Introduction to Complex Biological Systems
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Lecture 41
Introduction to microbial world and infectious diseases

Welcome back to the NPTEL online course on introduction to complex biological systems. This week, I will be discussing infectious diseases, specifically viruses and bacteria. This lecture, lecture number 41, I will mostly introduce the microbial world and infectious diseases. Here, I will cover a general introduction about microbes and their impact on our environment and the living world. This will be followed by a brief introduction to microbes and infectious diseases and their complex relationship, such as between microbes and humans. Now, what are microbes?

So, microbes, I would say, are organisms and acellular biological entities. As a result, microbes can be some acellular biological entities. For example, viruses are not cells; they are not considered living organisms. That is why I am including both cellular and acellular biological entities. The major feature is that they are very small to be seen clearly by the unaided eye. So, you need some microscope in order to properly visualize those small organisms or acellular entities.

So, those are the microbes. Now, if you see organisms and biological entities studied by microbiologists, microbiologists are professionals who study microbes, which can be cellular or acellular. Among cellular microbes, we can largely classify them into three major categories: one is bacteria, the other is Archaea, and the last one is Eukaryotes.

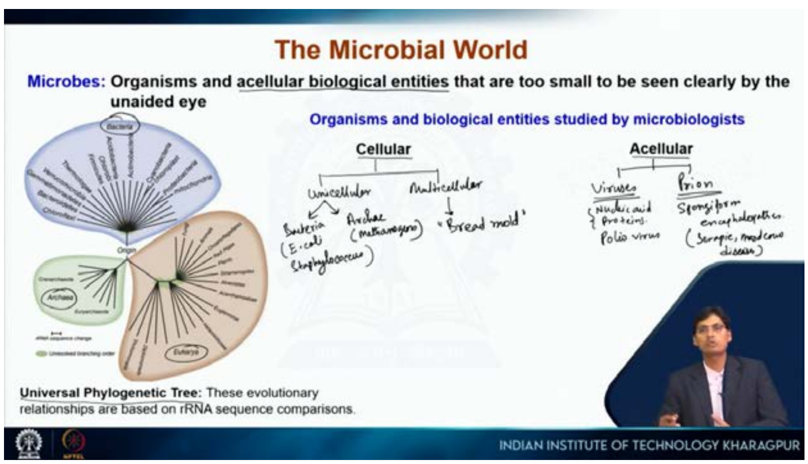
So, basically, if we consider prokaryotes and eukaryotes, bacteria and archaea come under prokaryotes, and the other one is eukaryotes. So, now this classification here is based on rRNA sequence, the ribosomal RNA sequence analysis, and this is like a universal phylogenetic tree. So, here also, another important aspect you will notice is that archaea are not directly related to bacteria. They have a huge difference in terms of classification or in terms of the phylogenetic tree. If you notice, they have some similarities with eukaryotes also in terms of RNA sequences. So, anyway, if we would like to concentrate on microbes now, here I would say, these can be prokaryotes and eukaryotes. The other way you can say it is unicellular and multicellular organisms. So, unicellular means here both will come, like bacteria, for example, E. coli, staphylococcus so all bacteria will come as unicellular microbes, and the other one is archaea. So, here, you can say methanogens, and now, multicellular organisms can also come under microbes because there are many multicellular organisms that are very small. Just one example, if I say bread mold. Sometimes, if we keep bread for a long time in moist conditions, you will notice some whitish filamentous stuff coming up. So, those are bread molds. So, there we have many, many cells in those fungi, but still, you need a microscope to properly visualize them.

So, these cellular microbes can be unicellular as well as multicellular and now, acellular entities. So, here the major two classes I would say are one, viruses. As you know, viruses do not have a lot of machinery; they are missing there so they only replicate inside the host cell.

So, as a result of that, we do not consider viruses as living organisms. They just have some kind of nucleic acid; it can be DNA or it can be RNA. So, RNA can be genetic material for viruses, along with some proteins. The structure of a virus is very simple; for example, poliovirus and influenza virus. There are many viruses and now, another major category of acellular microbes is prions. So, prions are actually proteins with no nucleic acid. So, they are just protein particles. But the thing is, these protein particles are infectious. So, what happened?

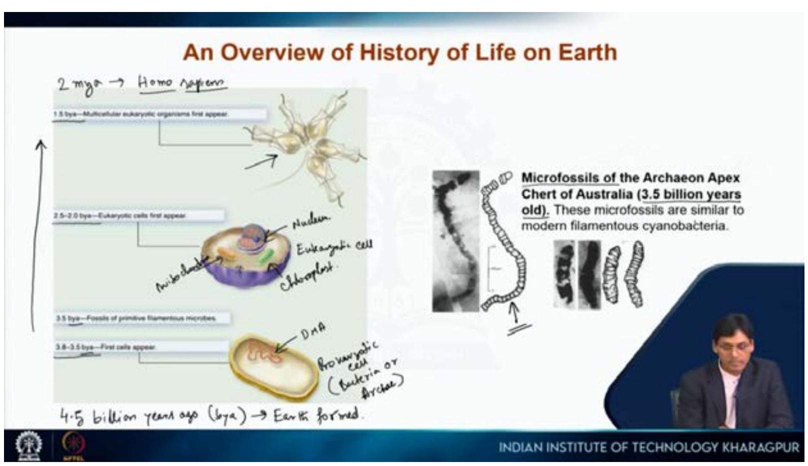
This protein somehow their folding and their character has been changed due to various different types of reasons and now those proteins can convert other proteins into a misfolded state and they can actually make other proteins into prions. So they are actually causing diseases for example, they cause some spongiform encephalopathies. So, for example, scrapie mad cow diseases.

I am little bit elaborating about prion because I am not going to discuss in more details in the in the next class, but I will be discussing about viruses and bacteria in great details in the following lectures. So this is prion and all together they are microbes and now let us see when they evolve in terms of the evolution of earth these microbes. So although we considered the microbial world, microbes evolved at first and then this complex organism like multicellular organism eukaryotic evolved much later, so here if you see this is the timeline So, I would say that approximately 4.5 billion years ago. So, BYA as you can see is mentioned BYA billion years ago. So, 4.5 billion years ago earth formed.



Now in this time scale if you see the origin of different types of organism you will be noticing that 3.5 billion years ago first cells appeared. What kind of cell? Those are nothing but prokaryotic cells, some kind of bacteria. They do not have a proper nucleus as you can see this is the DNA and I would say this is just a prokaryotic cell. It can be bacteria or archaea. Now, again it took a long time and approximately 2.5 to 2 billion years ago eukaryotic cells developed.

So, this is a eukaryotic cell but they are still single cell, single cell eukaryotes. So, as you can see here this is the nucleus and here mitochondria and this is chloroplast and it took a long time to get the multicellular eukaryote. Approximately 1.5 billion year ago as you can see here this is multicellular primitive eukaryotes not properly differentiated organisms like us like humans or big plants not like that. I should mention here it took million billions of years and finally, I would say approximately 2 million years ago million years ago homo sapiens humans developed. So what I am trying to say at the beginning, there are only microbes, only unicellular organisms. Now what we see is that we have different types of organisms with a lot of diversities here, from microscopic organisms like virus bacteria to very complex organisms like humans, plants and so many organisms are present in the present world. Here in order to support whatever this time scale I am just discussing here, if you see this microfossil which was found in the Apex chart of Australia, this is around 3.5 billion years old and these microfossils are very similar to modern filamentous cyanobacteria. So, cyanobacteria is also present now. So, they are photosynthetic bacteria, but whatever is found in this Apex chart of Australia, this is not true cyanobacteria what is present now, but this is very close to that. So, as you can see this is found in this microfossil again it suggests if you see the time scale that 3.5 billion years old. So, as a result of that we mention here that 3.5 billion years back the first cell appeared and here 3.5 billion years ago fossils of primitive filamentous microbes originated. I would like to emphasize that this early cellular life that means both archaea and bacteria save our environment and drives evolution of complex life forms.

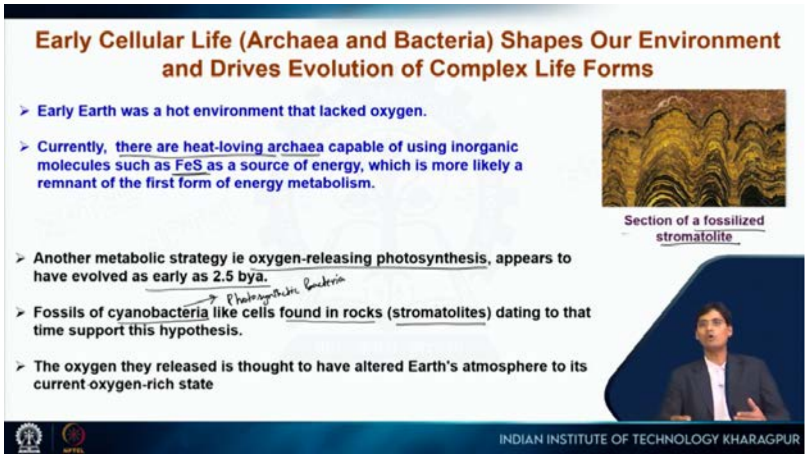


I would like to explain this part that if you see early earth was a hot environment that lacked oxygen. So, as a result of that, if you see nowadays, in the present world, almost all of us rely on oxygen for energy metabolism. Without oxygen, we cannot survive. But when those organisms evolved at the beginning, I would say the very beginning when earth formed, during that time, no oxygen was there and it was very hot. So, currently there are heat loving archaea.

So, archaea are sometimes considered more primitive than bacteria. So, they are capable of using inorganic molecules such as iron sulphide as a source of energy instead of oxygen. Oxygen was not there at that time so they are using iron sulfide as energy source which is more likely a remnant of the first form of energy metabolism and over the time oxygen generated and that also drives evolution of different types of organism So, here that is why I mentioned that another metabolic strategy is oxygen releasing photosynthesis and it appears to have evolved as early as 2.5 billion years ago. So, as you can see here this is some kind of section of fossilized stromatolite.

So, what happened here? Fossils of cyanobacteria, this is already mentioned as photosynthetic bacteria. So, they are bacteria, but they can carry out photosynthesis.

So, here I am just clarifying that photosynthetic organisms like plants have chloroplasts and there are a lot of pigments inside the chloroplasts, which is why they can carry out photosynthesis. But cyanobacteria do not have chloroplasts; they have some kind of pigments that can carry out photosynthesis. Those cyanobacteria are found in rocks like stromatolites, dating to that time around 2.5 billion years ago. So, that supports this hypothesis that during that time, they generated oxygen because of these different types of metabolic activities and the oxygen they released is thought to have altered our atmosphere to its current oxygen-rich state. As I already mentioned, almost all organisms rely on oxygen. Besides their role in shaping our environment, they also drove the evolution of complex life forms.

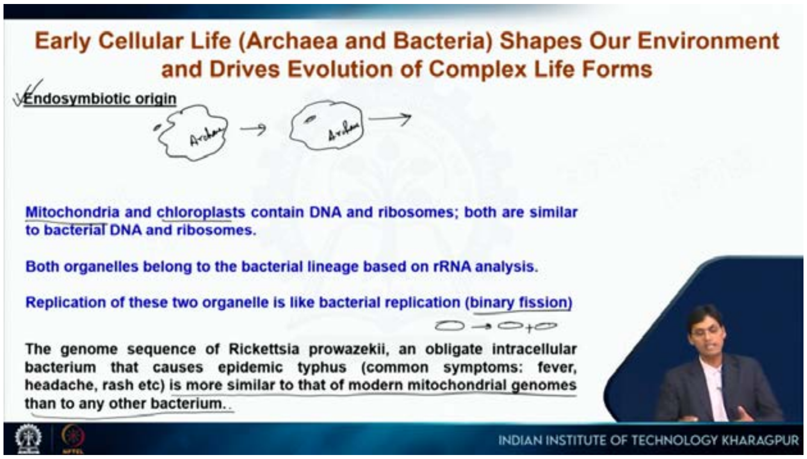


At the beginning, we had only unicellular organisms, particularly prokaryotes like archaea and bacteria. But then eukaryotic cells developed, followed by multicellular organisms. Now, how eukaryotic cells developed? So, there are many hypotheses, and the endosymbiotic origin is one of the most important. Scientists really believe this hypothesis to support the origin of eukaryotic cells. So, what happened is that a primitive eukaryotic cell, for example, some kind of big bacteria, I would say archaea, so if this is archaea, they phagocytosed small bacteria. So, as a result of that, we would say that this is the bacteria or archaea or it could be both and this is some kind of ancient eukaryote, not yet a developed eukaryote. The bacteria came inside this ancient eukaryote and now, over a long period, after millions or billions of years, today's complex eukaryotic cells developed the nucleus and all those complexities evolved. But now, if you see, this is some kind of symbiotic relationship. The bigger cell, whether it is archaea or bacteria, does not matter, but the bigger cell, which I am referring to, is that ancient eukaryotic cell.

So, that actually phagocytoses this bacterium. Now they are in a symbiotic relationship, and over time, this modern eukaryotic cell developed where these bacteria inside the cells are still present, like mitochondria and chloroplasts. So, they are still present; if you see mitochondria and chloroplasts, they contain DNA and ribosomes. So, although they are cell organelles, they still have their own DNA and ribosomes. More importantly, both are similar to bacterial DNA and ribosomes. They are more similar to bacterial DNA and bacterial ribosomes. Particularly, I would like to mention that the DNA of mitochondria and chloroplasts is circular DNA, which is again similar to bacterial DNA also, both organelles belong to the bacterial lineage based on ribosomal RNA analysis.

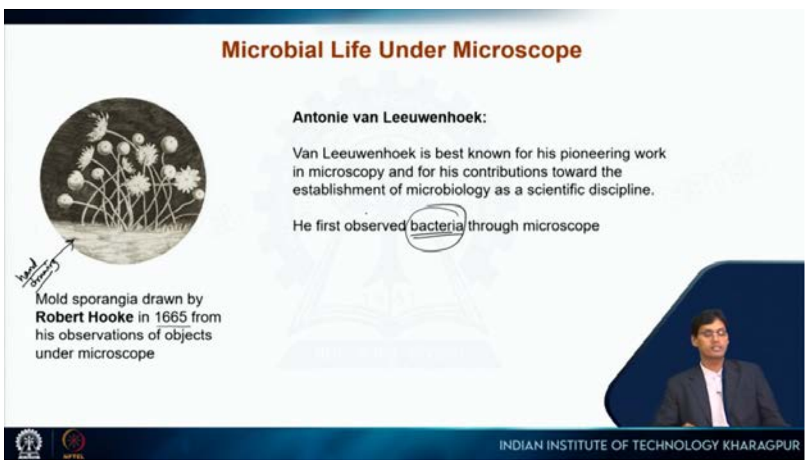
Another important thing is the replication of these two organelles, mitochondria and chloroplasts, which is just like bacterial replication, like binary fission. That means one bacterium here divides into two. Chloroplasts and mitochondria undergo binary fission and divide in this way. So, all these support the endosymbiotic origin of eukaryotic cells. More importantly, the genome sequence of this bacterium, Rickettsia, is an obligate intracellular bacterium that causes typhus. It is a disease, particularly fever, headache, and rash, which are the common symptoms of epidemic typhus.

If you see the genome sequence of this bacteria, it is more similar to that of the modern mitochondrial genome sequence than to any other bacterium. This is very interesting. So, it again suggests that mitochondria might have evolved from bacteria itself. That is why you can see a lot of similarity between the mitochondrial genomes and the genome of this bacterium, Rickettsia and now, I would just like to focus on microbial life under a microscope.



Whatever in modern day currently we are studying about microbes, we need a powerful microscope also in order to understand microbes in a better way. But at the beginning it is, I would say a long time back, in 1665, during that time these mold sporangia was drawn by Robert Hooke, and his observation of these sporangia is based on whatever he saw under the microscope. So, this is although just a hand drawing, not the microscopic image; this is just a drawing by Robert Hooke, who also discovered the cell and that the cell is the unit of life, and almost all of you know about that. So, now, Robert Hooke first draw this picture about this mold sporangia and almost at the same time, Antonie van Leeuwenhoek, he is best known for his pioneering work in microscopy and for his contribution toward the establishment of modern microbiology or microbiology as a scientific discipline.

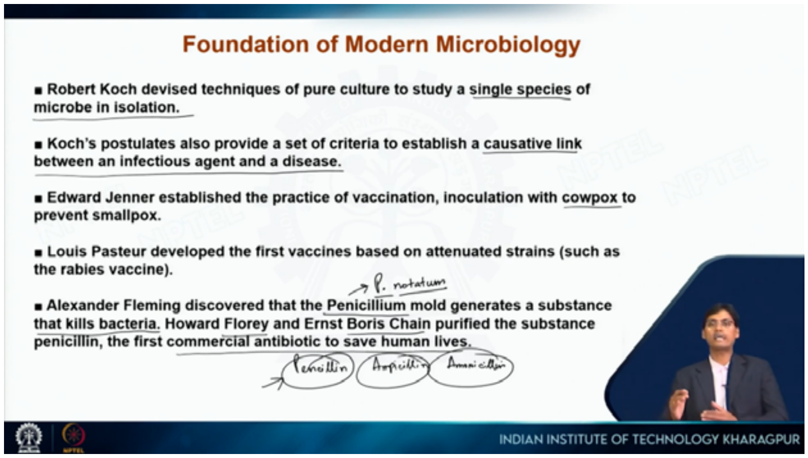
He first observed bacteria through a microscope. So, Robert Hooke first observed a cell under a microscope for example, mold sporangia. So, as a result of that this is not bacteria, this is some kind of eukaryotic cell, bread mold for example is a eukaryotic cell, but here Antonie van Leeuwenhoek first observed bacteria under a microscope, and then a long way to go; now we have a lot of information, a lot of understanding about bacteria, viruses, and so many things. Now I would like to mention a few of the important discoveries. I would say that those are the major pillars and that actually are the foundation of modern microbiology. First one is there are many; I cannot cover all those things but some important points I will be covering here. Robert Koch devised the technique of pure culture to study a single species of microbe in isolation. Now, it is almost in all labs whenever we are working with some microbes, we work on a single species of the microbe, particular bacteria for example, and in isolation not in the environment.



So, as a result of that robust watch, actually first discovered this technique of culturing single species and then Koch’s postulates also provide a set of criteria to establish a causative link between an infectious agent and disease. It is very important that a particular microbe can cause a particular disease. That causative link between a microbe and the disease was also established by Robert Koch and then this is again another milestone that Edward Jenner established the practice of vaccination. So, what he did was inoculate cowpox to prevent smallpox, as you know, smallpox is a very deadly disease during that time. But cowpox, it is again caused by some kind of viruses, and what it did if someone is inoculated with cowpox, it can prevent the smallpox disease, so this is again a great discovery, and this is modern day whatever we are taking vaccine immunization, the basic study coming from here the first one. Then Louis Pasteur developed the first vaccines based on attenuated strains such as the rabies vaccine. Nowadays many attenuated strains of microbes are available for vaccination and Alexander Fleming discovered that penicillium. This is particularly penicillium notatum. So, this is some fungus. So, it generates a substance that kills bacteria. This is a very important discovery. This is the beginning of the discovery of antibiotics.

So then, over time, Florey and Boris Chain purified the substance penicillin from this fungus, and this was the first commercial antibiotic to save human lives. Now, we have a number of antibiotics available, but this was the beginning of that. Because of their remarkable work, all three of them shared the Nobel Prize in Physiology and Medicine in 1945. So, penicillin was the first antibiotic used to save human lives. So, I am just giving one example: penicillin. So, now if I say ampicillin and amoxicillin, all those antibiotics are very similar. So, penicillin was the first one, the natural one and then, over time, scientists developed slightly different antibiotics. But all three of these antibiotics work in the same way. They actually block the synthesis of peptidoglycan.

Peptidoglycan is a polymer present in the bacterial cell wall. As a result, if these antibiotics stop the synthesis of peptidoglycan, the bacteria cannot survive. They cannot make their peptidoglycan, so the bacteria will die and cannot divide. That’s why this antibiotic is very important. Here, when discussing archaea and bacteria, I must mention one major difference: bacteria have peptidoglycan in their cell wall, but archaea do not. Now, I would like to briefly introduce a few microbial infectious diseases. Microbes cause diseases, and some of these diseases have had a huge impact on human history. So, I will just mention a few of them.



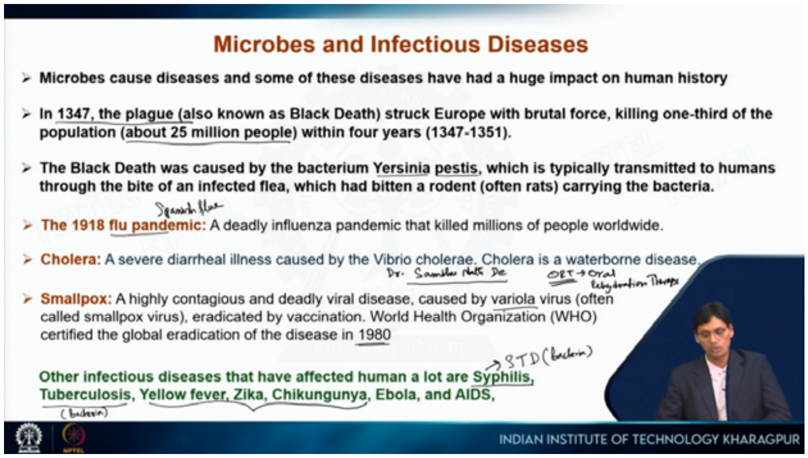
If you look at 1347, the plague, which is also known as the Black Death, struck Europe with brutal force and killed one-third of the population, which is almost 25 million people within four years, from 1347 to 1351. So, this was a huge load, a huge burden and later on, it was discovered that the Black Death was caused by the bacterium Yersinia pestis. So, this is the bacteria, the causative organism for this disease, which is typically transmitted to humans through the bite of an infected flea that had bitten a rodent, such as a rat. That carries this bacterium. But nowadays, these kinds of diseases, like bacterial diseases, can be managed much better because, as I already mentioned, there is a spectrum of antibiotics available commercially nowadays.

So, it is much easier to handle this kind of bacterial infection. And then another important infectious disease outbreak was the 1918 flu pandemic. In the first module, when I discussed the Griffith experiment, that was in the backdrop of the 1918 flu, also known as the Spanish flu. This was a deadly influenza pandemic that killed millions of people worldwide. Then, cholera, a severe diarrheal illness caused by Vibrio cholerae, is a waterborne disease. Here, I must mention that, long ago, many people used to die from cholera, and one of the major problems was in the case of cholera, the symptom is severe diarrhea. As a result, people suffered from dehydration and lost a lot of water, making it very difficult to manage. One of the pioneering scientists in this field, whom I must mention here, is Dr. Sambhu Nath De. He used to work in Kolkata. His work particularly demonstrated that the pathology of cholera, the dehydration during the disease, directly contributed to the development of ORT therapy, meaning oral rehydration therapy. Why? As I already mentioned, the pathology is that people lose water, and because of dehydration, they die. and as a result, this was mostly observed by Dr. Sambhu Nath De. From there, oral rehydration therapy came into place.

So, for example, electoral and ORS, whatever, sometimes if we are really suffering from different types of diarrhea, then we take ORS or electoral powder. So, this is the link between this whatever I am discussing right now. Now another important disease is smallpox, a highly contagious and deadly viral disease caused by variola virus and often it is also called smallpox virus. This is a very deadly disease; if it gets into a village or a town, then almost all people are getting contaminated, they are getting infected by this smallpox, and it is creating a lot of problems, but because of the vaccination, the disease has been eradicated, and WHO declared in 1980 that it is not there anymore; this disease itself is completely eradicated. There are many other infectious diseases as I already mentioned. I am just covering a few of them which are very important.

So, here if you see syphilis, this is one sexually transmitted disease. Tuberculosis is again an airborne disease both syphilis and tuberculosis are caused by some bacteria. So, a bacterium is the causative organism for these two diseases. In case of tuberculosis, all of you know that mycobacterium tuberculosis is responsible for this disease, and then yellow fever, Zika and Chikungunya all these three are diseases caused by viruses and here particularly mosquito is the carrier of those viruses.

So, all are viral diseases, and similarly here Ebola and AIDS are not carried by mosquitoes. But I would say Ebola is a very deadly disease, and AIDS, many of you know, is acquired immunodeficiency syndrome caused by the HIV virus. So that is all. I would say a few infectious diseases I just mentioned here, but if you see, because of those infectious diseases, people used to believe that microbes are always bad, a kind of common perception because they are creating a lot of problems like different types of diseases and so many things.



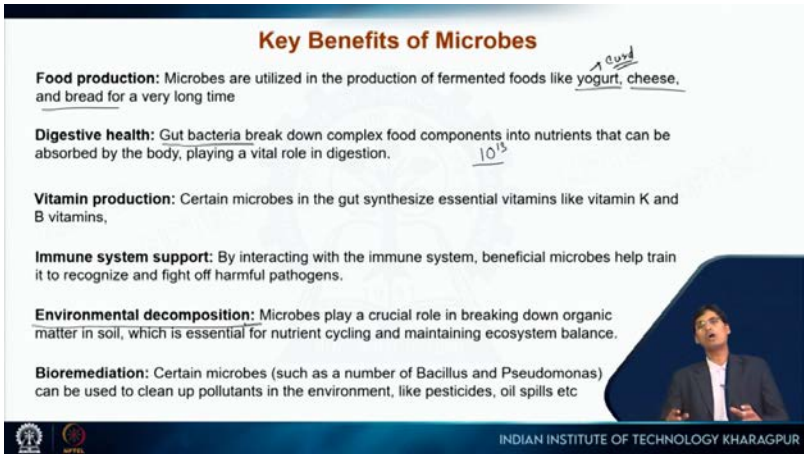
But microbes are also very helpful, as at the beginning I told, because of the microbial organisms oxygen developed on the earth, for just one example, and then I also mentioned that Alexander Fleming found penicillin from some fungus. This is also another microbe, penicillium notatum, from there. Not only that, there are many microbes which are associated with humans and many other organisms. They are actually helping.

So that's why I am trying to say that it has some kind of complex relation between microbes and their host. For example, microbes and humans. So here I will give a few beneficial sides of microbes. In food production, microbes are utilized in the production of fermented food like yogurt, cheese, and bread for a very long time. So this is curd, so for example, when we try to make curd, what we do is we just whatever curd we have, we are taking a little bit of that, just a pinch of that, and we are putting that on some fresh milk, and then again that fresh milk will be converted into curd. The reason is that in that curd we have a lot of live bacteria. Mostly they are lactobacillus, and now they will make this fresh milk into curd again, so as a result of that, I am just giving you one example. Similarly, cheese, bread, and all those things everywhere have bacteria involved so sometimes bacteria, sometimes fungus like yeast all those things are involved here, but for food production, they have a huge role and then digestive health. Gut bacteria, particularly those present in our mouth and intestines, break down complex food components into nutrients that can be absorbed by the body; therefore, they play a vital role in digestion. I must say here that a healthy individual is actually a healthy human being. We have a lot of bacteria in our body;

so the number of bacteria is more compared to the number of human cells present in our body. If you are healthy enough, sometimes I mentioned that in adult humans we have approximately 10^{13} cells, but now I am telling. In healthy human beings, we have much more bacterial cells compared to the 10^{13} cells; because they are very small, they can still be present in our body, and they are helping in different ways as already mentioned, digestive health.

Another example is vitamin production. Certain microbes in the gut synthesize essential vitamins, for example, vitamin K and different types of B vitamins, particularly vitamin B12. It is very important for us, and it is mostly synthesized by some bacteria present in our gut and then supporting our immune system by interacting with beneficial microbes, they help train our immune system. This is one positive side of these bacteria, although they don't cause any disease to us but are helping in this way by giving training to our immune cells. If a lot of these bacteria, which are in a good relation with humans, are not causing disease, and if those are present in our body, then some pathogens, which are disease causing bacteria or disease causing organisms, cannot easily colonize inside our body, so as a result of that, they need to compete with these good bacteria present in our gut. So this is another strategy I would say it's developed over time.

So, we are in some kind of mutually beneficial relationship with bacteria. They are surviving, and that is helping us as well. Besides all those things, there are two major points I also mentioned here. One is environmental decomposition, as you know, microbes play a crucial role in breaking down organic matter in soil, which is essential for nutrient cycling and maintaining ecosystem balance. So microbes such as bacteria and different types of fungi are part of our ecosystem and then, bioremediation, certain microbes, such as a few members of Bacillus and Pseudomonas, can be used to clean up pollutants in the environment, like pesticides and oil spills. So, they can be taken care of by these bacteria, which can directly clean these pesticides and oil spills. So if you see, microbes are also very beneficial. They are playing a very important role in our day-to-day life, and that is all.



So, for more details, you can follow Prescott's Microbiology. This is a very good textbook of microbiology. Thank you very much.