Design for Biosecurity

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Lecture 9

Bacillus Anthrax Bacteriology in context to Biosensor Development

Welcome back to the ninth lecture of this series. In our previous sessions, we delved into the Marburg virus, and before that, we explored Ebola. Today, we shift our focus to one of the most infamous category A bioterrorist agents, anthrax. As we progress through this journey, we will be making some modifications in our approach. Alongside discussing the pathogens themselves, we'll also touch on the various biosensors that have been developed to detect these agents. By the time we reach the fifth or sixth week, we will revisit some of these detection systems to explore their mechanistic details, allowing you to develop a comprehensive understanding of the pathogens and their corresponding detection modules.

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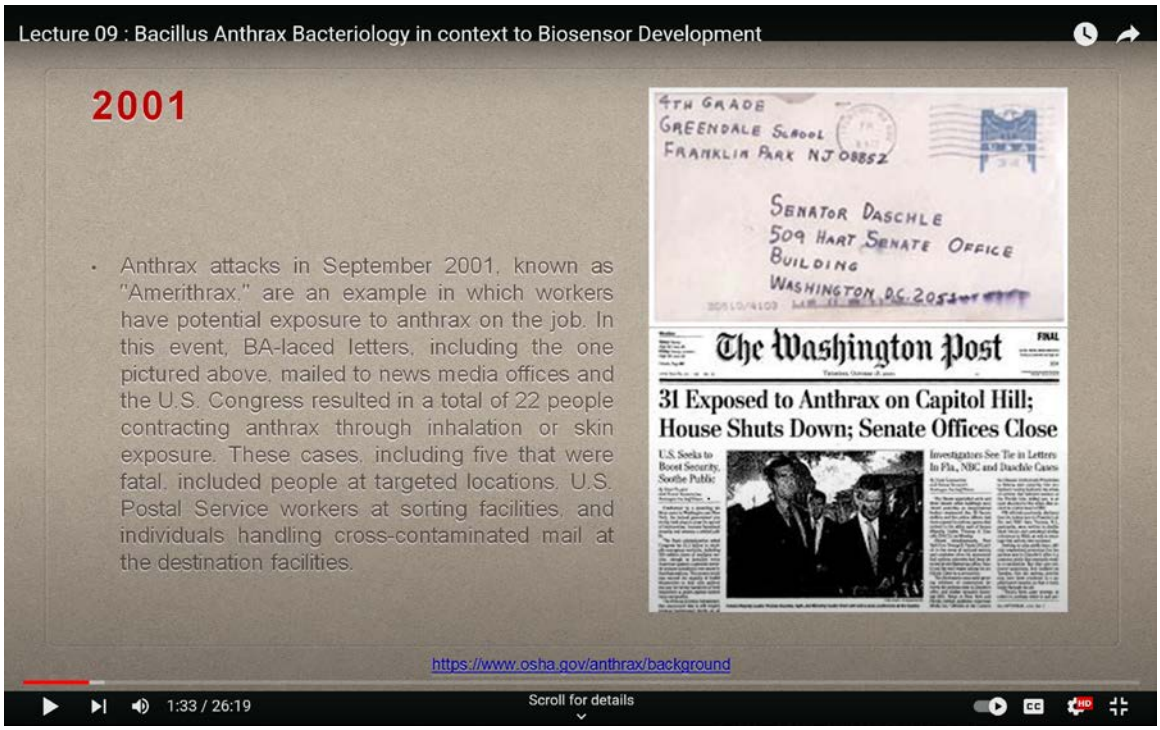

Let's begin today's lecture with anthrax. On a personal note, anthrax is a well-known pathogen, it’s far from being a new discovery. However, in recent history, especially over the past 25 years, anthrax has gained notoriety as one of the most significant bioterrorism threats to strike one of the world's most developed economies, the United States. And here, I must mention my personal connection to this incident. The most high-profile bioterrorism act involving anthrax occurred in 2001, shortly after the 9/11 attacks on the Twin Towers.

At that time, the United States was still reeling from the horrors of 9/11. The nation was in disarray, and global agencies such as the FBI were fully engaged in investigating the terrorist involvement in the attacks. Against this chaotic backdrop, an anthrax attack was carried out in the same year. It was a strikingly calculated act, preying on an already traumatized nation.

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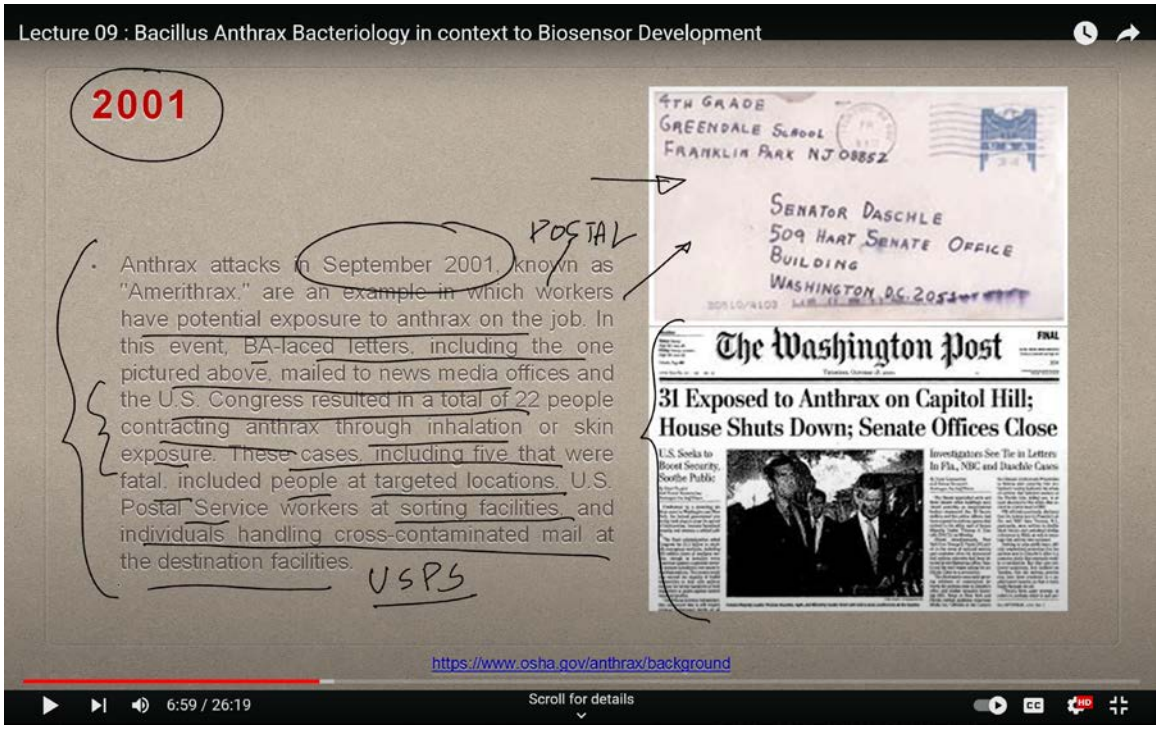

In January 2001, I migrated from Switzerland to the United States. I still vividly remember that cold evening when my flight landed. Like many others, I expected my time in the U.S. to be a wonderful experience as I was there for a new job opportunity. Little did I know

that by mid-year, the global narrative would undergo a drastic shift, a shift that would leave a permanent mark on the world. By the end of that year, everything had changed, and in ways that would shape the next decade.

The anthrax attack that followed 9/11 left a deep impression on me, and over the next 10 years, I closely followed the developments surrounding this bioterrorism case. In the next two or three lectures, I will be sharing my understanding of anthrax, an understanding that evolved over years of research and observation.

When I first arrived in the U.S., my knowledge of anthrax was limited to what most people glean from textbooks. I knew it was a pathogen that could cause disease, but nothing more. However, when such textbook knowledge is weaponized and turned into a tool of terror, you begin to realize the true gravity of the situation. It was an eye-opener for me, this wasn't just a simple bacterium; it was a dangerous agent of destruction.

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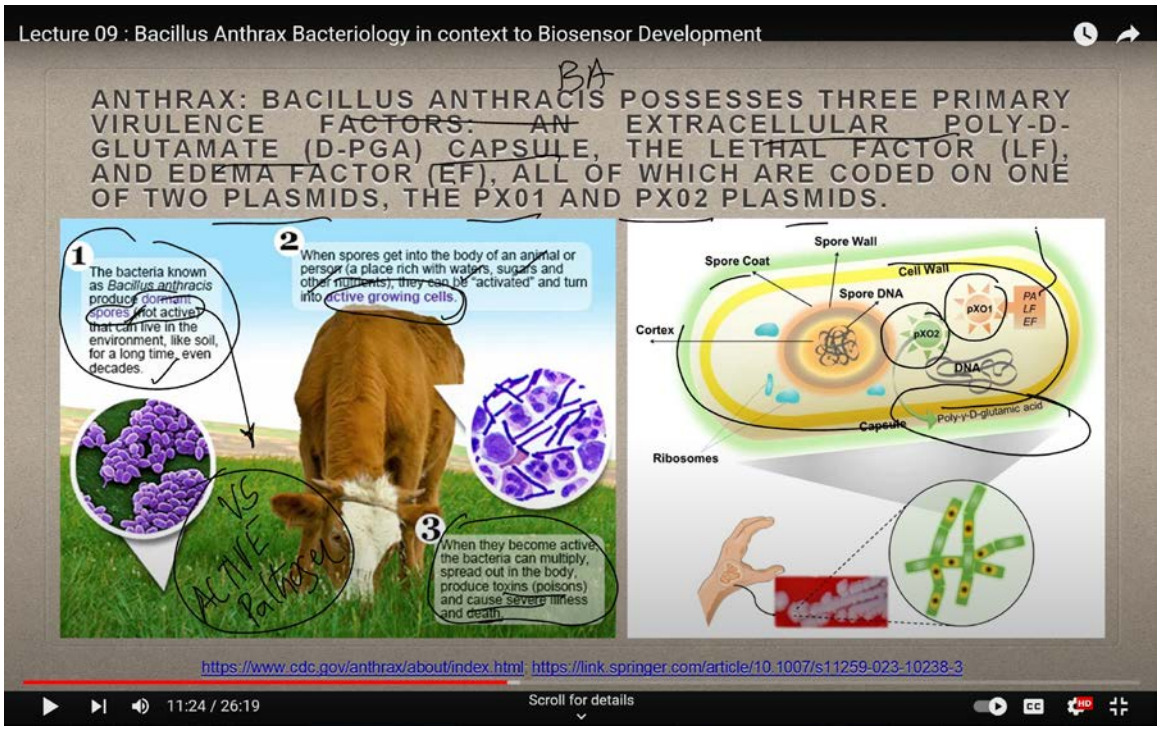

As we move through this topic, you'll come to see the series of remarkable events associated with anthrax and why it's imperative to understand them thoroughly. This isn't

just about anthrax; it’s about all pathogens that can be weaponized. To begin, the infamous anthrax attacks started with something as mundane as postal mail. And that’s where we’ll start this exploration into anthrax and its terrifying legacy.

So, if you look at the slide here, you’ll see an example of a postal letter sent to a United States senator. Now, what did the sender or group of senders do to introduce anthrax as a weapon into the envelope? Imagine, for a moment, holding an envelope like this. Although, by that time, the world was gradually transitioning to emails and other electronic forms of communication, postal mail was, and still remains, one of the most reliable methods for sending materials from one part of the world to another. But what happens when you open such an envelope?

As you tear it open and breathe in, the spores inside are released into the air and can immediately enter your nasal cavity. Once these spores are inhaled, infection begins, a process that was carefully and deliberately planned in this case. As you can see from the slide, this occurred in 2001. It was widely reported, with headlines like The Washington Post stating, "31 exposed to anthrax on Capitol Hill, House shut down, Senate office closed." The September 2001 anthrax attack, also known as Amerithrax, is a striking example of how postal workers were subjected to potential exposure to anthrax spores. The letters, laced with Bacillus anthracis (BA), were mailed to both the news media and the U.S. Congress. This attack led to 22 people contracting anthrax through either inhalation or skin exposure. We’ll dive into these exposure types in the following slides, but it’s critical to note that five of these cases were fatal. Among the victims were individuals working at targeted locations, including the U.S. Postal Service (USPS) sorting facility and those handling contaminated mail at the final destination facilities.

Now, consider the immense level of fear and chaos this caused across the nation. The sheer innovation behind using the postal service to create paranoia on such a large scale was significant. It threw the entire country into a state of frenzy. People became terrified to open their letters. Even the simple act of receiving a parcel became fraught with fear. This period marked a modern, meticulously pre-planned bioterrorist attack that instilled unprecedented fear in the public.

With that context in mind, let's dive into understanding Bacillus anthracis, the bacterium responsible for anthrax. According to standard textbooks, Bacillus anthracis is a pathogen, a bacterium, or a microbe that naturally resides in the soil. In its spore form, it is generally harmless, it remains inactive. Now, as you see on the slide, Bacillus anthracis (commonly referred to as BA) possesses three primary virulence factors. But before we get into those factors, let's first understand what makes this bacterium so tricky to detect.

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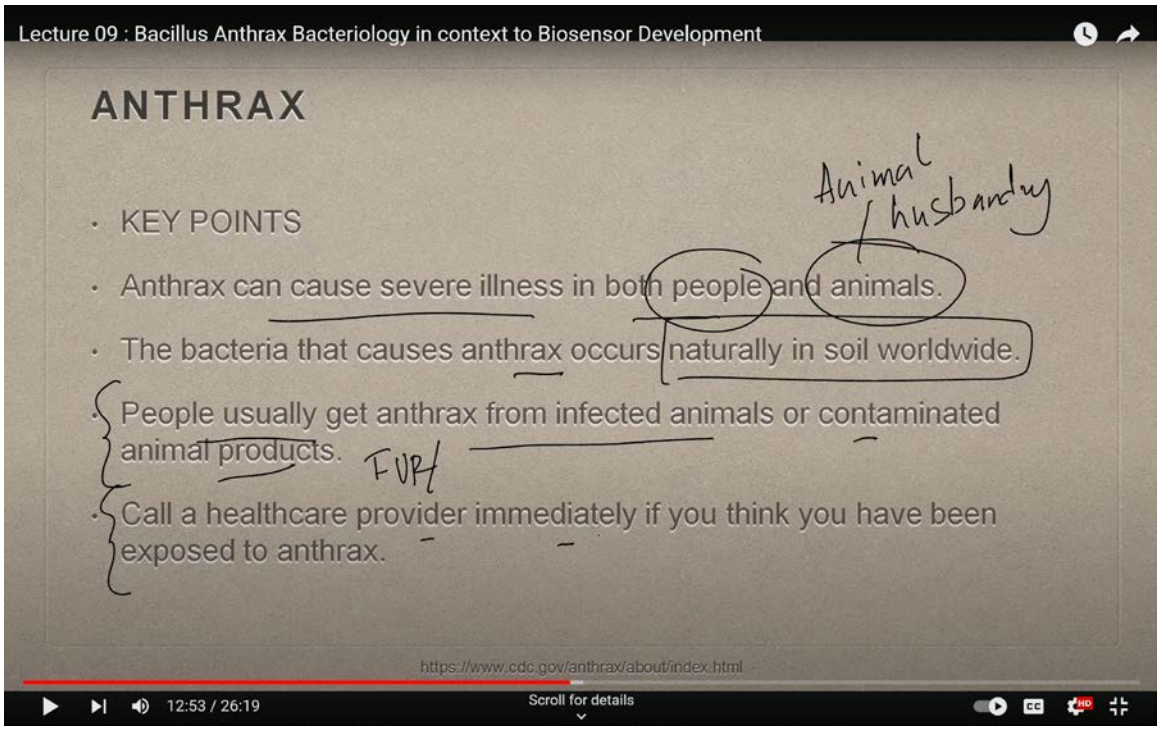

The bacterium produces dormant spores. Keep in mind, these are dormant spores. So, the challenge arises: unless you have a sensor that is specifically capable of detecting dormant spores, you won't be able to determine whether anthrax is present. This dormancy presents a unique challenge because it effectively silences all metabolic activity. With no metabolic activity, there is nothing to measure, no emissions or detectable signatures. Let's say, for instance, someone is active, like I am right now. I'm taking in oxygen, producing carbon dioxide, emitting volatiles from sweat, and generating heat. All of these things can be detected through various sensors, such as infrared (IR) signatures, which locate me based on the heat I produce.

But imagine if all my metabolic activities slowed down to a dormant state, rendering me completely inactive. I would enter what is called a calm, quiescent phase. In this state, without any metabolic signatures, it becomes exceedingly difficult to detect my presence. That's the problem we face with dormant anthrax spores.

Could you identify me if I entered a dormant state, with no visible signs of activity? Probably not. And that is exactly the problem scientists and medical professionals face when they have to detect dormant bacteria, such as tuberculosis or anthrax. It's important to understand the complexity of these pathogens, particularly how they adapt and survive under different environmental conditions. These are some of the critical factors we need to consider when discussing pathogen detection: what strategies do these microorganisms employ to survive, and how do they interact with their surroundings?

Now, back to the slides. Anthrax spores can live in the environment, such as in soil, for long periods, sometimes even decades, surviving over 10 years or more. When these spores enter the body of a host, whether it's an animal or a person, where conditions are rich in water, sugar, and nutrients, they become active. They transition from a dormant state to active, growing cells. Once active, the bacteria multiply, spread throughout the body, and release toxins that cause severe illness.

These toxins are the real threat. So, consider this: when dormant in the soil, anthrax is fairly benign, harmless even, until it finds a host. This is the challenge we face when detecting dormant spores as opposed to active pathogens. Detecting active anthrax bacteria is far simpler than identifying its spores during dormancy. This is where sensor technology struggles, and why research in this area is so vital.

Now, looking at the bacterium's makeup, anthrax contains three primary virulence factors along with an extracellular polyglutamate capsule, commonly referred to as DPGA. As shown in the illustration, the DPGA capsule forms a protective outer layer around the bacterium. The bacterium's virulence factors include the lethal factor (LF), the edema factor (EF), and a protective antigen (PA), all encoded by two plasmids, PXO1 and PXO2. These plasmids carry the genes responsible for the production of these virulence factors, factors that make anthrax so dangerous.

This highlights why it’s not enough to simply have a detection system for anthrax. You also need a deep understanding of its cellular and genetic makeup. Knowing the genetic structure is key to developing an effective sensor. Without this knowledge, detection systems could miss the spores entirely, especially in their dormant state.

Now, moving on to some key points about anthrax: it can cause severe illness in both humans and animals, and the bacterium that causes anthrax, Bacillus anthracis, occurs naturally in soil worldwide. People usually contract anthrax through contact with infected animals or contaminated animal products. This could include fur, hides, and potentially even meat. The possibility of meat contamination is a point that requires further investigation, but fur, hides, and other products are known to pose a risk. Therefore, if you believe you’ve been exposed to anthrax, it’s crucial to contact a healthcare provider immediately.

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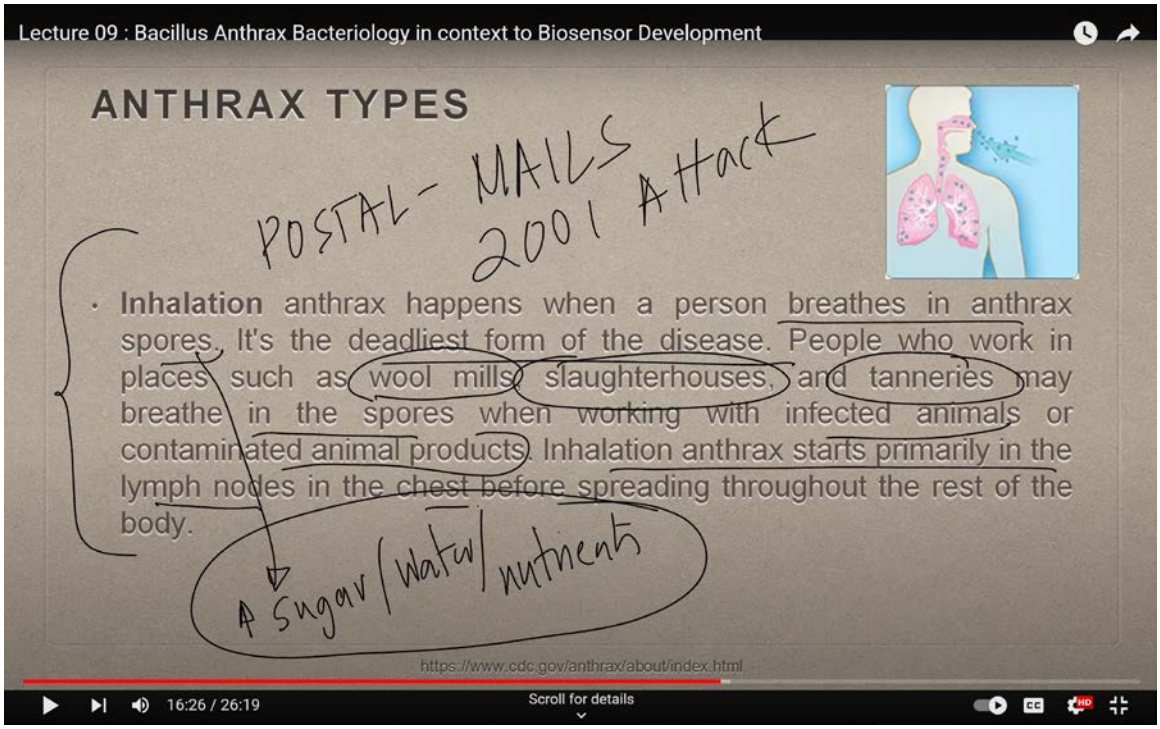

These are the fundamental points to understand before we move further into the specifics of anthrax. Now, let's talk about the different types of anthrax, which are categorized based on how a person becomes infected.

The first type is cutaneous anthrax, which affects the skin. This type of anthrax occurs when spores enter the body through a cut or scrape on the skin. It typically affects people who handle infected animals or contaminated animal products such as wool, hides, or hair. This means workers in industries like wool processing, leather manufacturing, and fur collection need to exercise extreme caution. The spores can enter through any wound or exposed area on the body, granting the microbe access to the body's intracellular fluids. Cutaneous anthrax primarily presents on the head, neck, and forearms, so remember, these are the areas where symptoms are most likely to appear.

In this slide, you see an example of anthrax infection on the forearm and hands, which is the most common and, fortunately, considered the least dangerous form of anthrax infection. However, there is another form known as injection anthrax, which was first identified among heroin-injecting drug users in Northern Europe. Interestingly, it hasn't been reported in the United States. Injection anthrax behaves similarly to cutaneous anthrax, but the infection occurs much deeper, either under the skin or within the muscle tissue, wherever the drug has been injected. This aspect is crucial because it highlights a troubling connection between drug abuse and anthrax infection. If a batch of drugs is contaminated with anthrax spores, and these are injected directly into the body, it can lead to a deadly infection. The danger here is significantly elevated compared to cutaneous anthrax since the spores bypass the skin's defenses and enter directly into the bloodstream.

Cutaneous anthrax, on the other hand, tends to remain on the skin's surface. Your innate and adaptive immune systems can generally contain it before it spreads too deeply. However, when the infection becomes systemic, whether through injection or inhalation, it can be fatal if not caught early.

Speaking of inhalation, let's revisit the infamous 2001 postal anthrax attacks. These attacks were specifically designed to cause inhalational anthrax, which occurs when a person breathes in anthrax spores. Once the spores enter the lungs, they find an ideal environment,

rich in sugar, water, and other nutrients. Inhalational anthrax is the most dangerous form of the disease. Workers in certain industries, such as wool mills, slaughterhouses, and tanneries, are particularly vulnerable to this type of infection. These individuals may unknowingly breathe in anthrax spores while handling contaminated animal products like wool, hides, or fur.

Inhalational anthrax starts its invasion in the lymph nodes within the chest, eventually spreading throughout the body. This highlights the importance of safety precautions for workers in industries that handle animal products, from the slaughterhouses to the wool and carpet industries. The risk is real, and it only takes a small misstep for a worker to become exposed to these dangerous spores. That's why there needs to be stringent screening and safety measures in place, especially as large quantities of animal products like leather and fur are processed.

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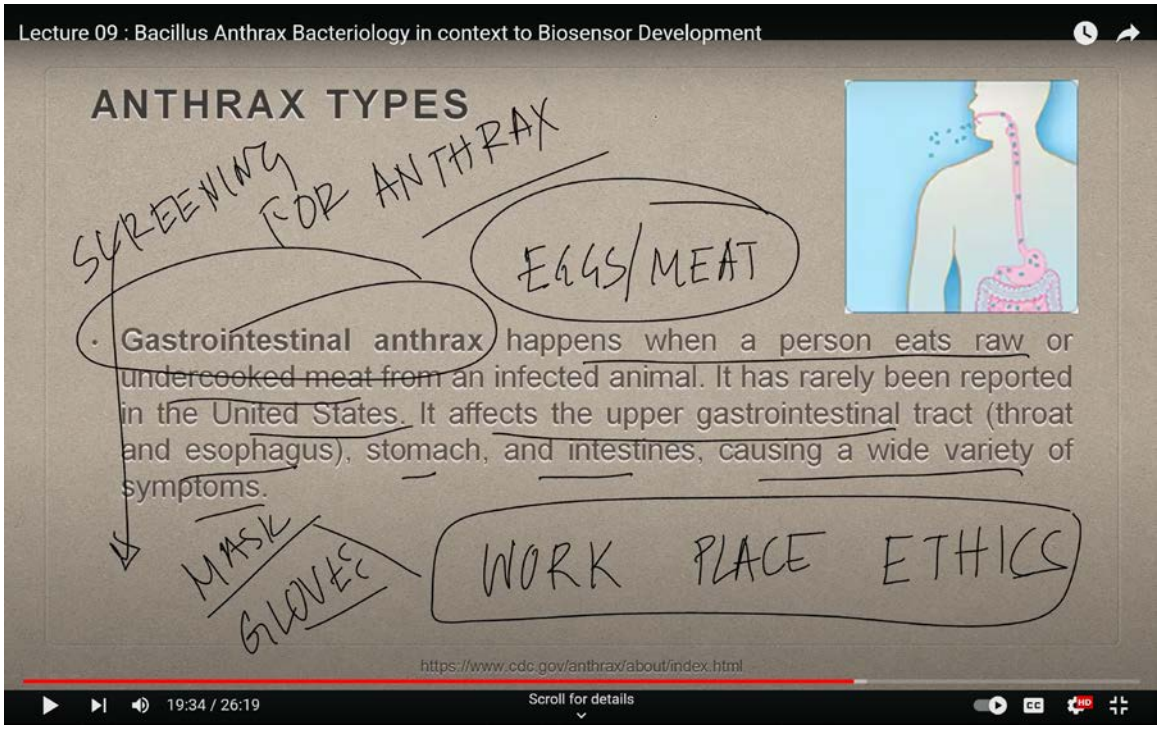

Imagine the severity of a scenario where a worker in a tannery inhales anthrax spores, it could happen without detection. The symptoms could start off as minor as a cough or cold,

and before anyone realizes it, the infection has already taken hold. This is why extra caution is required, particularly after the global COVID pandemic, which has taught us how easily airborne pathogens can spread.

The third form of anthrax is gastrointestinal anthrax, which occurs when a person consumes raw or undercooked meat that is contaminated with anthrax spores. So, as I mentioned earlier, anthrax can indeed enter the gastrointestinal (GI) tract. If the meat you're eating is contaminated, the spores can infect your system. This reinforces the need for extreme caution with animal products such as eggs and meat. These products should always be thoroughly cooked, as proper cooking will destroy any anthrax spores or active pathogens. However, if the meat is undercooked, you run the risk of anthrax infection.

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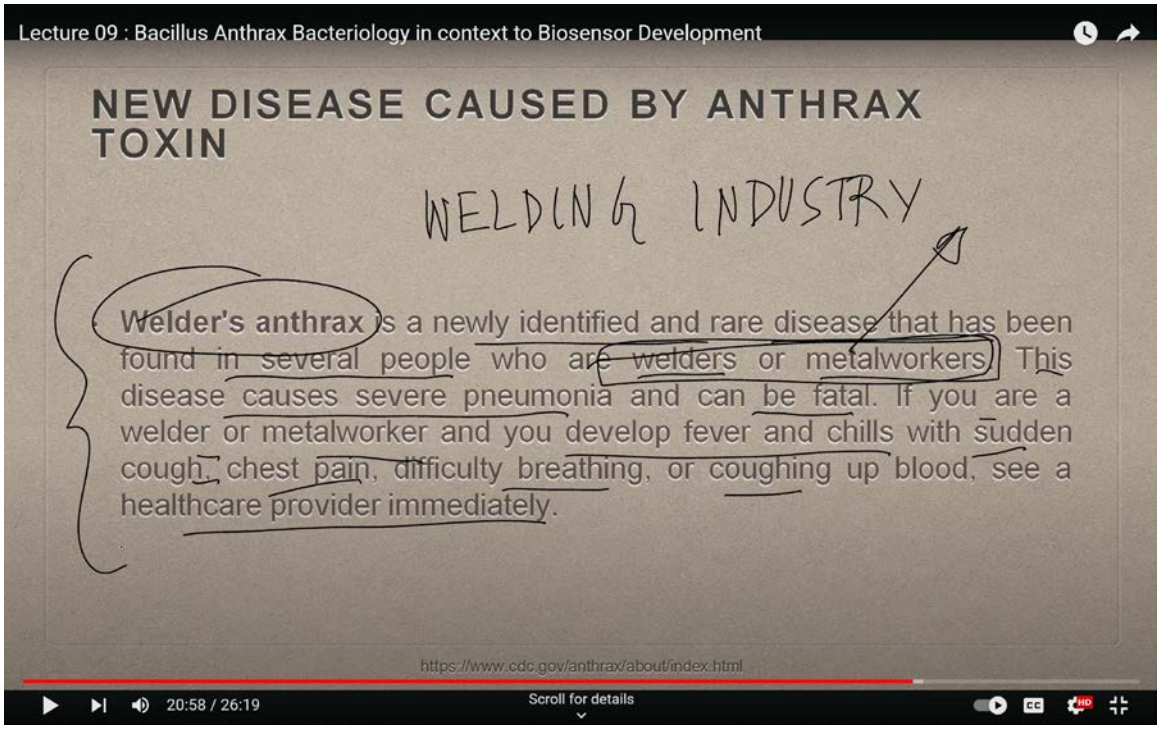

In the United States, gastrointestinal anthrax is rarely reported, but when it occurs, it can affect various parts of the upper gastrointestinal tract, including the throat, esophagus, stomach, and intestines. It presents a wide range of symptoms. This underscores the importance of vigilance and care because anthrax can enter the body through multiple

pathways. Understanding this is crucial for maintaining workplace safety and biosecurity, particularly in industries at risk of exposure. For example, wearing masks and gloves becomes an essential measure to prevent infection. Regular screening of animals, particularly for anthrax, should be mandatory in certain workplaces like slaughterhouses and wool industries, ensuring a higher standard of biosecurity.

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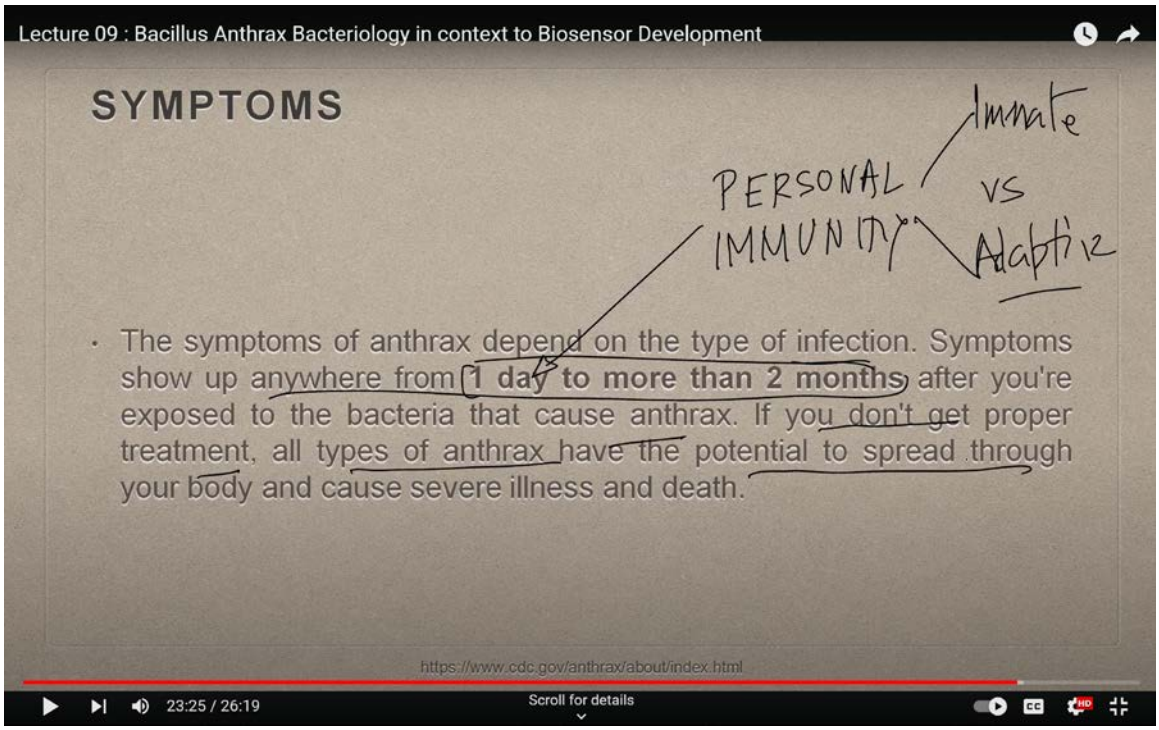

Another emerging concern is a recently discovered anthrax-related disease called welder's anthrax, a condition that is of particular interest to the iron and steel industries, where welding is a common practice. Welding, as we know, is integral to construction and the manufacturing of metal structures. But in recent cases, it has been linked to a rare and potentially deadly illness found in welders and metal workers. This newly identified disease causes severe pneumonia, which can become fatal if not promptly treated. Welders or metal workers who suddenly develop symptoms like fever, chills, persistent cough, chest pain, difficulty breathing, or coughing up blood must seek medical attention immediately.

Often, this illness is misdiagnosed as tuberculosis (TB) due to the similarity in symptoms, but without proper detection, a misdiagnosis can lead to devastating consequences. Welder's anthrax is a newly emerging issue that we must address carefully within the metalworking industry. It's alarming to think that people working with animals, leather, fur, and now metals can be at risk of contracting anthrax, not from a bioterrorist attack but simply through contaminated environments.

The essential takeaway from all this is that biosecurity measures, workplace hygiene, and understanding the mechanisms of anthrax exposure are key to preventing infection. It’s not about living in fear; it’s about being informed. The more we know about how anthrax operates, the more effectively we can develop sensors and detection systems. And if we can design a sensor that detects dormant spores, the form of anthrax that lies inactive in the environment, we will be much better equipped to prevent outbreaks.

Let’s touch on the symptoms of anthrax now. The symptoms vary depending on the type of infection, and they can manifest anywhere from one day to as late as two months after exposure. The range is quite startling: one day to 60 days. This variation is largely a function of the individual's immune system. Think about that for a moment, your immune response can either delay or accelerate the onset of symptoms, making it even more important to detect and address anthrax exposure as early as possible.

The strength of your immune system, particularly the balance between your innate and adaptive immunity, plays a critical role in how well you can fight off an anthrax infection. If you are exposed to the bacteria that cause anthrax, and you don't receive timely treatment, all forms of anthrax have the potential to spread throughout your body, leading to severe illness and possibly death. Fortunately, there are medications and vaccines available, but early detection is key to successful treatment.

Now, when we talk about cutaneous anthrax, it is generally considered the least dangerous form, but that doesn’t mean it’s harmless. The classic symptom of cutaneous anthrax is the formation of itchy, small blisters or bumps, followed by significant swelling around the affected area. You’ll notice this swelling is concentrated around the painless sore, which

often forms on the face, neck, arms, or hands. What makes it distinctive is the black center that appears as the condition progresses.

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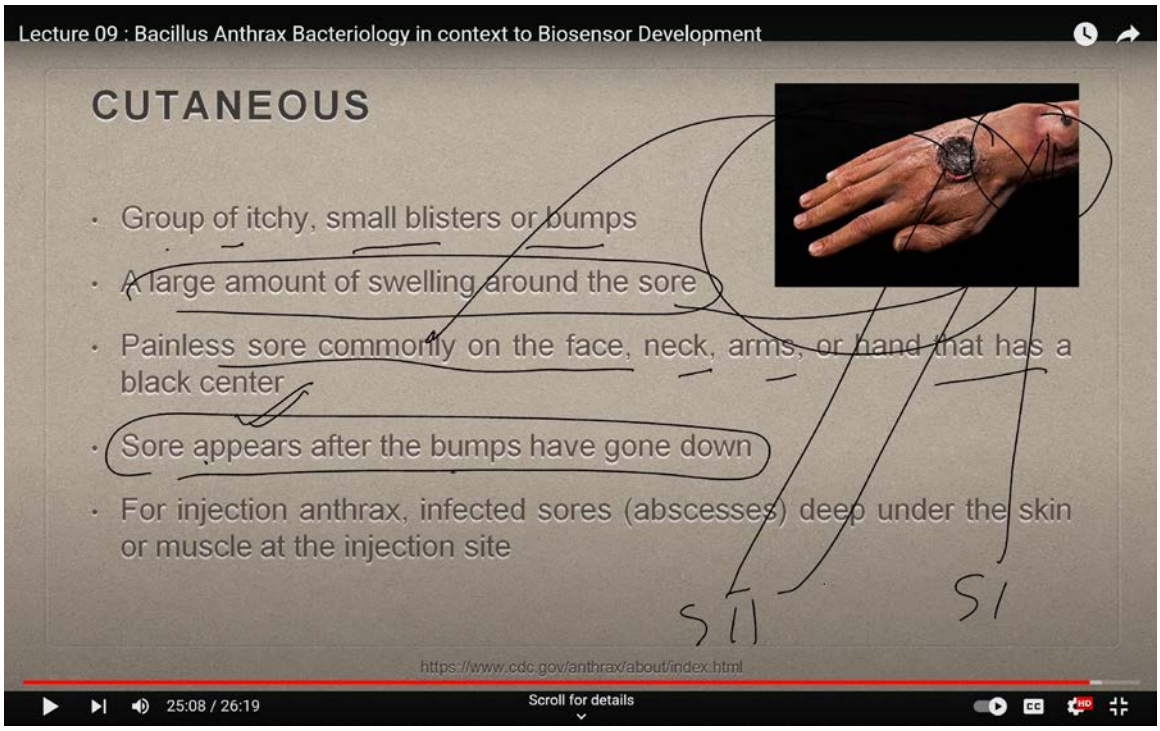

The development of cutaneous anthrax occurs in stages. Initially, you have the itchy bumps, which later subside, leading to the formation of a sore. As the infection advances, fluid accumulates in the area due to the body's immune response, immune cells rush to the site in an attempt to stop the infection. This fluid buildup is normal and results from damaged blood and lymph vessels. Once the infection has established itself, the fluid eventually dissipates, leaving behind a black scar at the infection site. This progression is a classic indicator of cutaneous anthrax.

For injection anthrax, often seen in cases of drug abuse, abscesses develop deep beneath the skin or muscle at the injection site. This form is particularly dangerous as it bypasses the outer skin layers and injects the bacteria directly into the body, making it more difficult to treat.

This concludes our discussion for today on cutaneous anthrax. In our next session, we will delve into the other forms of anthrax and their respective symptoms. It’s essential that you grasp these foundational details because understanding these limited but critical scenarios will equip you to handle more complex challenges that may arise in the future. Thank you.