

Applied Environmental Microbiology
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Lecture – 39
Exposomes I

Dear students, up till now we have talked about how microbes are present everywhere. So, they are ubiquitous in nature or essentially ubiquitous because wherever there are even slightly hospitable conditions, microbes will survive some microbes wealth right there and the other thing we have learned is how microbes are integrated with our public health and our own well being. Not only in terms of their pathogenicity that some microbes are pathogenic, but also that some microbes some commensal microbes are necessary for good health.

For example, in the previous lecture we talked about if the gut micro biome is healthy and is adequate enough to promote lean body mass; then the person or the rat is likely to have a lean body mass. On the other hand if this gut micro biome is affected and it changes to another profile it changes its profile; then it is quite possible that now the new profile will not support a healthy lean body mass and will affect the body mass index of the person or the rat.

We also learned about IBS; which is Irritable Bowel Syndrome and how it is; now, we are suspecting and we have good reasons to believe it is largely governed by the microbial flora inside our gut; obviously, we do not know exact; we can we have not been pointed the exact reasons which affect the constitution of microbial community in the gut in the first place.

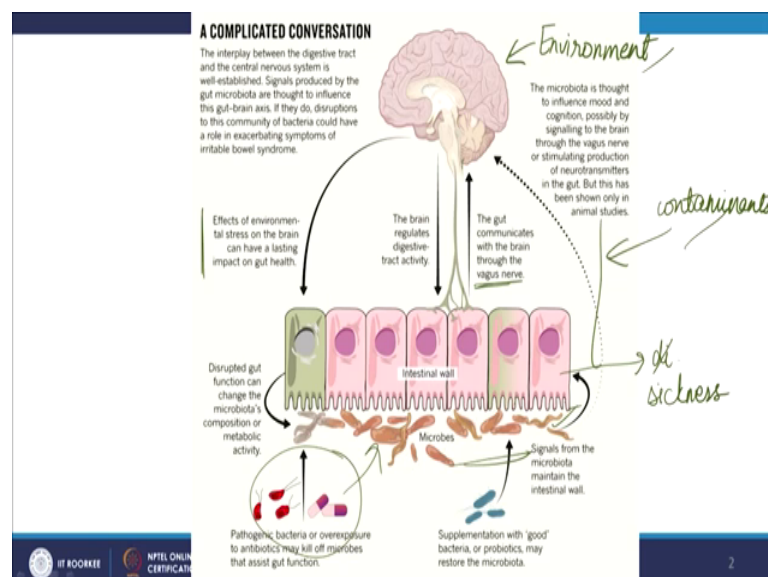
And if you remember one of the examples that I gave you in the one of the previous lectures was when the cow or a ruminant is died of a ruminant is shifted from a grass or hay fair based diet to grain based diet then that results into acidosis because now the microbial community is overtaken by streptococcus bovine; which recur which used to utilizes the starch in the grains and causes acidosis which can be fatal for the ruminant. Similarly we are trying to find out what are the factors that affect our microbial community, also the microbial communities around us how they interact with the

microbial community within us and how that affects our public health and in our personal well being and health.

Now, with that we come to the concept of exposome that I will be talking about today. So, what is exposome if you look at it as spelled as E X P O S O M E S and its pretty much similar sounding as other own omec words such as metagenomes. So, metagenomics or proteomics, metabolomics; so, omics is whenever we talk about the entire um; if you are talking about metagenomics for example, we are talking about all the meta genes that are present in the sample. So, omics means all encompassing; so, when we are talking about exposome there are two words here expose and the other is omse. So, omse means all encompassing and expose it comes from the word exposure.

So, everything that is x we are exposed to our environmental systems and public health systems are exposed to comes under the exposome. So, let us take a look into exposome and I must tell you that exposome the conversation on exposome started in 2005. And by the time we started the conversation about exposomes, we already knew how our gut micro flora affects the way our mind works and the way our mind works affects our gut micro flora.

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And we realized that apart from this particular condition also the microbial community in our environment we already knew that in our environment, in our bodies and everywhere else affects everything else. So, we had already appreciated the importance of microbes

the importance of our exposure to them. And we had started questioning certain practices as indiscriminate utilization of anti antibiotics.

So, if for example, if this intestinal wall is exposed to anti microbials then these microbes will die out which will prevent the proper fermentation of the food as its supposed to be in the hindgut. And that will impact the kind of messages that the gut sends to the brain and the way the brain feels. Also when these microbes have been remove using antimicrobials and the pathogens have a higher chance of surviving where they are no living microbes that wait waiting for to compete.

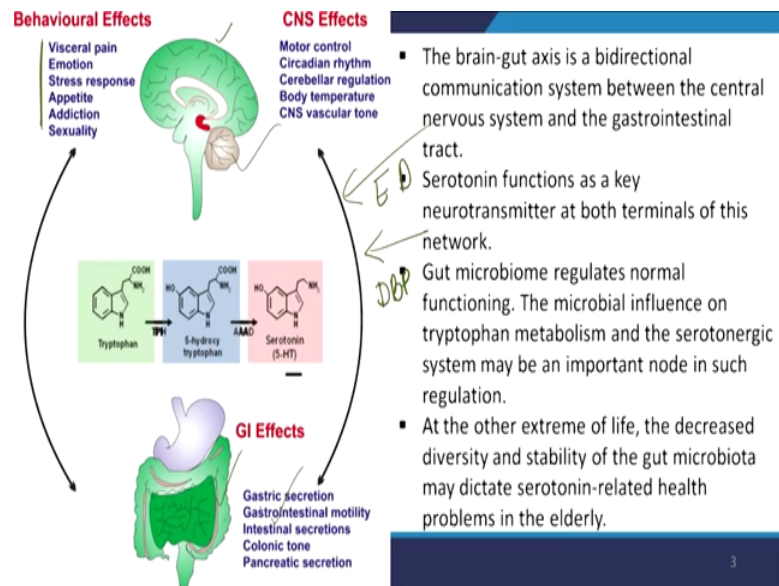
So, let us look here in this particular diagram that I shared in the previous lecture; we talked about the interplay between digestive tract which is are intestinal wall here represented by this. And our central nervous system which includes our neurons and our brain and we talked about how the signals produced by our gut are given to the brain used through this gut brain axis.

So, the gut is communicating will brain through the vegas nerve and the brain is regulating the digestive tract activity. Now note this thing here this thing effect of environmental stress on the brain can have lasting impact on gut health. So, the environment might affect the brain for example, it is too hot, too cold or stressful or lack of sunlight or whatever or the circadian rhythms have are changing or whatever the reasons are that we are we do not know yet or maybe there may be the body is exposed to other contaminants.

So, body is exposed to other contaminants which have stressed the entire body; all of these exposures these environmental conditions, exposure to contaminants which may be chemical, biological or physical in nature will impact the microbial community flourishing within our bodies. And that will impact our gut health in this schematic and will also impact our well being in other respects and when that happens.

Now, our for example, in case of gut health we are more susceptible to diarrhoea and we are more susceptible to sickness in general. And this can be because we do not have the good microbe and it can also be that now pathogenic microbes have a higher chances of infiltrating these places and over popping pop colonizing them.

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The next thing we also talked about in the previous lecture was how the behavior; these are the behavioural effects how they are dependent upon our microbial community and how our behaviour also affects our microbial community? Now what we know is that it is not just our mental state of being, but it is also the environmental state of being. So, what is missing in this picture and has been added since 2005 is the environmental stressors.

So for example now here I am exposing the body to endocrine disruptors or if I am exposing the body to low grade into green disruptors less them out or if I am disposing bodies to disinfection by products; now, in this case the microbial community here the functioning of brain everything will get impacted. So, it is not just if I am being exposed to pathogens or not which decides my susceptibility to develop diarrhoea, but also what else I am being exposed to in the environment how stressed and vulnerable my system is.

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EXPOSOME

- The exposome concept was initiated within epidemiology in 2005 to encompass “the totality of human environmental exposures from conception onwards, complementing the genome” (figure 1)
- The exposome concept calls for providing a description of lifelong (from the prenatal period) exposure history. It was developed to highlight the need for **more comprehensive environmental exposure data**.

Three overlapping domains within the exposome:

- 1) a general external environment (urban–rural environment, climate factors, social capital or education);
- 2) specific external environment (diet, physical activity, tobacco, infection, occupation, etc.);
- 3) internal environment (internal biological factors, such as metabolic factors, gut microbiota, inflammation, oxidative stress or ageing)

Handwritten notes and diagrams on the slide include:

- A diagram showing 'Cause' leading to 'Effect' with 'acute & chronic' written above it.
- A diagram showing a person with arrows pointing to 'Diet', 'X', 'J', and 'X'.

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And this is what brings us to the exposome which is the topic for today’s lecture and the lecture after this. So, the exposome concept as I mentioned was which came in 2005 and this was as a result of public health studies. Now conventionally the public health studies they look for cause and effect; I mean there are many different kinds of studies we can do, but in many epidemiological studies we are trying to figure out the cause and effect for example, in the famous London Cholera case; we wanted to find out what was the source of Cholera that spread the cholera outbreak in London and then we found out it was a hand pump etcetera, etcetera.

So, we want to find out the source now by this time many studies in public health had demonstrated that; it is not always one single soul that makes all the difference; at times the body, the health of the community members is already compromised. And then there is the trigger which allows the pathogen to infiltrate and to colonize the bodies and make them fall sick.

So, when this happened then the when this understanding gathered momentum then in 2005 in a seminal paper scientists started talking about the totality of human environmental exposure from conception onwards complementing that you know. Now if you also mention that when we are talking about this aspect of public health lot of research especially by for example, Doctor Gillian Banfield in US and other similar researchers had showed that the early colonization. So, when the infant is about to be

born that the infant's body is not colonized by microbes, but when the infant is got out in the open in the environment depending on whether it is a c section or normal delivery the child will be differentially colonized by microbes. Now this colonization of microbes and then so, this is microbial exposure and then we might have other things such as chemical exposure.

For example now, we know that there are many flame retardants that break the blood milk barrier and come in the breast milk. So, now, the infant might be exposed to these flame retardant domain based fear of flame retardants which are not good for its health and growth. So, all the exposures starting from not even not just birth, but even conception for example, if the mother was exposed to smoke alcohol or drugs or some other contaminants like flame retardants; then many of them will permeate, will pass through the blood and blood barrier and blood fetal barrier and in damage the fetus or affected.

So, right from the conception what exposures were involved and how they have affected the genome. And the reason why they started talking about this is that before this 2005 seminal paper there was; it was believed by many microbiologist in a environment microbiologist that it is a genes that determine our ability. So, for example, if now people are talking about there should be a gene for alcoholism, a gene for homosexuality, a gene for this, a gene for that.

So, let us say a putative gene for alcoholism and what the research started gathering up by 2005 was its not just the presence or absence of the gene, but a lot about regulation of the gene. There is a lot of things talking about how the environmental exposure complements the genome and this is where the exposome concept came from. What it does is it calls for providing a description of lifelong from prenatal period exposure history. So, right from birth and even birth from conception to this current moment what are the different chemicals you have been exposed to; what are the different kinds of smoke you have been exposed to environmental stressors. So, body accumulates the stress from all of that.

So, there are two kinds of responses or reactions from the body when it is exposed to as antibiotic or high amounts of any concentration or any contaminant one is acute effect the other is chronic effect. So, acute effect will happen on a short term range for

example, if I am exposed to mustard gas high amount of it an acute effect would be fatality; however, if I am exposed to trace amount of mustard gas very little not enough to kill me and maybe the explosion happens once or twice here and there nothing happens on (Refer Time: 12:05) cool nothing happened for 1 day for 1 week for 1 month one year 10 years, but then by the time the 10 years have passed it was quite possible that that minute exposure to mustard gas 10 years ago started causing changes in my genes which over time have had a cascading effect and now, I am developing diseases and cancer.

For example, cancer that are now lethal to me. So, we can have both acute and chronic effect as I mentioned earlier the public health studies were often designed to be pro acute conditions because they want to find out cause and effect. So, ideally we have a cause and it is causing an effect. So, we have a pathogen or we have an environmental problem for example, a particular kind of fungus is growing in the sludge. So, we are having a particular effect right of protozoa is increasing in the sludge.

So, again noticing these problems with every sludge. So, these a cause and effect relationship investigations work really well if the time lag between cause and effect is not significant. So, time if it is small if the effect is acute on an acute scale that is a small time scale, then it is then this these studies are possible, but many a times the cause is so, remote in time it has happened in such distant past that we are looking for the nearby causes cause 1 is this caused is this the cause is cause 3 the cause.

And none of them are singular causes, but a cause that happened very past and past might be and that is the reason why people are talking about since conception till until. Now, but as you can imagine these studies are very difficult to do and this is where our environmental microbiology comes into picture because for example; let us say I have a human being here and this human being is eats something which is not good for his or her or drinks water with laden with hepatitis a and e and gets to on this.

There is another person who does not get drunk this is what determines the susceptibility of person to get jaundice and not get jaundice. Now the in this case we want to look at the exposure to all microbes and exposure to all chemicals and all physical conditions and emotional condition conditions and social etcetera, etcetera conditions; all of them which come under exposome that make one person more susceptible to hepatitis a or e

infection and the other person not so, susceptible. So, if we can figure out this what causes a person to be susceptible to an allergy to chronic condition or even to infections; then we can figure out novel ways of treating our patients and also taking care of our environment.

So, let us look into it in order to understand our exposome we need to understand have information on three different domains. The first is your general external environment for example, you need to have general information about external environment for example, is this person from which developing country or developed country, are these people from rural area or urban area, what kind of occupation they do, what kind of climate they live in do they live in hilly; terrain, do they live in hot tropical climate places, what is their social status, what is their economic status, what is the educational status? So, we need to know the big things.

Now we know that the mind affects the gut mind affects the microbial community and well being of the gut. So, we also know that social factors emotional factors education etcetera would affect the microbial community in the body. Next thing we want to know very specific external environment tell cues for example, we want to know what is there any difference in their diet in the physical activity you consumption of tobacco or did they have any prior infection.

For example, this particular person whose susceptible to getting hepatitis a or e after drinking contaminated water that is developing jaundice like symptoms after double drinking contaminated water. Then maybe this person already had certain amount of liver damage or had some certain amount of compromised in the immune system. And whereas, the other person did not and that is what this person had symptoms of liver and liver damage and the other person did not.

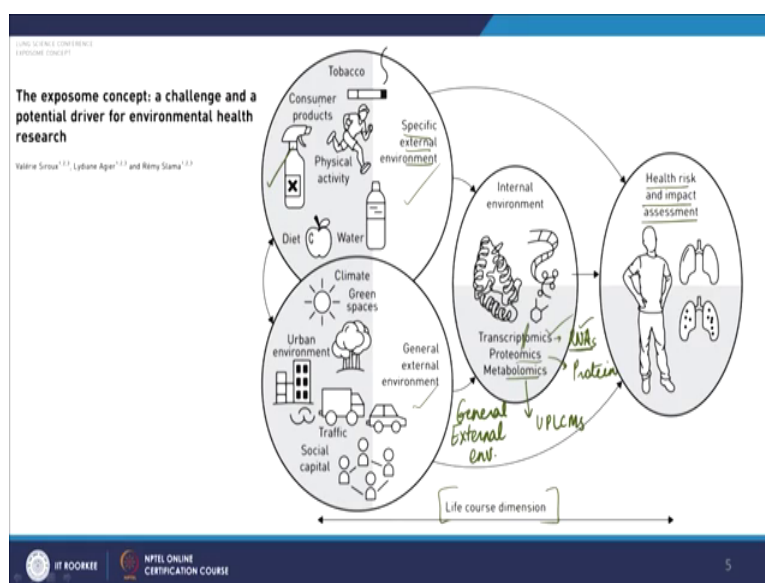
So, we would now we want to find out very specific external conditions such as prior infection, tobacco, physical activity, occupation. Now the next thing you want to understand is; so, we have figured out the external environment the general and the specific. Next thing you want to understand is your internal environment for example, what are the metabolic factors in your body, what is the what are the different characteristics of the your serum, your blood, your microbial communities, the juices in your body. What is your gut micro bio flora and what we are finding out that the gut

microbial flora effects not only gut related diseases and allergies and chronic conditions, but also has impact on the entire health.

So, we also want to see the degree of inflammation in the body apparently when body suffers from high inflammation; it is more susceptible to certain diseases. Similarly with oxidative stress and aging; we already know that elderly population are more susceptible to infectious diseases; so, maybe this person whose susceptible is basically elder.

So, you will not to understand or maybe it is the same age as the other person, but the body has aged much more in this case and in this case because of some specific or a general external environmental or internal environmental conditions. So, once we have figured out all these three; only then we can go and start identifying putative causes. And then we get more data, we can perhaps gather evidence in favour that this cause seems very likely.

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So, we noticed here that the exposome takes care of your external environment; so, this is your external environment and this is your general external environment. So, it is very general what kind of place you live in what is its demography, its economy, social life and what is your urban environment. And then we talk about specific external environment; so, what is a specific external environment of the person and then we look at the internal environment of the person; we can do right now we are doing three

different analyses for internal environment. One is the transcriptome if you remember; so, omics means all transcriptome transcriptome comes from transcription.

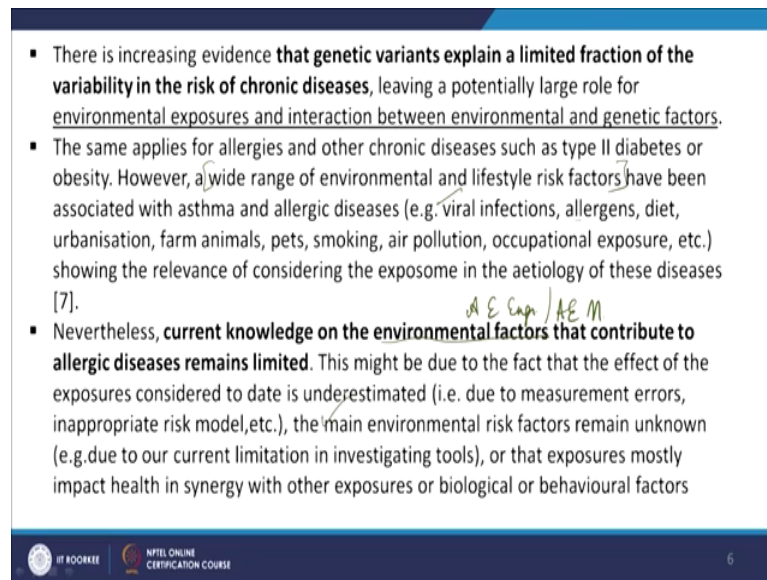
So, all RNS's in the body of the person or in the gut micro biome of the person are sequenced. So, we understand what genes of the body are being transcribed and then we look at the proteomics. So, we are looking at post translation; so, you want to know all the protein structure that are present in the gut micro biome or in the body and then we do it with work at metabolomics which looks at all metabolites typically done through liquid chromatography and mass spectrophotometry.

And nowadays we apply UPLCMS at times UPLCMS MS folding metabolomics; now this is your understanding of the internal environment. Using data from the general external environment specific in external environment, very specific internal environment over the life course in under the dimension of life course we understand better now the health risk and impact assessment.

What is this person likely to get as a disease now here I am talking about personal, but we can also isolate what are the specific external environmental cues or general external environmental cues or internal environmental cues which result in a particular disease. And what is the probability we will get a disease if we are using this consumer product versus another consumer products.

So, this exposome studies are very useful for risk assessment and health impact assessment alrighty.

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▪ There is increasing evidence **that genetic variants explain a limited fraction of the variability in the risk of chronic diseases**, leaving a potentially large role for environmental exposures and interaction between environmental and genetic factors.

▪ The same applies for allergies and other chronic diseases such as type II diabetes or obesity. However, a wide range of environmental and lifestyle risk factors have been associated with asthma and allergic diseases (e.g. viral infections, allergens, diet, urbanisation, farm animals, pets, smoking, air pollution, occupational exposure, etc.) showing the relevance of considering the exposome in the aetiology of these diseases [7].

▪ Nevertheless, **current knowledge on the environmental factors that contribute to allergic diseases remains limited**. This might be due to the fact that the effect of the exposures considered to date is underestimated (i.e. due to measurement errors, inappropriate risk model, etc.), the main environmental risk factors remain unknown (e.g. due to our current limitation in investigating tools), or that exposures mostly impact health in synergy with other exposures or biological or behavioural factors.

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Now, why we need them just study a revision of that we have we know this now that the genetic variants only explain a small fraction of the diseases that you are noticing specially in chronic diseases, allergies and other diseases such as type two diabetes and obesity.

We know that it is mostly your wide range of environmental and lifestyle risk factors that contribute to triggering these genetic factors. Especially in case of even viral infections, allergens, diet, urbanization all these affect the probability of getting asthma and other allergies; however, we would have very limited knowledge on the environmental factors that contribute to allergic diseases.

We know that there is a difference, but we there is an (Refer Time: 20:39), but we do not know which environmental factors have how much effect and this is where as applied environmental engineer, you come into the picture or applied environmental microbiologist; however, you want to call yourself. You come into this picture and you try to understand what are the environmental cues environmental factors that affect our microbial community such that we are more susceptible to a particular disease to the chronic or acute and in doing this kind of study is actually this is quite a hot research topic right.

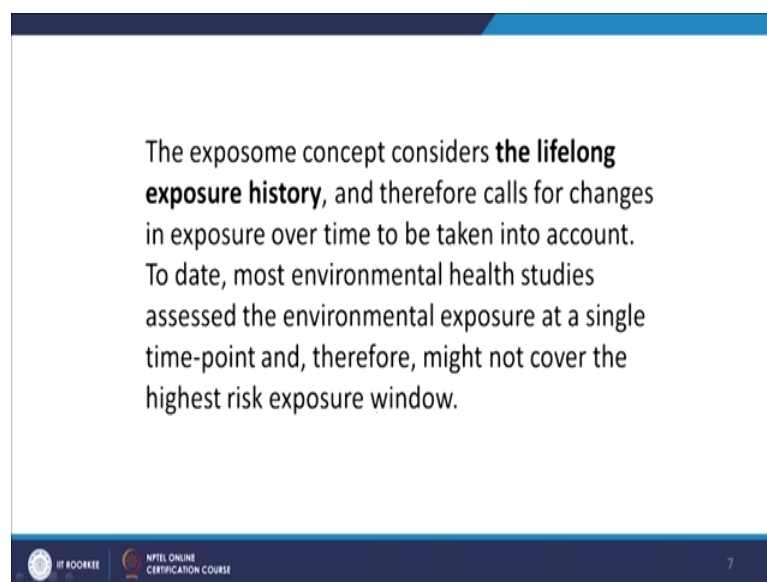
Now again for students who are interested in research please look up exposome and this week's homework we have lot of questions about exposome and I hope that will make it

more clear when you are trying to answer the assignment in this week alright. And why do we not know about environmental factors a because this understanding is a recent development. The other thing is the main environmental risk factors are unknown still because we do not have investigating tools to identify them to understand them. And the other is that environmental exposure is time varies with time, we do not have history of the person it is very hard for us to develop the history of the person.

Now, to catch back the history of the person who is sick now or healthy now what we can do is we can take babies like what did Doctor Gillian Banfield did was. In her one of her studies she took she had understood the microbial communities on skin and in the gut of children right before right after when they are born.

And then noticed it over period of time; so, how the microbes in our environment and in the mothers body colonized the infant and how that affected the health of the infant? So, these kinds of studies are exposome studies and the important thing is that they consider the lifelong exposure history. And therefore, they want to notice how changing a change in exposure over time will affect your health; I will give a very simple example.

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We live in India and in India air pollution is one of the largest killers it is; some reports say it is the fourth largest gathering in our country. Now most of these reports are based on direct impact of air pollution. For example, if I am living in a very polluted city for example, Delhi and do especially during it is highly polluted times, then it is likely that

my asthma might get worse I might develop long irritation and finally, lung cancer and then I die.

And then people say air pollution one more person dead; now these are it is very easy to observe them, but I live in Roorkee. So, in Roorkee when I am being exposed to a not hazardous levels of air pollutants, but still considerable amount of air pollutants over the course of my life. Now, I might be more susceptible to certain other infections for example, pneumonia or other viral bacterial infections that people exposed to the contaminants that I am being exposed to at a small concentration are susceptible to get.

Now this kind of, now if I were to die in few years from those diseases then we will not label air pollution as a reason, but we would call that the immediate cause which could be a certain kind of cancer or which could be a certain kind of bacterial or viral disease as the cause of death. And thus the amount of deaths due to air pollution are underestimated.

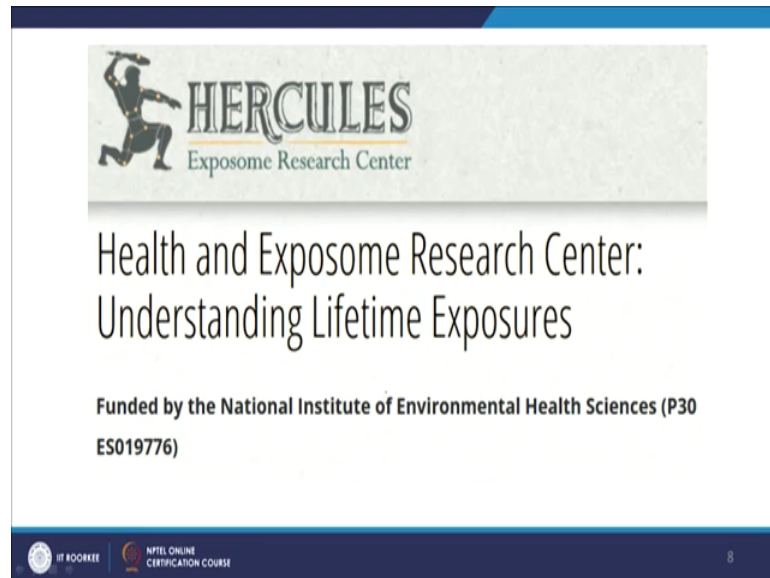
Now in this case if we know the chronic exposure history of the patient the person whose dead recently and we know that what is unique about this person this person lived in a Roorkee town high; highly populated town and was exposed to this amount of these contaminants, which people and then they can do a nice study cohort study or case study and figure out whether what contribution it was of the air pollution I was exposed to on a daily basis that resulted in particular disease.

So, this is where the exposome comes into picture; now another strain with the air pollution another thing is many of our working class members now spend more time indoors then they spend outside. Most of the middle class families and also upper class families when we talk about economic classes and that most of our countrymen now spend more time indoors then they would spend a few years earlier when we were largely rural economy. Now when we are spending time indoors, we are being exposed to volatile organic compounds and other contaminants that are found mostly inside the house and not outside. Now in this case our bodies have are exposed to different contaminants than the person who sits most of his time outdoors are not exposed to the contaminants in the air.

So, now, I might develop some disease because I spend more time indoors; they do not have a very good correlation with the contaminants found in the local Roorkee air. But if

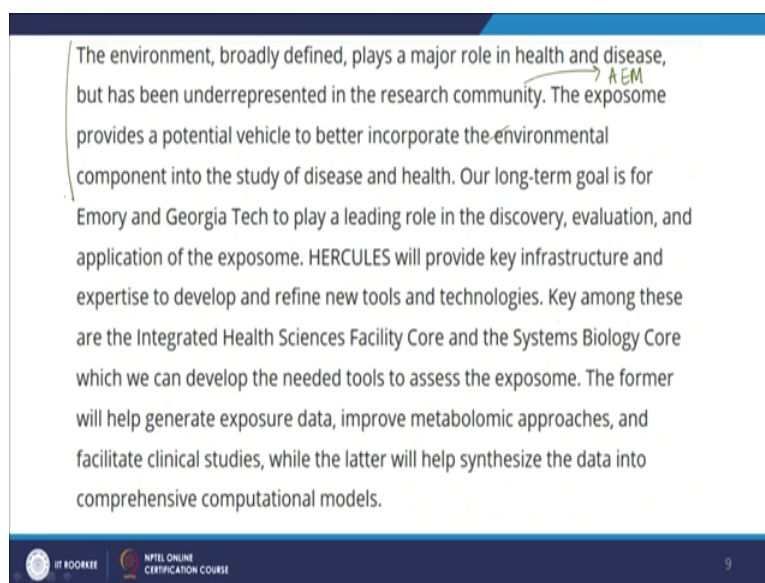
I look at my personal exposome then you will know oh god we develop this disease because of x y z exposure. This is again where the life line is lifelong exposure history, it is very important rule. So, let us read this to date most environmental health studies assess the environmental exposure at a single time point and therefore, did not cover or may not have covered the highest risk exposure window.

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So, now there are some really big research centers that are working on um; there are working to gather data on exposome. One of them is the HERCULES exposome research center and they are funded by NIEHS; National Institute of Environmental Health Sciences.

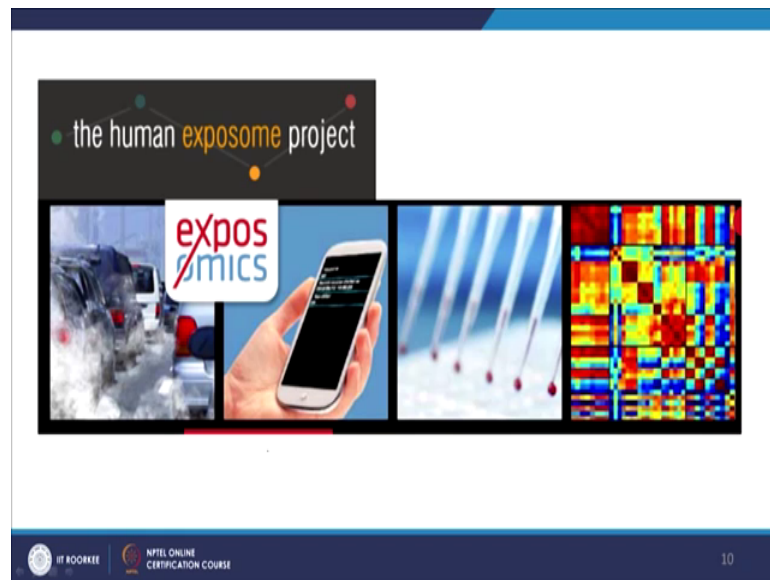
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And look at what they have written for the environmental exposome; the environment broadly defined there is a major role in health and disease, but has been underrepresented in research community. Dear students this is again where it is very important for us to understand applied environmental microbiology right. And this is also the scope of this particular subject that we are studying. Now the exposome provides a potential vehicle to better incorporate the environmental component into study of disease and health.

Once you understand our environment better; once we understand the environmental exposure better we will be able to explain why people are developing a particular disease having specific health challenges. Our long term goal is for every the place where they have the center in U S Atlanta, our goal is to play a leading role in discovery evaluation and application of exposome and now they have other kind of information about their center, but these first two lines are very very important for you to understand.

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Next there is this human exposome project which collects all data on human exposome and summarizes on their website. And then there is an expose omics, they are doing some very good research and water pollution, air pollution in biostatistics and in omics.

So, let us look at that; so, when it comes to air pollution they are finding out that we need to understand what is a person's personal level of exposure to different contaminants. And if you look at this particular figure and this is from one of their studies where in their backpack they had a bespoke crack inside this backpack that held sensors and batteries.

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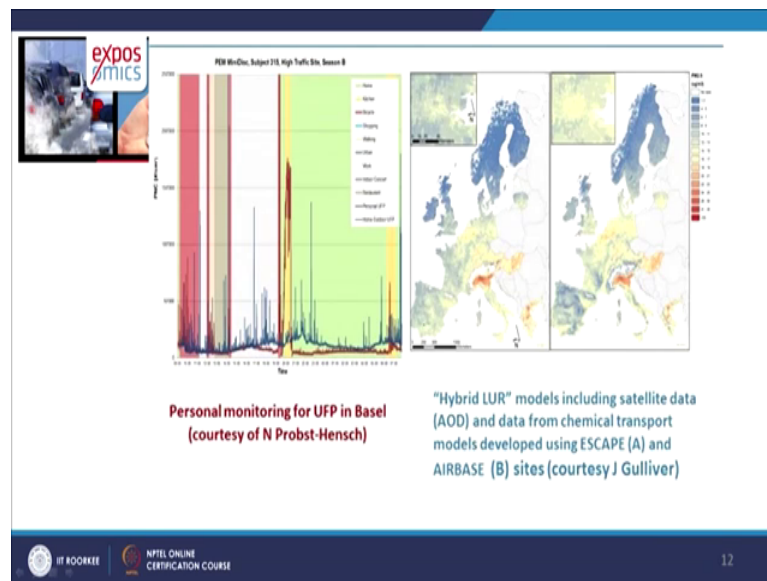
Now these sensors send different kinds of contaminants; this sends what were they there was battery for supporting the sensor; there was a pump, but PM 2.5 pump based on cyclone movement. What it would do is it was collecting here and measuring real time amount of PM 2.5, there was a UFP DISCmini which measured other kinds of contaminants; kept the information stored into SD card.

So, this information was available; it was shared to shared with the researchers. Now there was also separate the candidates who were carrying this backpack. So, people were supposed to carry this backpack wherever they went throughout the day. For example, I do not sit in this room for entire day or every day even, but I go to different departments, different places, I also take a walk around the campus, I go to market. So, as a typical person you also have a lifestyle and you do not stay confined within a room.

So, wherever you go you are being exposed to the contaminants present in that particular environment; that is the importance of why we use backpack for storing our sensor in collecting real time data. Now the person is also given a GPS and accelerometer for fine locating the person when person was in market; the person was exposed to these contaminants, when person who was in this room this contaminant accelerometer also helps us understand the velocity and this correct to validate the data that we are getting from GPS.

Now this data is again shared to the software; the best book software together this data is sent to the process data. Now when they did this study, they found out that of them that they found out that the exposure for different kinds of lifestyle is distinct and also when the exposure changes the contaminate contaminant, the effect of contaminant on health also changes.

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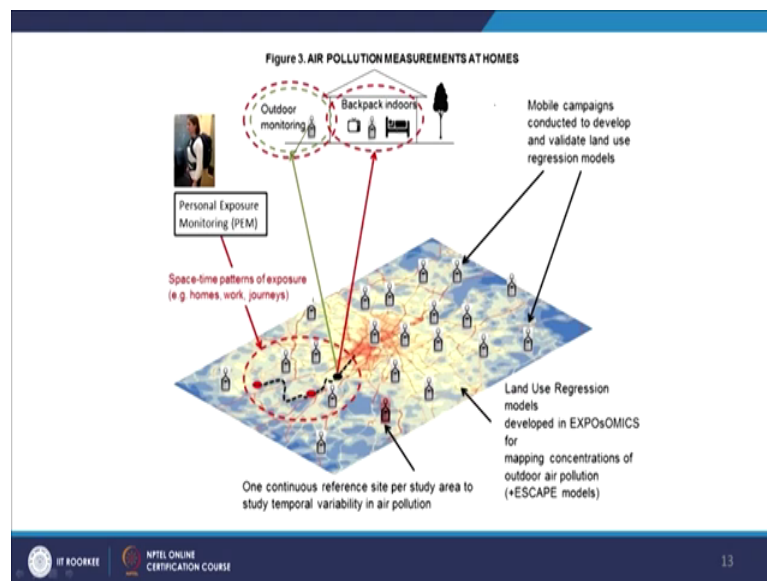


Now, this is based on personal monitoring now what they did was do a collected data based on personal monitoring. Over time how different kinds of people had different kinds of exposure and now they also have satellite data. So, this is satellite data usually will capture your outdoor data. So, what they did was in this study exposed omics people; they tried linking that if we have this amount of PM 2.5 here PM 2.5 is very low in this kind of (Refer Time: 29:56) countries north of Ireland, Scotland and England.

Now in this countries where the in this regions where PM 2.5 is very low let us find out what the person of exposure is. So, satellite data is easier to get personal exposure studies are hard to do more expensive more they were not capital intensive. So, if I know for example, this region has higher exposure to PM 2.5; what about people who are caring about their lives here. So, basically what I am trying to understand that how does the ambient air quality affect the exposome; not only when the person is spending time outdoors, but also when the person is spending time indoor because eventually the air will find a way to seep in.

Now, this is a very nice interesting ongoing study and I encourage you to follow exposomics and understand about the latest research that they are doing. Now what they look here these are the air pollution measurements at home, when the backpack when the outdoor monitoring was done. So, the outdoor monitoring gives is given to you by satellite and the backpack indoors is basically the person very person sleeping the person who put backpack right, there the person will move around the house maybe go out catch a bus.

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Again endure and then go to office and come back. So, when they compare this in the same location; I have some information from the satellite, I also have information on when I am doing personal exposure monitoring; I know the space time space time pattern of exposure. For example, person is journey, person is at home at work and when I do this what I am getting is they developed a very nice model a land use regression model for exposomics which map the concentration of outdoor air pollution.

Now, currently they are trying to link all of this and hopefully we will get very meaningful data on how the exposome varies when made air quality varies and how that effects would affect the public health. So, dear students this is all for today in the next lecture we will go ahead and talk more about exposomes and how they affect our health and what are the latest frontiers in research?

Thank you very much.