and a map of which nations have the lowest rates of parasite and worm infections, they are essentially the same.

It seems counterintuitive: why would exposure to pathogens help to prevent immune system-mediated diseases?

The answer may lie in how our immune system develops. For our immune system to work correctly there must be an exquisite balance of several different types of white blood cells, inflammatory proteins, and anti-inflammatory proteins. Our bodies have achieved this balance through generations of survival in the midst of infectious organisms. Remove the infectious organisms, and things can get unbalanced.

For example, one of the most important immune cells in the human body - CD4 T cells (also called T helper or T_H cells, a subgroup of lymphocytes) - develop in specialized subgroups.

One such subgroup, called T_H1, specializes in fighting viral infections. Another such subgroup, called T_H2, is more efficient at fighting worm infections (see table below).



Other subgroups of CD4 cells, such as T_H17 and regulatory T cells, play different roles. **These T cell subgroups expand in response to infection, and expansion of one subgroup can suppress another.**

For instance, in response to a viral infection, the T_H1 cells expand and may suppress T_H2 cells. Following viral infection, the immune system "remembers" the infection as memory T cells and remain in the body for years, sometimes for a lifetime.

Many autoimmune diseases, including IBD and type I diabetes, are referred to as T_H1-mediated, meaning that the autoimmune damage tends to be dominated by the T_H1 subgroup of T cells.

In countries where worm infections are more common, IBD is less common, presumably due to the fact that, by fighting off worm infections, the immune system is balanced more towards a T_H2 setting. In fact, there have even been case reports of IBD patients who have become infected with an intestinal worm, resulting in the resolution of all of their IBD symptoms. Interestingly, after these patients were treated with drugs to kill the worm infection, their IBD symptoms returned. Experiments in mice have confirmed this protective effect of worm infections in shielding against IBD.

In fact, researchers are now exploring the use of the pork whipworm, *Trichuris suis*, as a treatment for various autoimmune diseases.

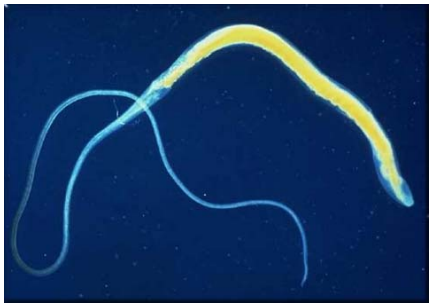


Figure 3: ***Whipworm (*Trichuris *spp.) has been used successfully in the treatment of autoimmune diseases.***

Clinical trials are under way in testing this treatment for IBD, multiple sclerosis, and even peanut allergies.

It isn't just our immune system that benefits from exposure to germs. Some germs might even have beneficial effects on the brain; relieving depression and even making us smarter!

Figure 4: ***Soil bacteria can increase neurotransmitters in the brain. Can exposure to dirt prevent depression? Increase intelligence? Research is underway to answer these questions.***

Researchers have studied the effects of exposure to a bacteria commonly found in soil, *Mycobacterium vaccae*, and have shown that this exposure can lead to increases in serotonin and norepinephrine (two important molecules in fighting depression) in the brain.

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In fact, when these bacteria were given to mice, it stimulated the growth of some brain cells, were able to run mazes twice as fast as their counterparts.

So what does all this mean? Certainly, there are benefits to killing germs. The control of life-threatening infectious diseases such as smallpox, polio, and cholera has made a big impact, not only our life expectancy, but also our quality of life.

Let's face it, no one likes staying in bed with a case of the flu or food poisoning. It is important to recognize that there may be a price to pay for trying to completely rid ourselves of all microorganisms in our environment, and there might even be a benefit to keeping some of them around.

As scientists learn more about the beneficial effects of microorganisms, perhaps we can better use them to our advantage. So put down the hand sanitizer and go play in the dirt. It might just make you healthier and smarter.

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