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The Dirt on Hygiene: From Microbe to Modern Medicine

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In 1670, Dutch cloth merchant Antonie van Leeuwenhoek peered through his homemade microscope and became the first person to observe what he called *animalcules*—tiny living creatures invisible to the naked eye (Kutschera, 2023). Although Leeuwenhoek meticulously documented these microscopic beings, he never connected them to disease. Two centuries would pass before this crucial connection was made. In the late 19th century, scientists Louis Pasteur and Robert Koch (along with many others) established what we now know as the *Germ Theory of Disease*—the revolutionary idea that specific microorganisms cause specific diseases (Blevins & Bronze, 2010). This discovery fundamentally transformed human society, launching a global campaign against these invisible enemies. Public health initiatives championed hand washing, cities built modern sewage systems, and surgeons adopted sterile techniques.

The 20th century brought antibiotics, vaccines, and antimicrobial products into our homes. We declared war on microbes, and for good reason—countless lives were saved. However, in our zeal to eliminate dangerous pathogens, we may have overlooked something vital: not all microbes are our enemies. Many are essential allies in maintaining our health. Recent research suggests that our increasingly sterile modern environment might be contributing to the dramatic

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rise in allergies, autoimmune disorders, and antibiotic resistance. This is the essence of what scientists call the *hygiene hypothesis*—the intriguing possibility that we might have inadvertently disrupted an ancient ecological balance critical to our immune development in our quest for cleanliness.

As a public health scientist partnering with an immunologist and translational bioscientist to co-author this article, I recognize that understanding the nuanced relationship between humans and microbes is essential for effective public health policy, especially as misconceptions about germ theory circulate widely, and some even attempt to refute this foundational concept that has saved countless lives through sanitation, vaccination, and antimicrobial treatments. This article explores the fascinating journey from our first glimpses of the microbial world to our evolving understanding of how these tiny organisms shape our health in harmful and beneficial ways. As Pasteur prophetically noted, microbes indeed have had the last word, but perhaps not in the way he imagined.

Germ Theory and a Science-based Hygiene Approach

The *Germ Theory of Disease* is simply the ability of separate organisms (e.g., bacteria, viruses, and parasites) to cause disease when introduced to a second organism, like us. This scientific breakthrough informed humans worldwide that millions of critters live on, in, and around us, many of which are capable of spelling our untimely demise. Naturally, this led society to devise ingenious methods of defending ourselves against this invisible threat. Following the work of Pasteur and Koch, global hand-washing campaigns began (and continue today), sterile surgical practices were adopted, and ethanol became a medical disinfectant of choice (Curtis, 2007; Michaleas et al., 2022). Breakthroughs began to accelerate in the 20th century, antibiotics were discovered and used en-masse, a plethora of effective vaccines were developed, and people began to adapt their behaviors and living conditions to limit their exposure to dangerous microbes (Bloomfield, 2006). In Western society, migration to urban centers and a growing association between dirt and grime with microbes and disease began to limit our exposure to all microorganisms.

Robert Koch's pioneering work with anthrax in the 1870s provided the first conclusive evidence that a specific bacterium causes a specific disease (Blevins & Bronze, 2010). Although some of these postulates are considered dated, scientists still rely on Koch's core principles to establish causal relationships between microorganisms and disease. We must recognize the impact of germ theory and scientifically backed hygienic practices on human health. Since the late 1800s, infectious disease death rates have plummeted. Infectious disease was once the leading cause of death in the United States and is now not even in the top 10 (except COVID-19 after 2020) (Murphy et al. 2024). We have eradicated diseases that previously claimed the lives of billions and are advancing every day in the fight against infectious diseases. However, it is also important to research and recognize the potential side effects of this progress.

Hygiene Hypothesis, Old Friends Hypothesis, and Danger Hypothesis

Immunologists have proposed several hypotheses to explain the relationship between hygiene and immune function: the hygiene hypothesis, the old friends hypothesis, and the danger hypothesis. The *hygiene hypothesis* suggests that fewer infections in childhood may increase our susceptibility to allergic diseases by suppressing the development of the immune system (Strachan, 1989). Over the years, research has shown that while viruses generally worsen or contribute to immune diseases, exposure to certain bacteria, especially the beneficial ones (called commensals), is crucial for a healthy immune system. About half of the cells in our body are bacterial, and these commensal bacteria that live within us help develop our immune systems (Sender et al., 2016).

Extreme cleanliness, like sanitizing every surface, may hinder immune development through decreasing exposure to environmental factors and a diverse array of microbes, including beneficial bacteria. In fact, some think that without this exposure, the immune system may become overly sensitive or hypersensitive (the actual scientific term for allergies) and react to harmless substances. Factors like cesarean sections, which limit exposure to the mother's beneficial bacteria, and diets low in fiber, which good bacteria need, also impact immune health (Dominguez-Bello et al., 2019). Living on farms or having pets can expose us to beneficial bacteria, supporting a healthy immune system. For example, owning a pet in early childhood has been shown to be protective against allergies and other immune diseases (Hesselmar et al., 2018).

The *old friends hypothesis* suggests that our immune systems need exposure to certain microbes, which humans have co-evolved with over thousands of years, to function properly (Rook, 2010). These old friends primarily include bacteria that have been common in our environment throughout history. Without regular contact with these microbes, our immune systems may become overactive, leading to allergies and asthma. The underlying idea is that these microbes help train our immune systems to distinguish between harmful and harmless matter. The old friends hypothesis is widely regarded as the most compelling explanation for the connection between bacterial species and the immune system.

The *danger hypothesis* proposes that the immune system is primarily activated by signals from damaged or stressed cells rather than by the presence of foreign substances alone (Matzinger, 2002). According to this hypothesis, the immune system responds to danger signals released by cells when they are injured or under threat, such as during an infection or tissue damage. This helps the body focus its immune response on actual threats that could cause harm rather than reacting to harmless substances such as old friends or commensal bacteria inhabiting our bodies. By understanding the danger hypothesis, we can see how the immune system is designed to protect us by targeting real dangers, which helps prevent unnecessary immune reactions that could lead to allergies or autoimmune diseases.

By considering all of these hypotheses, we can appreciate the importance of balanced exposure to microbes in shaping a healthy immune system and that the immune system is geared toward detecting and responding to potentially harmful microorganisms while maintaining tolerance to beneficial ones. This nuanced understanding helps explain why not all microbes trigger immune responses and why our bodies have evolved sophisticated mechanisms to distinguish between microbial threats and beneficial microbial exposures.

Antibiotic Resistance: The Consequence of Overuse

The clearest cause-and-effect relationship exists with antibiotic resistance. Our widespread use of antimicrobials has accelerated this crisis through direct selective pressure on bacterial populations, allowing them to evolve the ability to survive in the presence of antibiotics that once resulted in their destruction. The Centers for Disease Control and Prevention (CDC, 2019) estimates that antibiotic-resistant infections affect nearly 3 million Americans annually and result in over 35,000 deaths. This demonstrates how our specific practices around antimicrobial use have concrete, measurable consequences. It is important to remember that antibiotics are only effective against bacterial infections, not viral ones. Inappropriate use of antibiotics for viral illnesses contributes significantly to resistance development without providing any therapeutic benefit (CDC, 2019).

The Rising Tide of Modern Ailments: Understanding Complex Causes

The decades following our increased hygiene practices have witnessed a parallel trend: rising rates of allergic and autoimmune disorders, particularly in developed countries with the highest hygiene standards. Understanding these increases requires careful scientific consideration of multiple factors.

Allergies and Asthma: Complex Origins

Allergic conditions have increased dramatically since the mid-20th century. According to the CDC (Jackson et al., 2013), food allergies among children rose by approximately 50% between 1997 and 2011, while asthma now affects over 25 million Americans. This allergy epidemic displays a geographical pattern that is most prominent in industrialized nations and urban environments. A relatively famous example is the peanut allergy. Peanut allergies in the United States have increased over 3-fold since the late 1990s (Lange et al., 2021). Currently, about 2% of adults in the US have peanut sensitivities, and peanut allergies are among the most commonly fatal allergic reactions (Warren et al., 2021). In 2015, the *Learning Early About Peanut* (LEAP) study demonstrated that introducing peanut products to infants significantly reduced the risk of developing peanut allergies by over 80% (Du Toit et al., 2015). This groundbreaking research led to new guidelines recommending that infants should be introduced to peanut-containing foods as early as 4-6 months of age. These findings have revolutionized pediatric recommendations, aiming to drastically reduce peanut allergies through early exposure to induce oral tolerance (Togias et al., 2017).

Research has examined the relationship between parasitic infections and allergy development later in life. Importantly, many of the studies with humans with naturally occurring infections show conflicting results, suggesting the mechanism is likely more complex than simple exposure (McSorley et al., 2019). However, studies in mice show convincing evidence that pups born from parasite-exposed mothers were less likely to develop anaphylactic allergies (Gibbs & Fairfax, 2022; Yazdanbakhsh et al., 2002). While reduced microbial exposure appears to be one contributing factor, it is important to note that many variables influence these trends, including air pollution, childhood exposure, dietary changes, genetic factors, and altered intestinal microbiomes. Research consistently shows that routine childhood vaccinations do not contribute to allergic disease development and that vaccinated children do not have an increased risk for allergies or asthma compared to their unvaccinated peers (Navaratna et al., 2021; Zhang et al., 2023).

Autoimmune Disorders: A Multifactorial Challenge

Over 80 autoimmune diseases, from type 1 diabetes to multiple sclerosis, are increasing in prevalence (Fugger et al., 2020). These conditions involve complex interactions between genetic predisposition, environmental triggers, and immune regulation. Research suggests that without microbial exposure to beneficial bacteria early in life, immune development may be altered. It is worth emphasizing that autoimmune disorders typically result from multiple contributing factors, particularly genetic predisposition, rather than any single cause. Despite extensive studies, no credible evidence links routine vaccinations to increased autoimmune disease risk. The timing of vaccination schedules coinciding with early childhood development has sometimes led to correlation being mistaken for causation.

What Does Evidence Tell Us?

The scientific consensus points to a nuanced relationship between our modern environment and immune health. While reduced exposure to certain beneficial microorganisms appears to play a role in these rising conditions, researchers emphasize that many factors contribute, including:

- changes in diet and food processing;
- reduced outdoor activity and connection to natural environments;
- increased air pollution and environmental chemicals;
- increases in C-section delivery and a resulting decrease in early-life exposure to microbes while exiting the birth canal;
- genetic susceptibility interacting with environmental changes.

Understanding these multiple factors helps us avoid oversimplified explanations while identifying practical ways to support immune health in our modern world. The converging evidence suggests a profound irony: our zealous pursuit of cleanliness may have compromised the health outcomes it intended to improve. This realization has led researchers to reconsider what constitutes a healthy relationship with our microbial world.

Finding Balance: Moving Forward with Our Microbial Friends

The hygiene hypothesis does not suggest abandoning modern sanitation or returning to pre-germ theory practices. Rather, it invites a more nuanced understanding of our relationship with microbes. Research increasingly supports a targeted hygiene approach maintaining critical hygiene practices that prevent dangerous infections while allowing beneficial exposures that train our immune systems. This might include:

- encouraging outdoor play and contact with natural environments for children;
- limiting unnecessary antibiotics and antimicrobial products;
- embracing diverse, fiber-rich diets that support healthy gut bacteria;
- owning pets as beneficial sources of microbial diversity;
- maintaining traditional hygiene practices where they matter most (e.g., hand-washing during disease outbreaks, food safety).

Conclusion

Dr. Marsha Wills-Karp of Johns Hopkins reminds us, “Almost no virus is protective against allergic disease or other immune diseases. In fact, infections with viruses mostly either contribute to the development of those diseases or worsen them” (Rivers, 2022, para 5). The key distinction lies between harmful pathogens and the beneficial bacteria that have coexisted with humans throughout our evolutionary history. The path forward is not abandoning cleanliness but developing a more sophisticated understanding of which microbes we should avoid and which we should welcome. By reframing our relationship with the microbial world from one of universal warfare to selective partnership, we may find more balanced approaches that protect us from disease while supporting robust immune development. Ultimately, perhaps the greatest irony of the hygiene hypothesis is that it does not invalidate germ theory but completes it, revealing the complex ecological relationship between humans and microbes that extends far beyond simple notions of good and bad bacteria. In this more complete understanding lies the promise of healthier human-microbial coexistence.

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