Design for Biosecurity

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Lecture 8

Ebola and Marburg Virology in context to Biosensor Development

Welcome, everyone, to the eighth class. We are now in the second week of our course. Before we dive into today's topic, I'd like to note that there has been a slight spillover from the first week into this one, and similarly, the second week will extend into the third. This pacing will allow us to grasp the course material from a broader and more comprehensive perspective.

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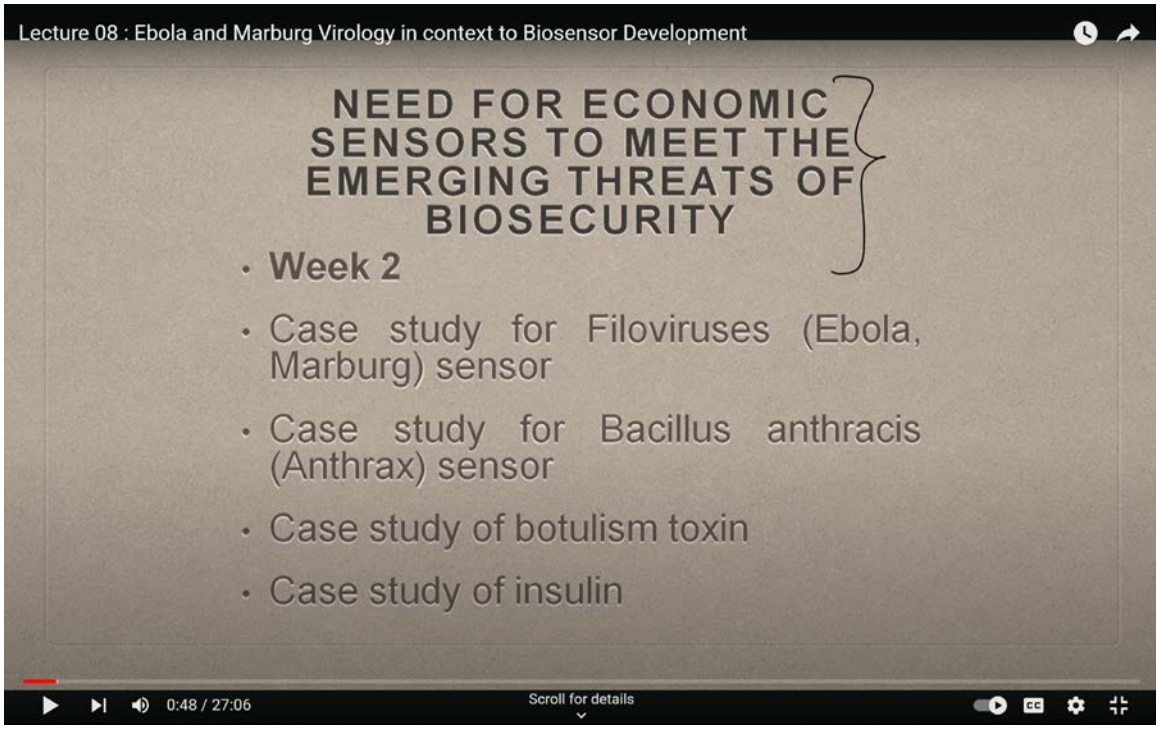

Today, as we look at the slides, we will address the pressing need for an economic census to counter the emerging threats to biosecurity. We will focus on case studies of filoviruses,

specifically Ebola and Marburg, followed by discussions on anthrax, botulinum toxin, and insulin.

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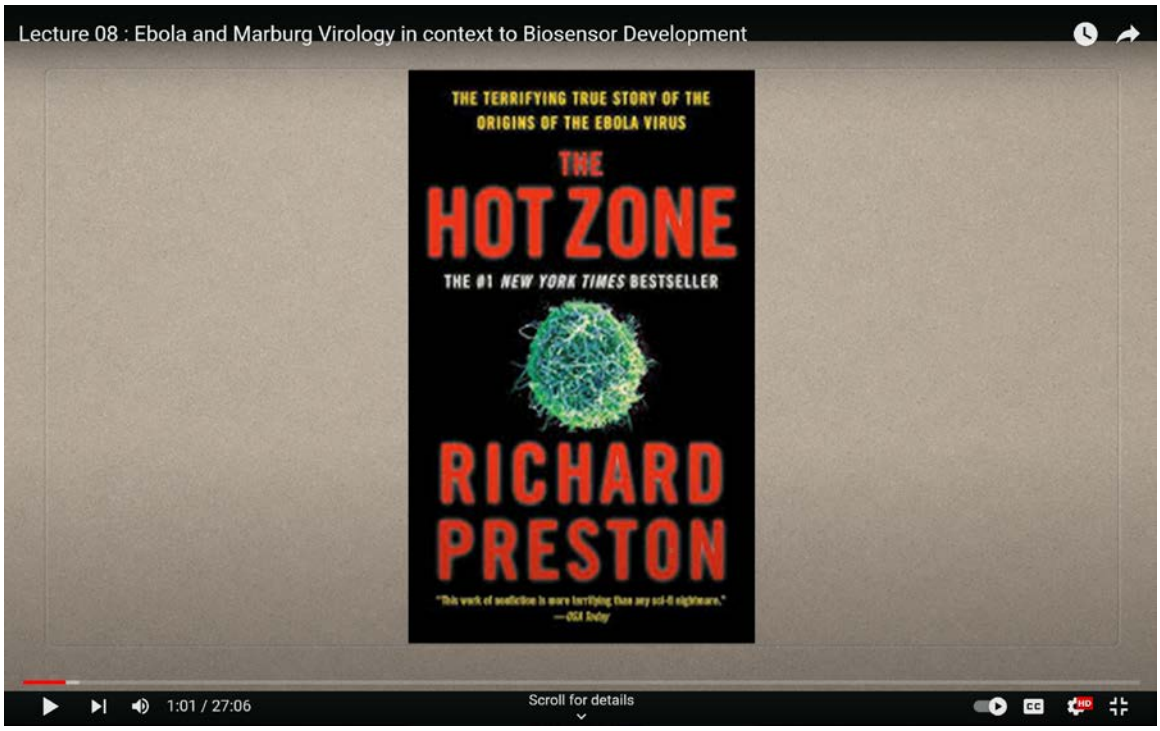

To begin with Ebola, I recommend a fascinating book titled The Hot Zone by Richard Preston. If you can find it online or purchase it, it will inspire you to understand the critical importance of research in this field. The book vividly illustrates how a disease or pathogen can travel across the globe, particularly via air travel, and how even the slightest negligence in quarantine measures can allow a carrier of a pathogen to slip through undetected, leading to widespread infection. It's almost as if a human bomb, laden with pathogens, is moving through borders, ready to infect large populations. This book will give you an in-depth understanding of how Ebola, one of the most feared pathogens, escaped the jungles of Africa and entered mainstream global consciousness. As we discuss Ebola, you'll realize the numerous epidemics it has triggered, especially in the African continent, and how it continues to pose a significant threat.

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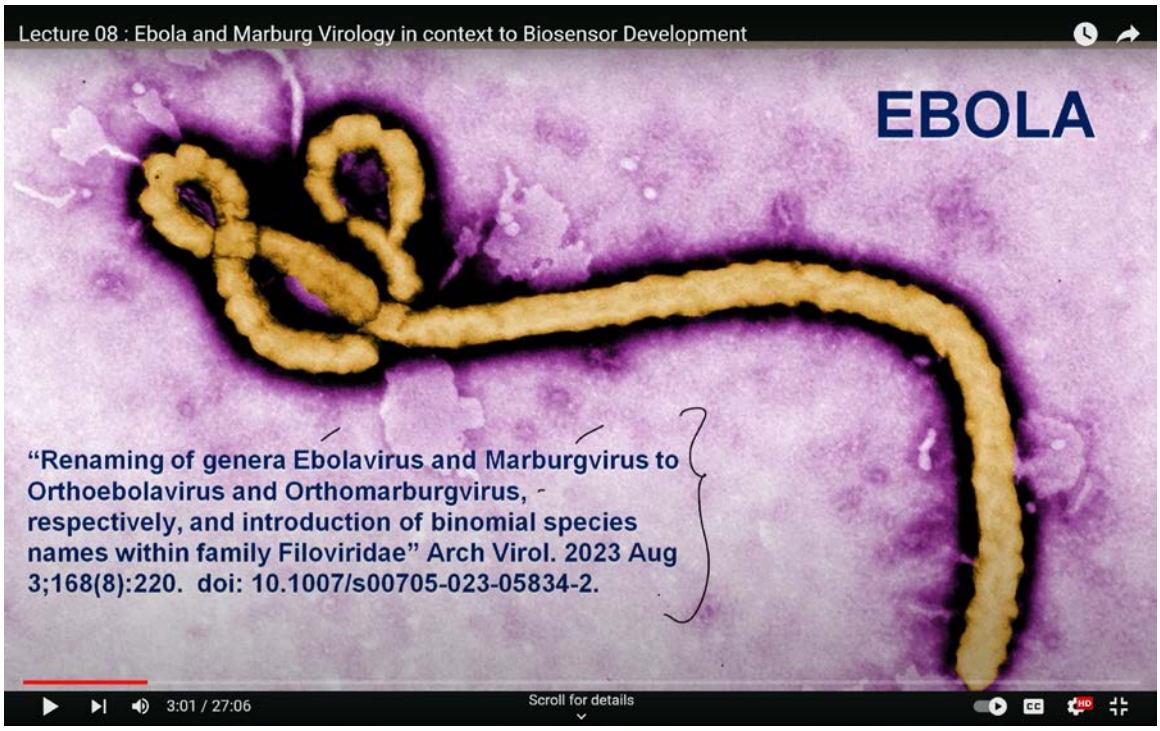

One important detail I want to highlight is the recent renaming of the genera Ebola and Marburg viruses to Orthoebolavirus and Orthomarburgvirus, respectively. This change occurred last year, so for those of you closely following this subject, it's essential to stay updated with this development. The structure of the nucleic acid of Ebola is crucial to understand, and we will delve into that in this lecture.

If we go back to the slides, you'll see that the name "Ebola" might sound unusual. The virus is named after the Ebola River, located near the area where the virus was first identified. There isn't a more profound scientific reasoning behind the name, it's simply derived from the region of its discovery. To give you a historical context, the Ebola virus, or EBoV as it's commonly abbreviated, was first identified in 1976. It has been nearly 50 years since two simultaneous outbreaks occurred, one in Sudan and another in the Democratic Republic of Congo (DRC), near the Ebola River, which gave the virus its name.

Ebola belongs to the Filoviridae family, a group of single-stranded RNA viruses. As I previously mentioned, this virus is primarily found in animal reservoirs, and various species have been recognized as potential hosts. Understanding the scale at which the Ebola virus operates is critical, and I encourage you to go online and explore more about the scale of the images depicting the virus to better appreciate the magnitude of what we are dealing with.

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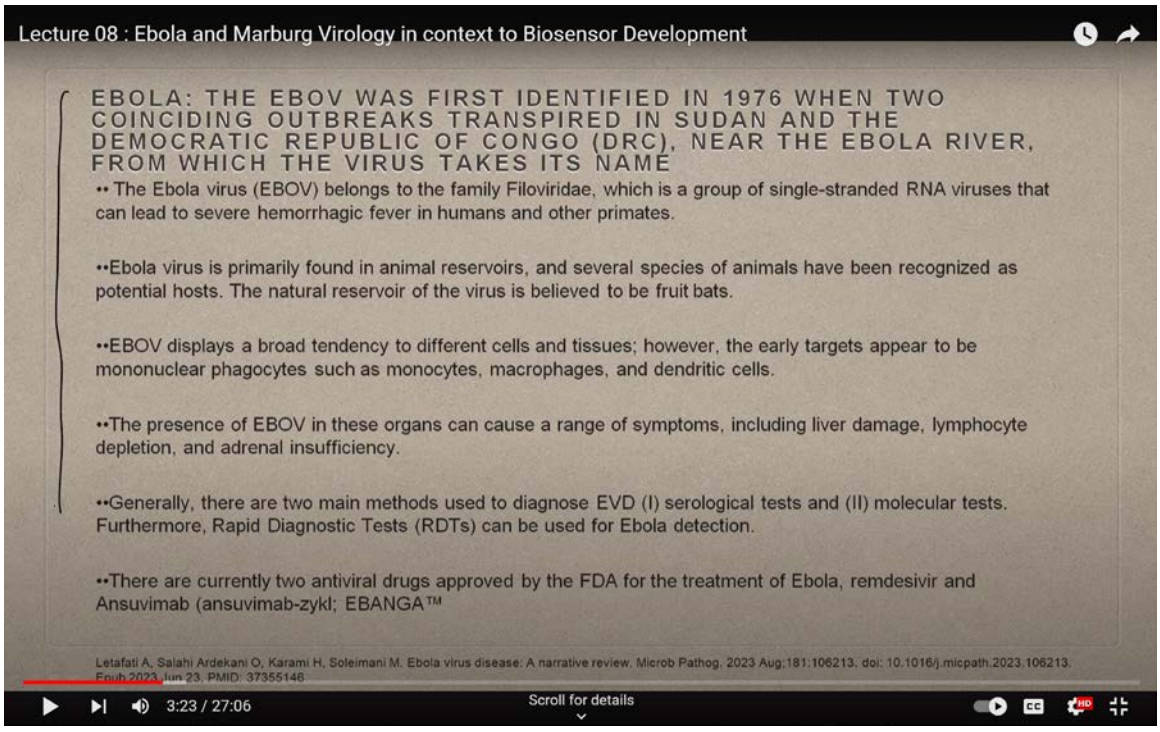

This lecture sets the stage for a deeper understanding of the Ebola and Marburg viruses and their implications for biosensor development.

The natural reservoir for the Ebola virus is believed to be fruit bats, which are quite common in tropical rainforests. These bats play a significant role in pollination, particularly at night, as they move from flower to flower. Most of these bats are vegetarians, subsisting on plant materials, and their nocturnal activities contribute substantially to the pollination process. There are numerous species of bats, and studying them can be quite challenging. I recall a few years ago, I visited a bat cave in the mountains near Madurai, which has a

well-established bat research program. It was a fascinating experience to observe these creatures in their natural habitat.

Now, let's focus on the bats deep within the jungle, which are heavily involved in pollination. Moving back to our slide, it shows that the Ebola virus exhibits a broad tropism for different cells and tissues. However, the early targets of the virus seem to be mononuclear phagocytes, such as monocytes, macrophages, and dendritic cells. This is a crucial point because these cells are integral components of the immune system. The virus directly attacks and compromises these immune cells, including dendritic cells, monocytes, and macrophages. The presence of the Ebola virus in these organs can lead to various symptoms, such as liver damage, lymphocyte depletion, and adrenal insufficiency.

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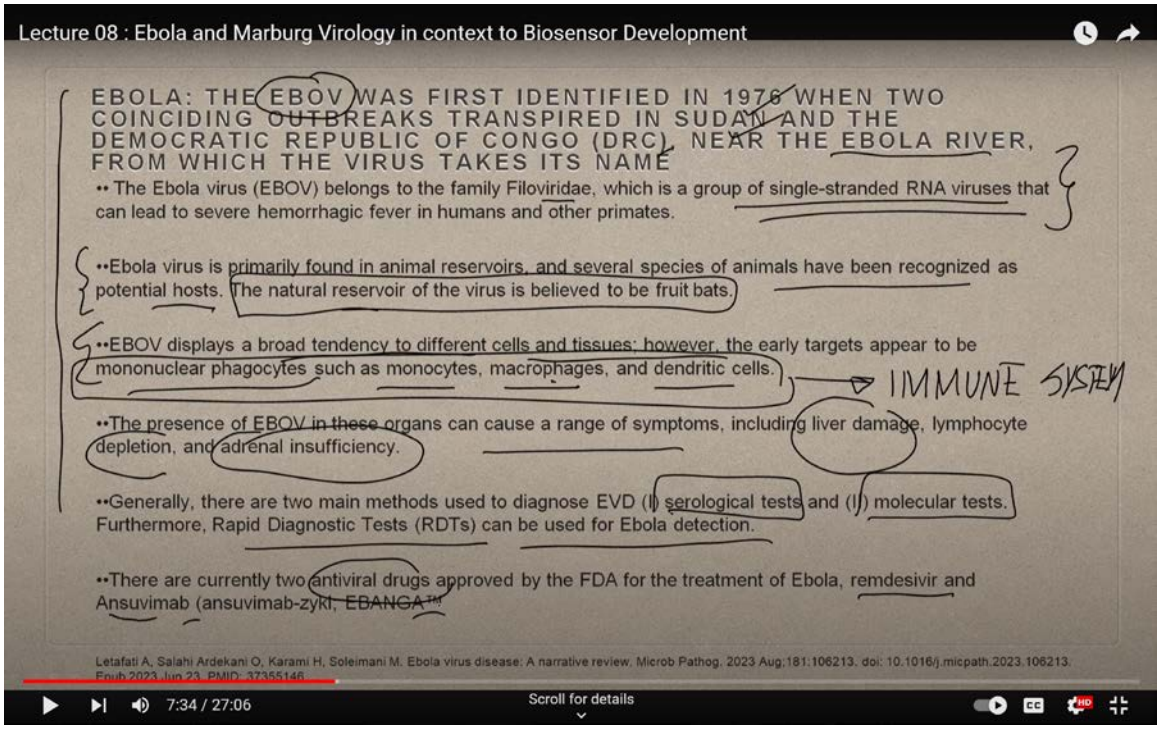

Currently, there are two primary methods for diagnosing Ebola: serological methods and molecular tests. Additionally, there are rapid diagnostic methods available for detecting the virus. At present, there are two antiviral drugs approved by the WHO that are used to combat Ebola. You may have heard of these drugs, particularly during the COVID-19

pandemic, Remdesivir and Favipiravir. These are broad-spectrum antiviral agents currently available for treatment.

Looking back at the history of Ebola, the first outbreak was recorded in 1976 in Sudan, where 151 people died, and in the Democratic Republic of Congo, where 280 fatalities were reported. After a two-year gap, the virus reappeared in Sudan in 1979. Then, after a significant hiatus, it surfaced again in 1994 in Gabon and in 1995 in the Democratic Republic of Congo. Notably, by 1996, the virus had spread from Sudan and Congo all the way to South Africa. This marked a significant geographical shift, as the virus traveled from Central Africa to South Africa and Gabon. By 2000-2001, it had reached Uganda.

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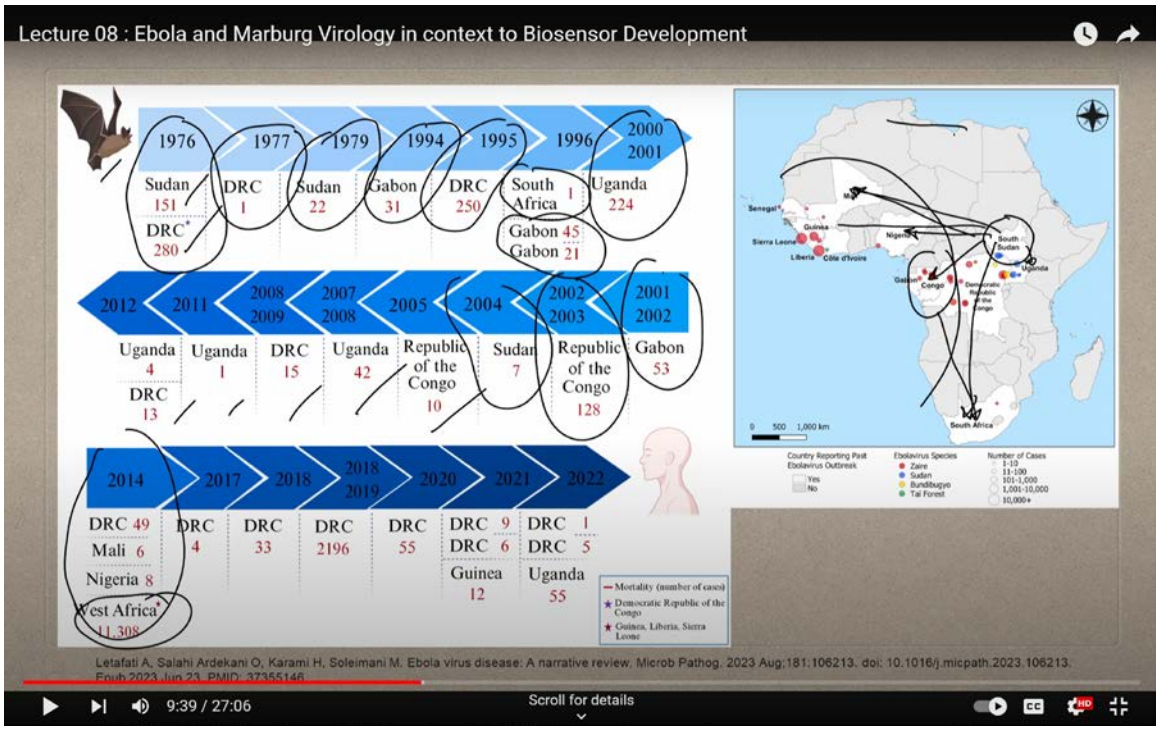

If you track the movement of the virus, you'll notice a pattern: it reappeared in Gabon, the Democratic Republic of Congo, Sudan, DRC, Uganda, and continued this cycle until at least 2014, according to reports. During this time, the virus spread significantly across West Africa, reaching countries like Mali and Nigeria. Observing the map of Africa, you can see how the virus expanded from one corner to many regions across the continent.

There is also the potential for the virus to spread beyond Africa through transcontinental travel, as has been documented in cases where the virus reached countries like Germany. Although these outbreaks have been contained, there is always a lingering concern that the virus could spread to other continents.

It's important to highlight that, despite this spread, the virus often remains confined to small, isolated pockets around the world. This brings us back to the concept of coevolution, which I mentioned in the first week. Understanding biosecurity involves grasping the concept of coevolution, how, in certain regions like the Himalayan belt or the Western Ghats, species and pathogens evolve together over time. This coevolution is a critical aspect of understanding the dynamics of viral outbreaks and biosecurity.

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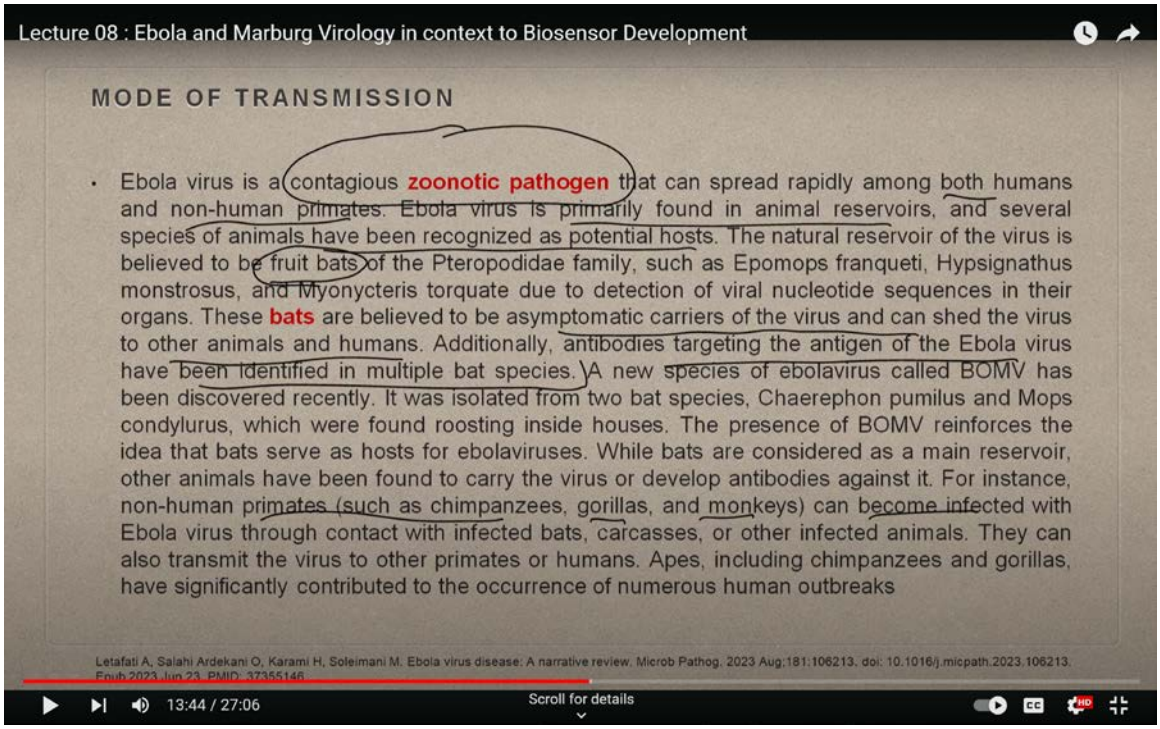

There is a unique blend of organisms, ranging from viruses to large animals, that coexist within an ecosystem. This delicate balance is typically maintained unless disrupted by external factors, such as natural migration. For instance, elephants naturally migrate along the borders of Karnataka, Tamil Nadu, and Kerala, and there is significant movement of

these animals from season to season. Similarly, migratory birds travel from Siberia to India and other warmer regions where the climate is more conducive to their survival. These migrations are part of natural cycles, and ecosystems have adapted to accommodate them over time.

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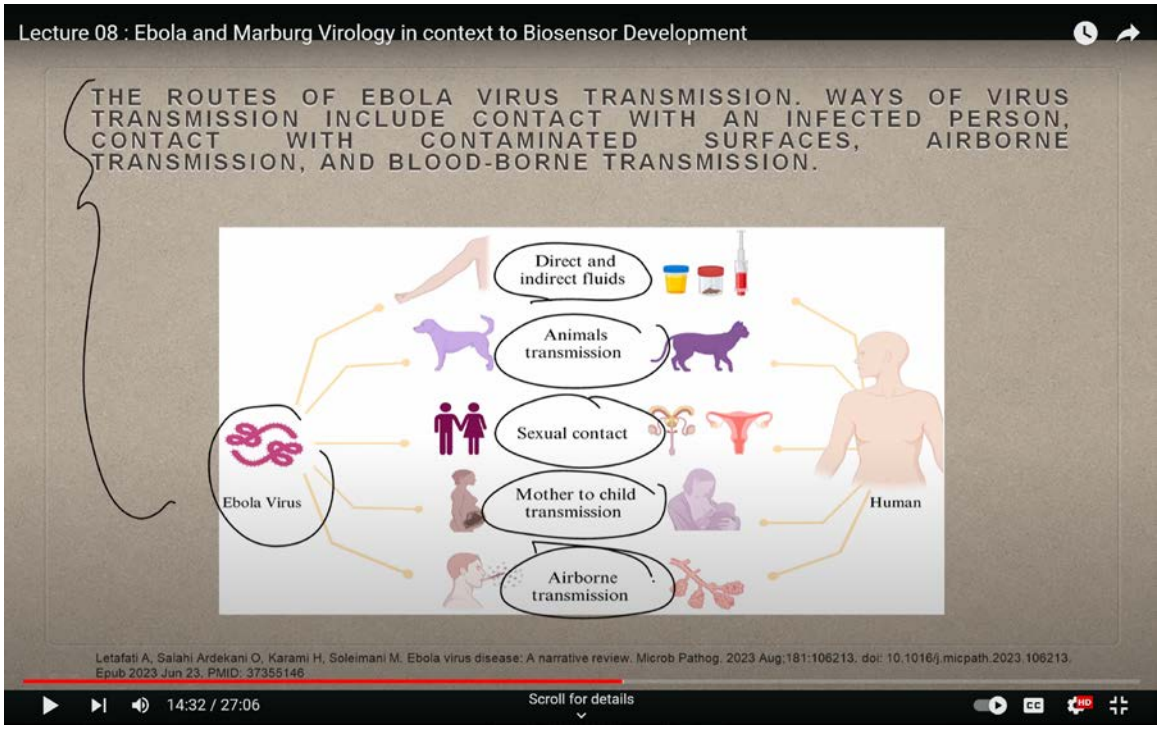

However, problems arise when migration is forced or when new species are introduced into an ecosystem. Many pathogen spreads are linked to such disruptions, often due to human activity. Moving on to the transmission mode of viruses like Ebola, it is important to note that these are zoonotic pathogens, meaning they can rapidly spread among both human and non-human primates. As mentioned earlier, Ebola primarily resides in animal reservoirs, with several species recognized as potential hosts.

The natural reservoir of the Ebola virus is believed to be fruit bats. Certain species of fruit bats have been identified as asymptomatic carriers of the virus, meaning they can harbor and shed the virus without exhibiting symptoms. Over time, scientists have discovered that a vast family of bats exists, many of which carry various viruses capable of infecting

humans. In fact, antibodies that target the Ebola virus antigen have been found in multiple bat species.

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This brings us to an interesting concept in nature, co-evolution. When we talk about species co-evolving in a particular environment, it signifies a peaceful coexistence, where organisms have developed immunity and survive together harmoniously. It's a mutual survival strategy, "I survive, you survive." However, this balance can be easily disrupted. For example, if a new species is introduced into an ecosystem, or if one element is removed, it can lead to significant problems.

In the case of non-human primates like chimpanzees, gorillas, and monkeys, these animals can become infected with the Ebola virus through contact with infected bats or the carcasses of other infected animals. This leads to another critical point: when disposing of the carcass of an Ebola-infected animal, it must be done in a highly controlled environment to prevent further transmission.

Let’s delve into the roots of Ebola virus transmission. The virus can be spread through direct and indirect contact with bodily fluids, animal transmission, sexual contact, mother-to-child transmission, and even airborne transmission. This is why I emphasized earlier the danger of airborne transmission, if an infected person travels to another country and coughs or sneezes, the virus can be transmitted to others.

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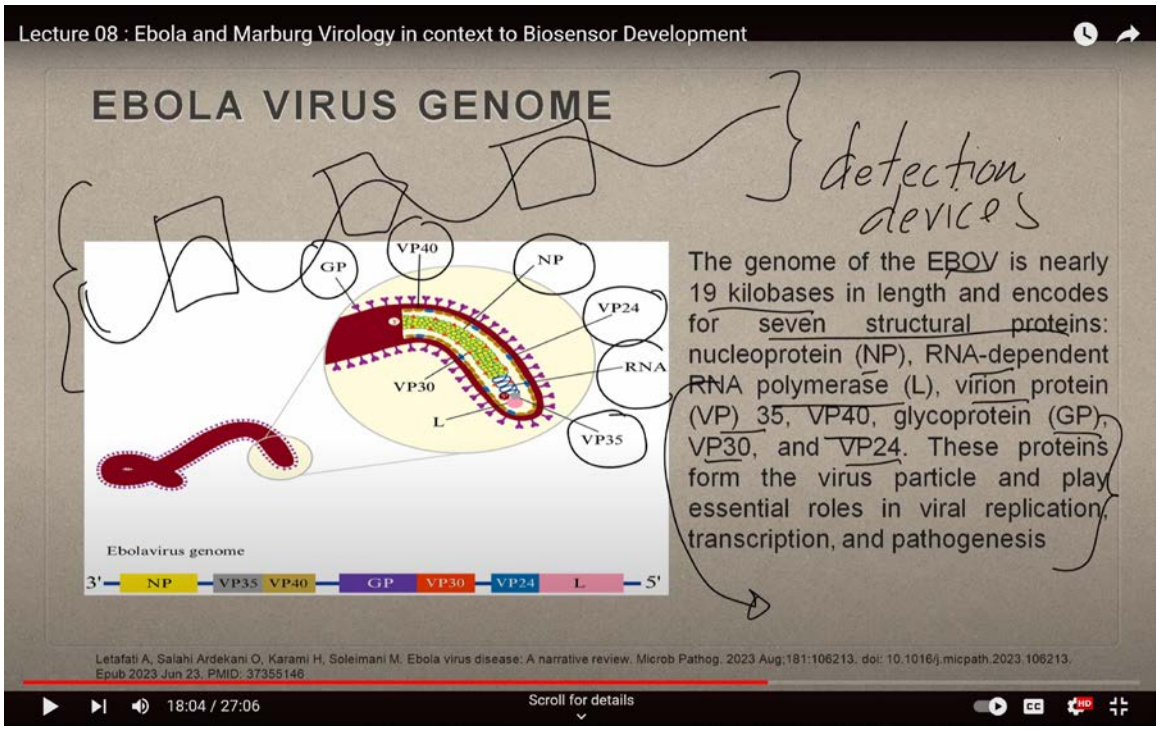

For a clearer understanding, let’s visualize the Ebola virus ecology and transmission. Bats are considered the primary reservoir hosts of the virus. They can spread the virus to other animals, leading to what is known as a spillover event. This occurs when a bat, monkey, or person becomes infected through contact with the reservoir host. Human-to-human transmission can occur through various means, including the exchange of bodily fluids and mother-to-child transmission.

Some individuals may have natural immunity to the virus, allowing them to withstand infection. However, one must be particularly cautious when dealing with the remains of those who have succumbed to the virus, whether human or animal. Proper disposal is

crucial, as is the need for healthcare professionals to exercise extreme care. Unprotected contact with blood and other bodily fluids can significantly contribute to the spread of the virus, making it imperative to maintain strict control measures to prevent further infections.

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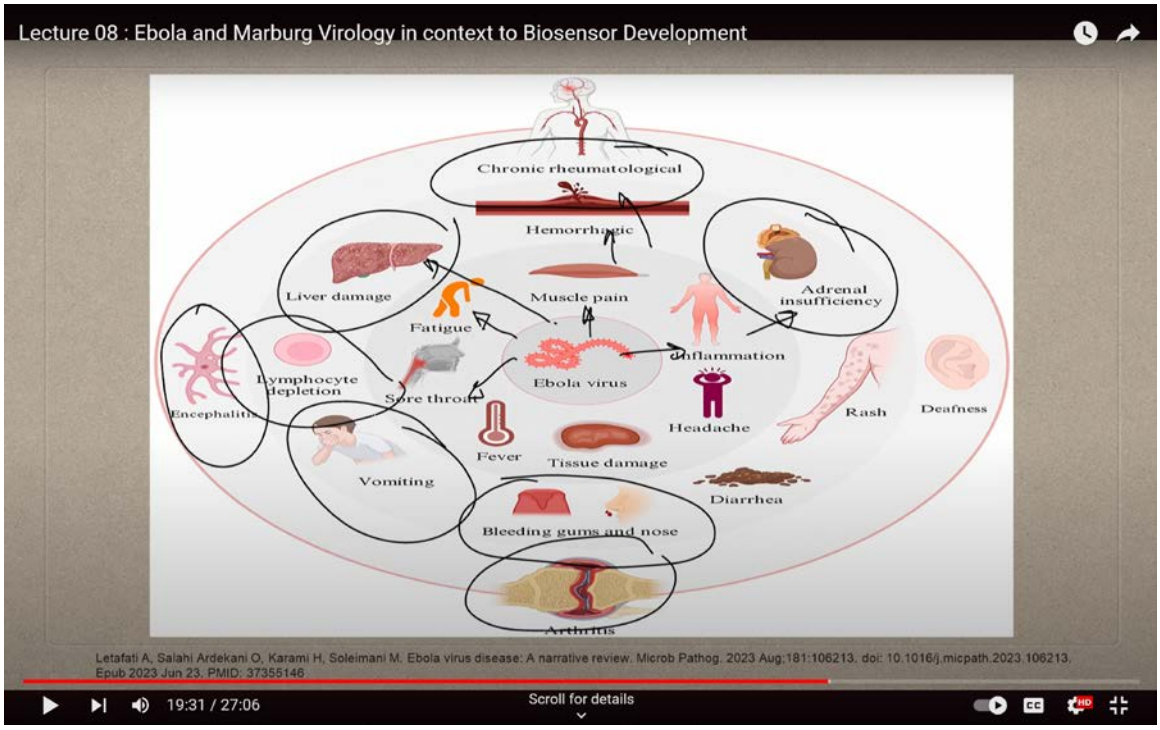

Now, if you examine the Ebola virus genome, it becomes quite fascinating. The genome spans approximately 19 kilobases and encodes seven structural proteins. These include nucleoproteins (NP), RNA-dependent RNA polymerase (RNApol), which is crucial for replication, and several virion proteins (VP30, VP40, GP, VP24). These proteins are responsible for forming virus particles and play essential roles in viral replication, transcription, and pathogenesis.

The importance of these particles, proteins, or molecules cannot be overstated. They are critical for how the virus attaches to a host cell, enters it, and replicates within. It's important to understand that all of this activity is driven by a fragment of RNA. This RNA has a specific sequence tailored to perform specific tasks. Understanding these sequences is key to developing antidotes, as antibodies can be raised to block these functions. The

RNA sequence is also vital for detection devices because it forms the foundation for understanding the proteins produced by the virus. Serological tests, for instance, rely on these sequences to detect the presence of antibodies.

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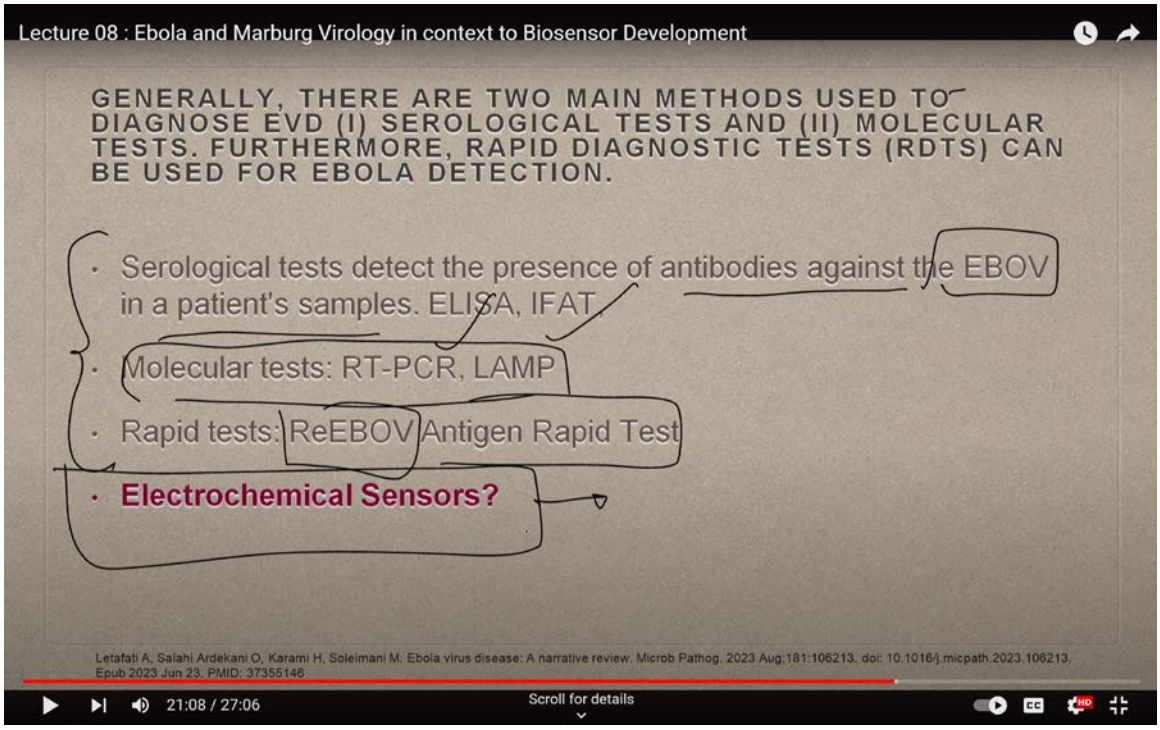

When discussing the symptoms of Ebola infection, the virus affects various bodily functions, leading to muscle pain, hemorrhage, chronic rheumatological inflammation, adrenal insufficiency, arthritis, encephalitis, extreme fatigue, sore throat, and lymphocyte depletion due to its attack on the immune system. The virus can also cause liver damage, bleeding gums, nosebleeds, and vomiting. These symptoms are critical because the damage to blood vessels often leads to fatalities, making it extremely difficult to save the patient.

There are two primary methods for diagnosing Ebola: serological testing, which detects antibodies against the Ebola virus (EBOV) using techniques like ELISA or IFAT, and molecular tests such as RT-PCR and LAMP. Many people became familiar with RT-PCR during the COVID-19 pandemic. Additionally, there is a rapid test called the RE-EBOV

antigen rapid test. All these tests rely on the structure of the virus's nucleic material, in this case, RNA, and the proteins it encodes.

Serological tests are based on these viral structures, making them essential for Ebola detection. Another type of diagnostic tool we'll discuss in this course is the electrochemical sensor, which is more economical, requires less sophisticated equipment, and provides rapid results. In the coming weeks, we will explore various electrochemical sensors, including those developed for Ebola detection. We'll examine their advantages, disadvantages, potential technological breakthroughs, miniaturization, and how they can be made widely available.

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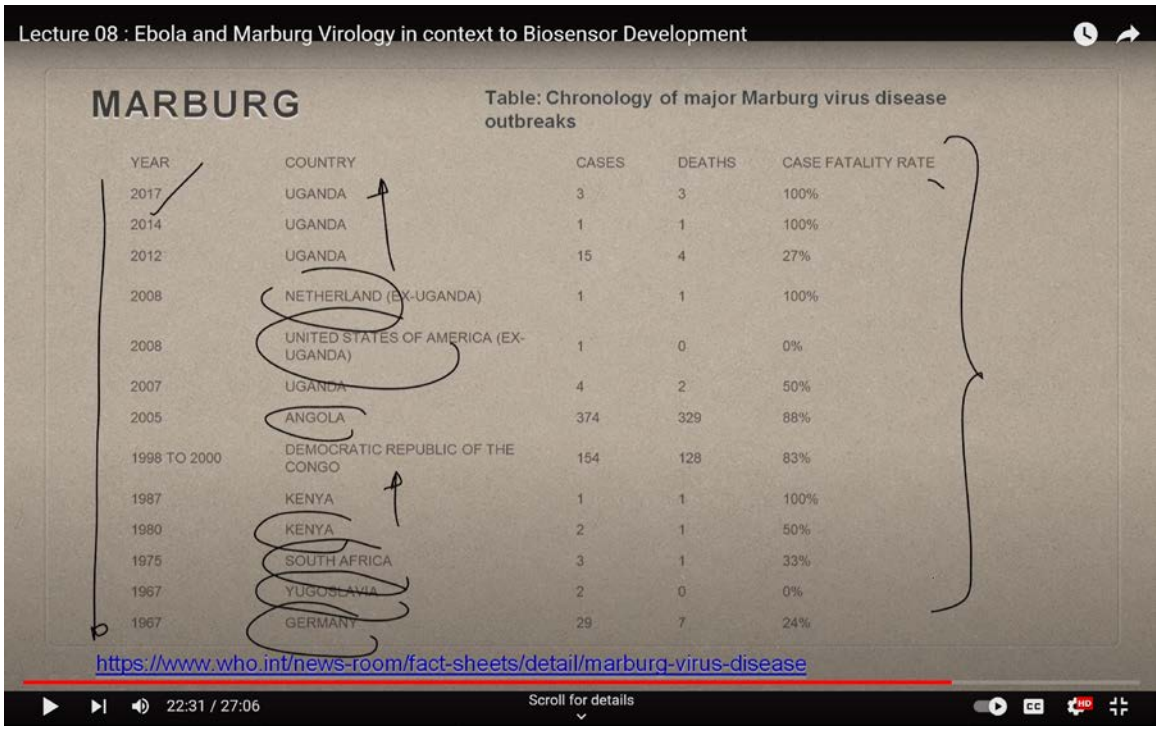

Moving on to the Marburg virus, which is closely related to Ebola and belongs to the same family, its history is also worth noting. The first known outbreak occurred in 1967 in Germany and Yugoslavia, with subsequent cases reported in South Africa, Kenya, the Democratic Republic of Congo (DRC), and Angola. In the United States and the Netherlands, carriers have been documented, with the last known case reported in 2017,

according to WHO. Although there are detection systems for Marburg, much remains to be done to understand how the virus has spread over the years.

Marburg virus, formerly known as Marburg hemorrhagic fever, is a severe and often fatal illness in humans. Like Ebola, it causes viral hemorrhage, with blood vessels being the primary area affected. Understanding this virus and its transmission patterns is crucial as we continue to develop more effective detection and treatment methods.

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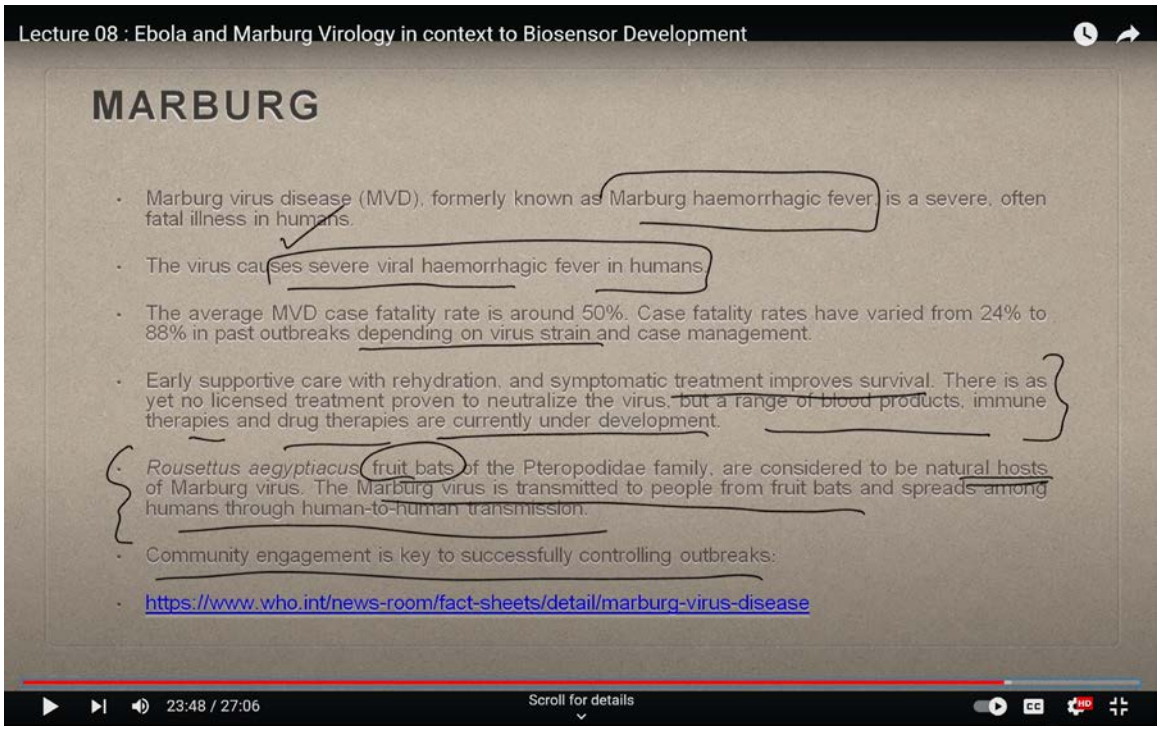

The primary concern with Marburg virus infection, much like with Ebola, is the severe bleeding it causes. This symptom is often the most critical factor in patient outcomes. The average case fatality rate for Marburg Virus Disease (MVD) is approximately 50%. Early supportive care, particularly rehydration and symptomatic treatment, can significantly improve survival rates. However, there is currently no licensed treatment that has been proven to neutralize the virus. Nevertheless, a range of blood products, immune therapies, and drug treatments are under development, offering hope for more effective interventions in the future.

Similar to Ebola, the natural host of the Marburg virus is believed to be the fruit bat. The virus is transmitted to humans through contact with bats and then spreads from person to person via human-to-human transmission. Engaging and educating communities is crucial for successfully controlling outbreaks of Marburg virus, as well as Ebola.

When we compare Marburg and Ebola, we see that they share very similar patterns of disease transmission and co-evolve in specific regions. However, if these viruses are removed from their native environments and introduced into new areas, they can act as "novel weapons." This concept, which we discussed in the first week, refers to how these viruses, when introduced to a new population that has not previously encountered them, can become incredibly dangerous. The new population's immune systems are not equipped to recognize or fight off these viruses, as they have not developed the necessary antibodies.

This rapid and severe impact on a new host population occurs because the virus is producing proteins that the new host's body has never seen before. The immune system is unprepared, allowing the virus to spread and cause significant harm before the body can mount a defense. This is in stark contrast to viruses that have coexisted with a population for an extended period, where the body has had time to develop defenses.

From an evolutionary perspective, this highlights the importance of understanding how viruses like COVID-19 have evolved over time. COVID-19, for instance, is not a new virus, it has existed for a long time in some form, but it reached a critical point where it suddenly spiked, causing widespread disruption and severely impacting the global economy.

Given the inevitability of human movement, trade, and international interaction, we must be prepared for the possibility of such viral spikes. This preparation includes the development of antidotes, therapies, and medications that can be deployed swiftly in response to outbreaks. Achieving this level of preparedness will require significant global cooperation and a concerted effort in research and development. Thank you.