Chemical Process Safety
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Lecture 6
Toxicology
Introduction, Routes and Exposure

Welcome to the toxicological studies module and toxicology is one of the most dangerous thing in the process industries apart from fire and explosion. Now it is not only possess the immediate danger but sometimes its affects you may observe in due course of time or even in the later part of your life. So in this particular module we will deal with what is toxicity, what is toxin and how we can go ahead with the toxicological studies? What are the different routes through which any toxicant can enter your biological system? What are the exposure symptoms, et cetera.

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Now, this as per the United Nation organization report published in year 2016-17 almost 8.3 percent of all deaths are attributed to the environmental exposure. These exposures are attributed to the selected chemicals each year and remember do not forget the Bhopal Gas Tragedy, it is because of one of the most toxic substance Methyl isocyanate. Now major contributors to this toxicological aspect are indoor smoke from solid fuel used, outdoor air pollution and second-hand smoke, followed by the occupational particulates, chemicals involved the acute poisoning and pesticides involved in self-poisoning.

Now remember, whenever we talk about the pesticides they are intermediate during the production and even raw material causes a severe problem.

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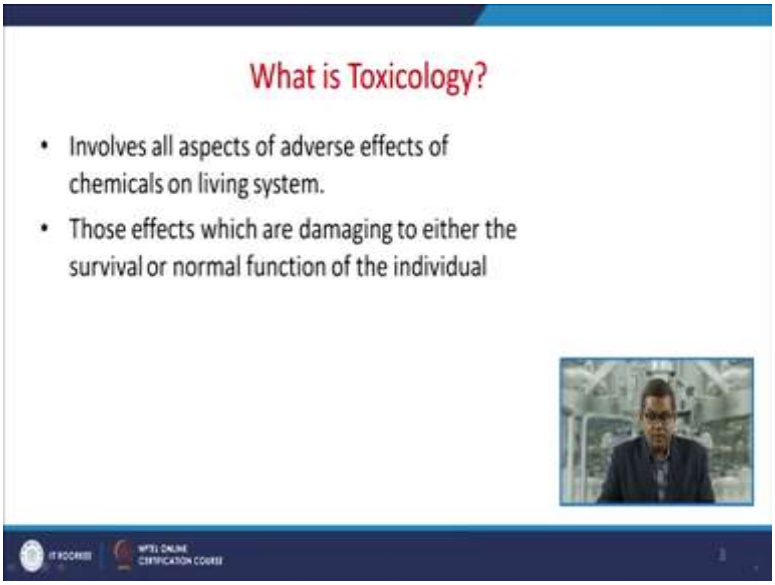

Now, question arises what is toxicology? This involves all aspect of adverse effect with the chemicals on the living system. Those effects which are damaging to either the survival or normal function of individual, so this is toxicology. So whenever we study the toxicology then question arises what is toxicity?

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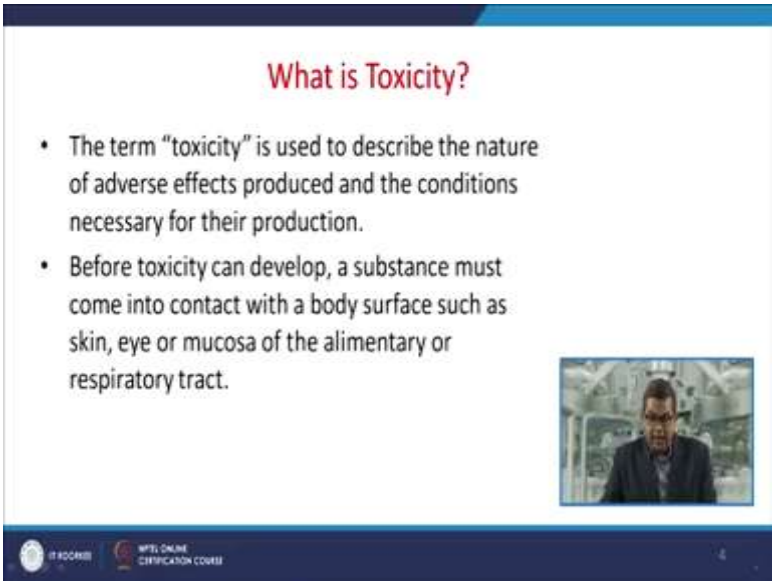

So, the term toxicity is used to describe the nature of adverse effect produced and the conditions necessary for their production. So remember we will consider the process as well

as end use. Now before toxicity can develop a substance must come into contact with a body surface such as skin, eye, mucosa or any other alimentary or respiratory tract. So in this particular chapter we are going to deal with all these aspects.

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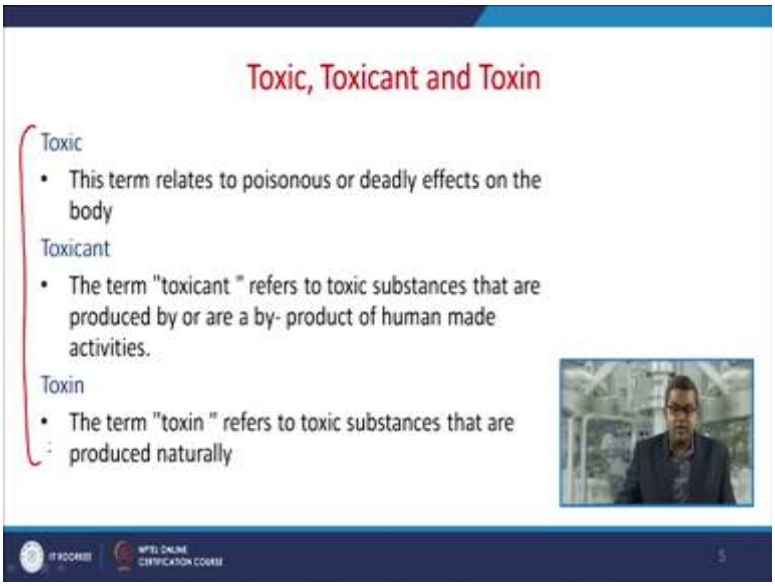

Now, before we go ahead, let us understand that what is toxic, toxicant and toxin. Now toxic substance they are available in two forms, one is the nature oriented and second is the man made toxicants. So toxic, this term relates the poisonous or deadly effect on the body. Now toxicant, this term toxicant refers to the toxic substance that are produced by or are by a by-product of human made activities. Now the term toxin refers to the toxic substance that are produced naturally. So you can clear cut remark it the three different aspect of toxicity.

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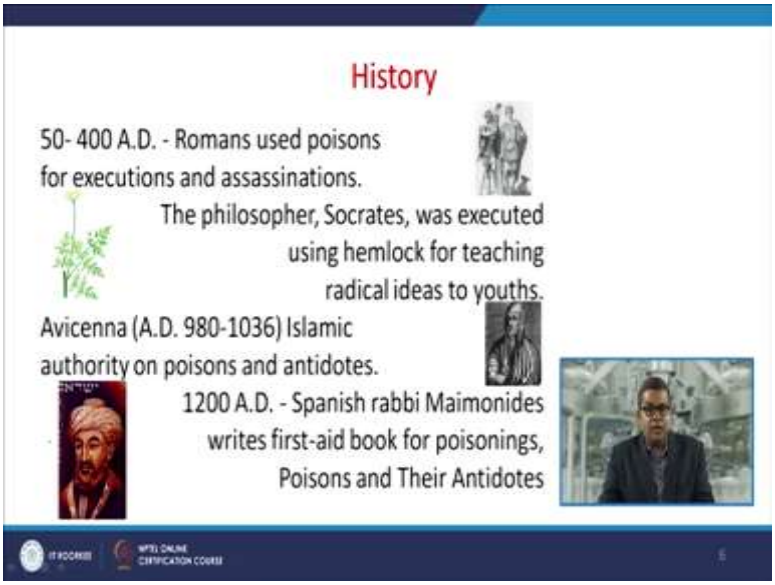

Now, if we consider the history of toxicity or toxicological studies; in between 50 to 400 AD roman used to poison for execution and assassination of their enemies. The philosopher, Socrates, was executed using the hemlock for teaching radical ideas to youths. Avicenna between 980 to 1036 AD Islamic authority on poison and antidotes. 1200 AD is Spanish rabbi Maimonides writes first-aid book for poison and poison and their antidotes because whenever we talk about the poison, whenever we talk about the toxicity, whenever we talk about the toxin then definitely must think about their remedial measures.

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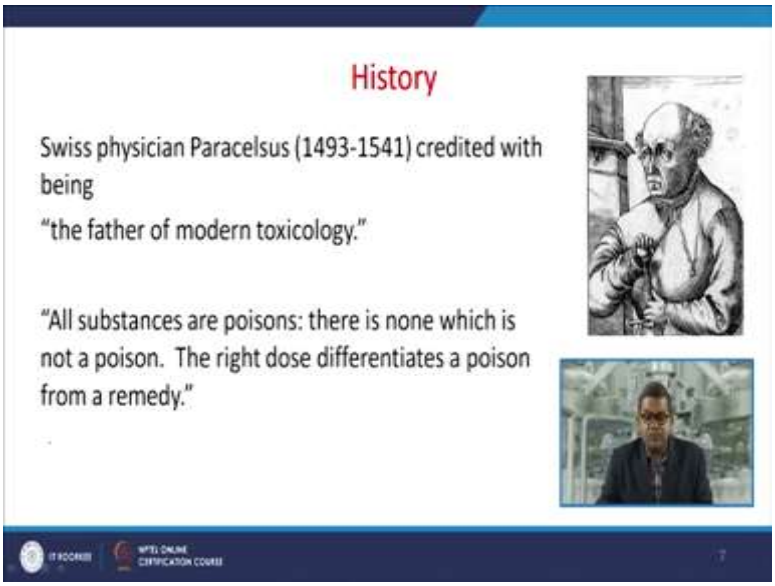

Now, Swiss physician Paracelsus in 1493 to 1541 credited with the being "the father of modern toxicology" because it is a science rather than the poison, it is a science. So all

substances are poison it is his verdict, there is none which is not poison. The right dose differentiate a poison from a remedy. Even water may become fatal if you take the access dose of water definitely it may become fatal and sometimes it may create a further problem.

So that is why all substances are poison and you have to find out that what is the actual dose which is required for the body system and if you take the access dose then definitely it may create a problem to your body structure as well as environment.

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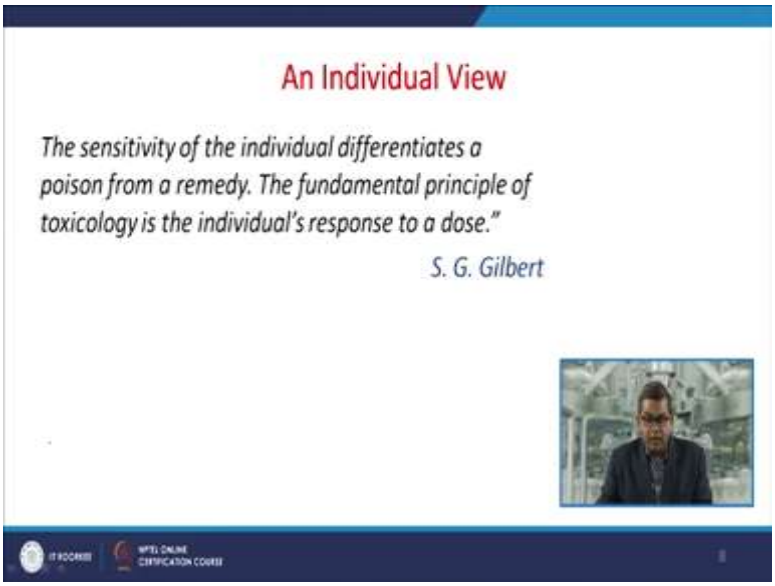

I would like to quote an individual view by S G Gilbert; the sensitivity of the individual differentiates a poison from a remedy. The fundamental principle of toxicology is the individual's response to a dose. Now remember whenever we talk about the individual's response that discovers the age, atmospheric condition, sex, et cetera because sometimes if you are young then you may overcome any kind of toxic exposure, but if you are a kid or if you are little bit older then definitely you may be over exposed to those kind of dose and if you go to the doctor then definitely based on these parameters they decide the actual dose of any medicine.

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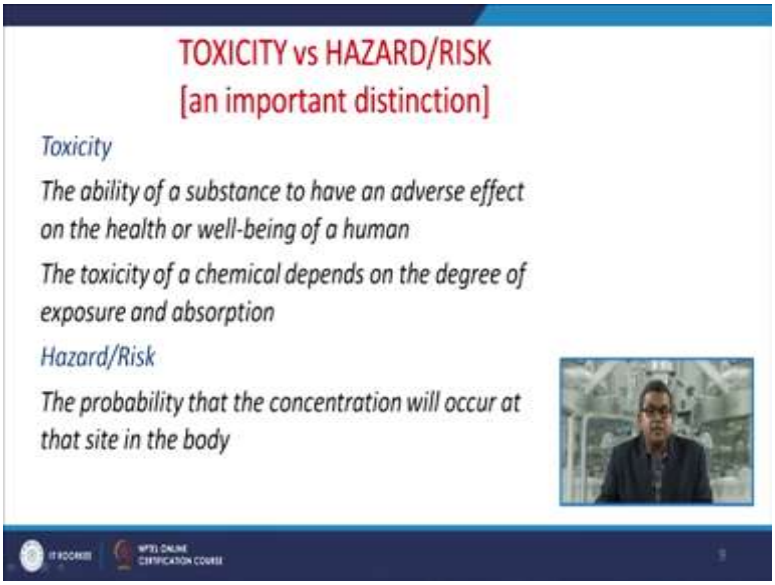

Now, there is hairline difference between the toxicity, and hazard. The toxicity; the ability of a substance to have an adverse effect on the health or well-being of human. The toxicity of a chemical depends on the degree of exposure and absorption. However, the hazard is the probability, hazard/ Risk is the probability that a concentration will occur at the site in the body. So you need to find out that whenever you got an exposure with the toxic substance, what is the route and at which point of time and at what point of time it is going to affect your body? And what is the target organ which is being affected? So in this particular chapter, in this particular module we will discuss all these things.

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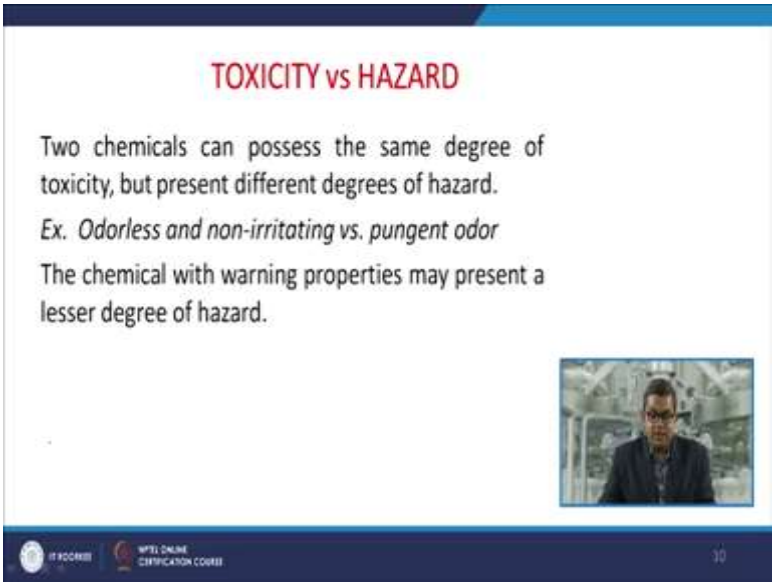

The two chemicals can possess the same degree of toxicity, but present in different degrees of hazard. It also attributes several other parameters like your age, weight, physical conditions, etc. The best example is odorless and non-irritating versus pungent odor. Remember nature gave you a beautiful things to determine that which one is correct and which one is not correct? So chemical with the warning properties may present the lesser degree of hazard.

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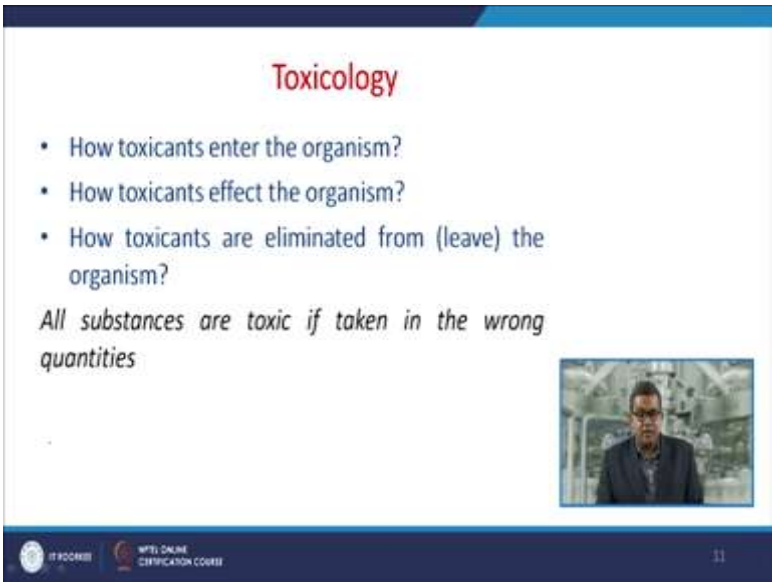

Now, when we go ahead with the systematic study of toxicology, we must know that how these toxicants can enter into the biological system means your human body or animal body et cetera or to the environment? Then second question must be asked that how these toxicants cam affect the organism? Means whenever you are under the contamination of those toxicants then how these can affect your body system?

Now, once these two questions are answered then you must answer the things that how toxicants can be eliminate from your body system or they can leave from your body system? Now all substances, remember again; all substances are toxic if taken in a wrong quantities. So you must know that what is the dose and what is the actual response for that particular dose?

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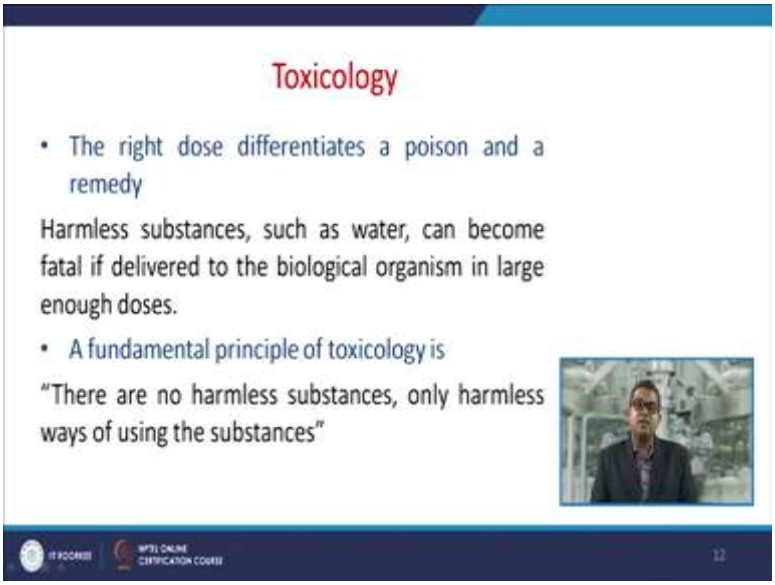

So based on these particular aspects the right dose differentiates a poison and a remedy. It is just like that whenever we got the vaccination then a limited quantity or required quantity of that particular virus being injected into our body system. So the harmless substance such as water even becomes the fatal if delivered to the biological organ in a large kind of doses which is not required to your body system.

So the fundamental principle of toxicologies is; there are no harmless substance, only the harmless ways of using the substance.

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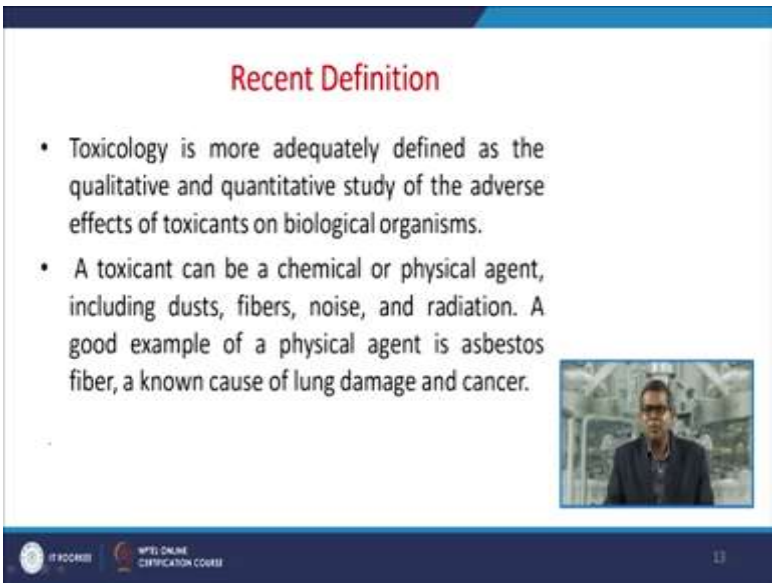

Now, based on all these discussion the people have predicted the most advance definition for the toxicology. Now toxicology is more adequately defined as the quantitative and quantitative study of adverse effect of toxicant on biological system. So a toxicant can be a chemical or a physical agent, including dust, fiber, noise, radiation, etc. A good example of physical agent is the asbestos fiber a known cause of lung damage and cancer.

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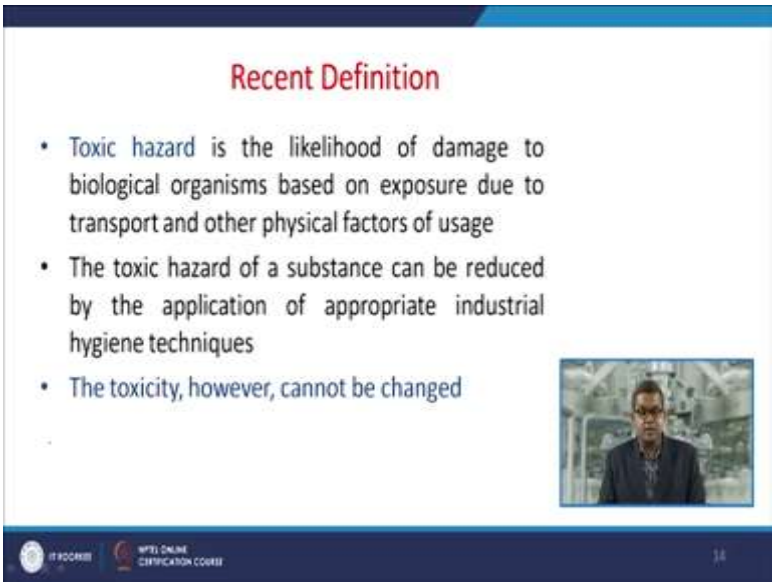

So government is now thinking to ban all kind of asbestos fiber, previously it is used as asbestos sheet for roofing or panelling. Now toxic hazard is the likelihood or damage to the biological system based on exposure due to the transport and other physical factor of usage. The toxic hazard of a substance can be reduced by the application of appropriate industrial hygiene technique.

So, you must create a barrier between yourself and exposure of toxic substance, but the toxicity of particular substance cannot be changed under any circumstances. So you cannot change the toxicity of methyl isocyanate, you cannot change the toxicity of arsenic. The only thing is that you must know that what is the barrier and what is the threshold limit for the intake for MIC to intake the body system.

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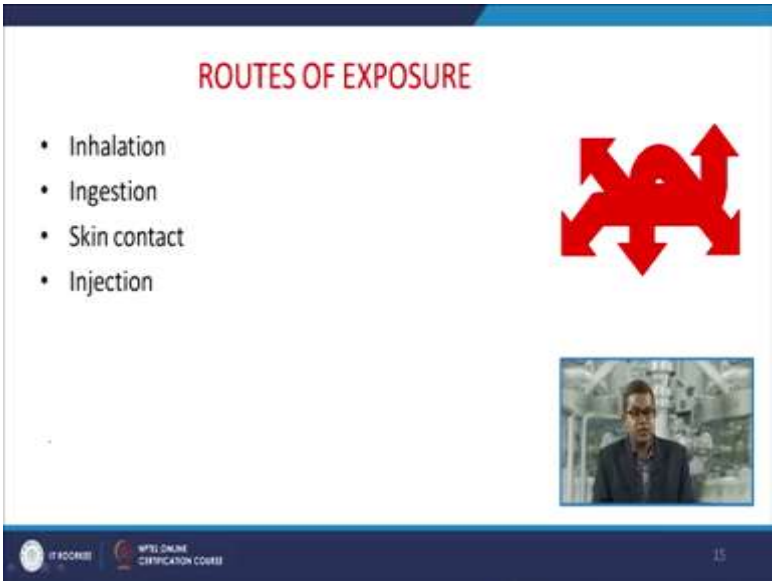

Now, there are basically 4 routes of exposure for any toxicant entry into a biological system. One is inhalation, ingestion, skin contact, and injection. Now these are the 4 prominent routes through which anything can enter into your body system.

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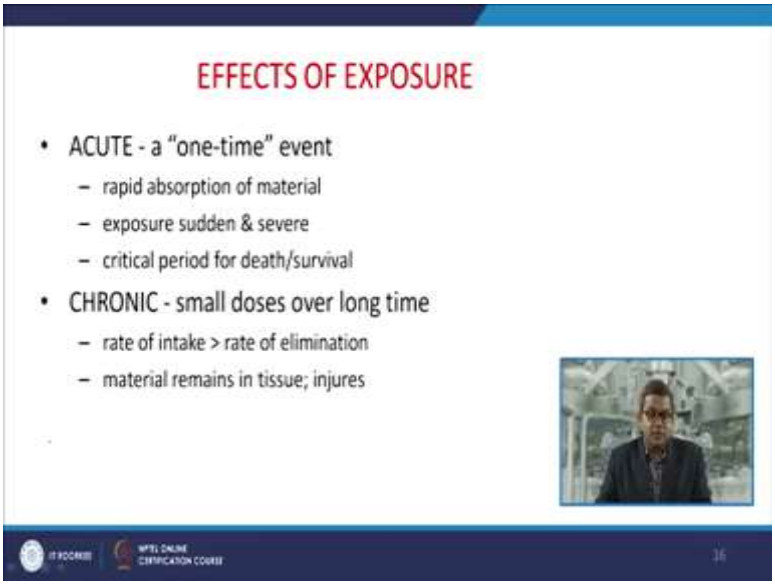

Now, before we go into the detail that how injection, how inhalation creates a problem we must know several other factors like acute that is the effect of exposure, the acute a one-time event that is the rapid absorption of a material and sometimes it may cross the threshold limit values, the exposure sudden and severe, the critical period for death or survival. Similarly the chronic that is a small doses versus over a long time sometimes if you are working in a workplace and where the small quantity of toxic substance being released then you may get a

very small doses, those doses of toxicant may accumulated within your body system and the effect may appear after a long time, so sometimes suppose you are working for a year or two and you are continuously bring exposed to that particular toxic and that may create a chronic problem.

So it all depends on the rate of intake, the rate of elimination it is both things are all together substitute to each other, the material remain in the tissue, injures like if the material remain in the tissue that may get deposited into the fatty tissues and when you become progressive and you are become older then all those fatty tissues may decomposed and the effect of that particular component or toxic substance may be prominent.

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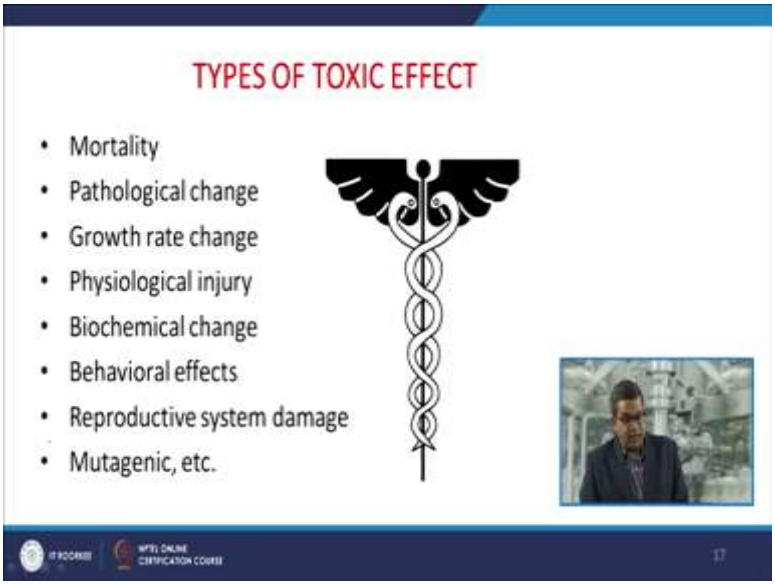

Now, there are various type of toxic effects like mortality, pathological changes, sometimes the growth rate changes, physiological injury, the biochemical change, behavioural effect, sometimes reproductive system may get damage and there are mutagenic changes. So you must know that what kind of effect is going to take place within your body system by the exposure of any toxic substance.

Now, sometimes these toxicity or toxic effects are govern by the target organ. So you must know because sometimes if you inhale something first it goes to your upper or lower respiratory tract and then it may go into your lungs and if you sometimes if you take or if you things or any toxic substance through a dermal absorption then the target organ maybe little bit different. So you must know that which of the organ is going to be affected by any toxic substance which you are going to take.

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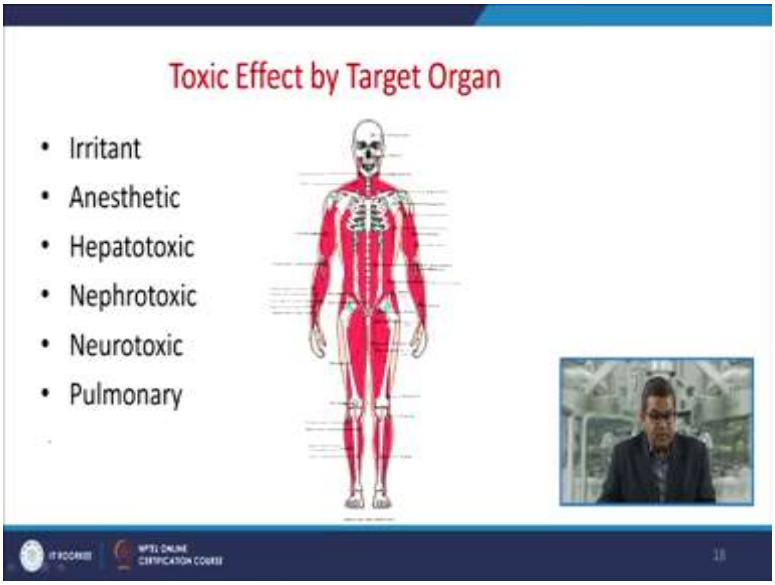

Now, these are the things which are important in this particular thing irritant sometimes suppose if you are exposed to the chlorine environment then first prima facie you may experience the irritation, then anesthetic, the hepatotoxic, nephrotoxic, neurotoxic and sometimes pulmonary so you must identify the target organ.

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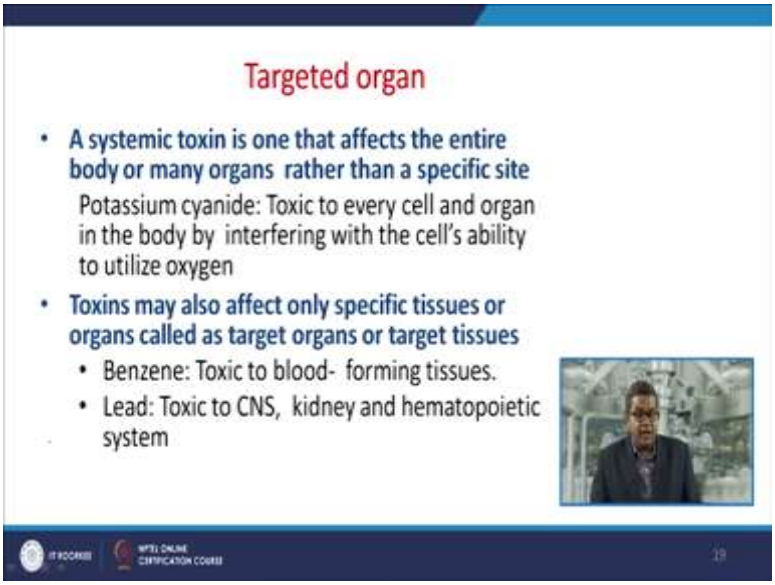

Now, target organ that is a systematic toxin is one that affects the entire body or many organs rather than a specific site. Like potassium cyanide, toxic to every cell and organ in the body by interfering with the cells ability to utilize oxygen. The same happened in the Bhopal Gas Tragedy. The toxin may affect also affect only to specific tissues or organs they are called the target organ or the target tissues like; Benzene toxic to blood forming tissues, Lead toxic to

CNS, kidney, hematopoietic systems. So you must know that which kind of toxin and which kind of toxic substance is there.

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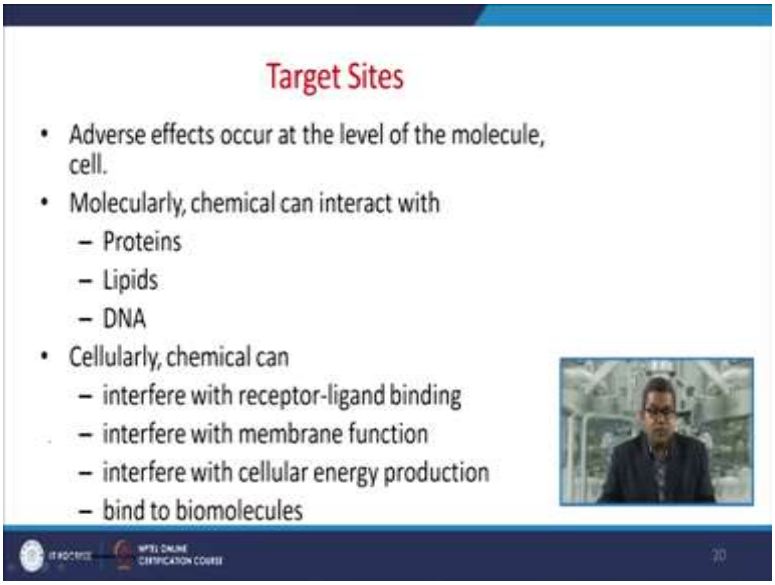

The adverse effects occur at the level of molecular cell. The molecularly, chemical can interact with the proteins, lipid, DNA. Cellularly, chemicals they can be effected by interfere with the receptor ligand bindings, interfere with the membrane function, interfere with the cellular energy production, bind to the biomolecules. Remember all four factors they play a very vital role when you study the toxicological effect for the later part of life.

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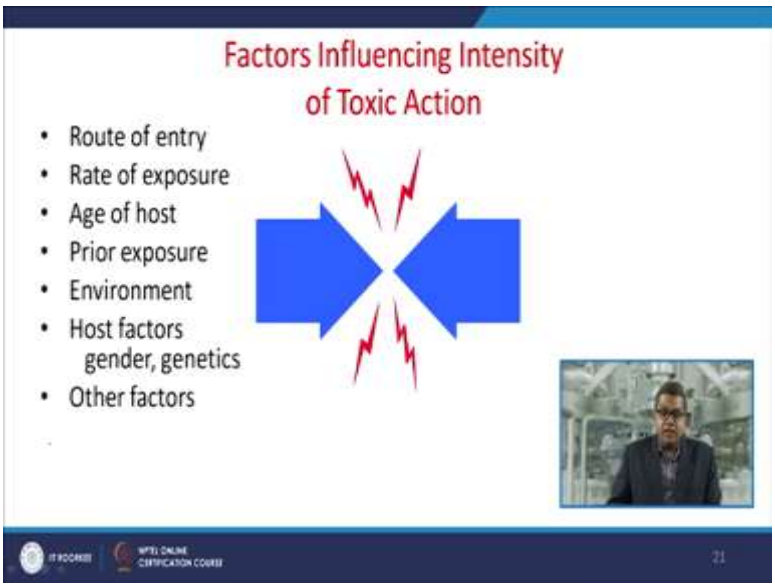

Now, there are various factors influencing the intensity of toxic action. Usually they depend on route of entry if it is being inhaled by your nose then definitely at what part is going to effect, then the rate of exposure sometimes acute, sometimes chronic, sometimes the concentration of toxic is on the higher side then you may get exposed more spontaneously, then age of your body system. Suppose if I am young my physic is good then there is a prominent production of different fatty tissues within my body system then I may be in a position to retaliate all those toxic exposure so it all depend on age of host and suppose a person is old then definitely because of lesser number of excretion routes he or she may be get exposed on a dangerous level.

Then prior exposure sometimes you are acclimatized to the system of toxic environment then definitely all those exposure may play a vital role for the multiple exposures, then environment suppose I am working in a humid environment and most of the toxicants they are hygroscopic in nature so they may get deposited in your body system or they may enter into your body system through the skin or inhalation or sometimes ingestion.

Again the host factor that is your human body that is gender male or female, genetics what is your pedigree, et cetera and there are several other factors which we are going to discuss in due course of time.

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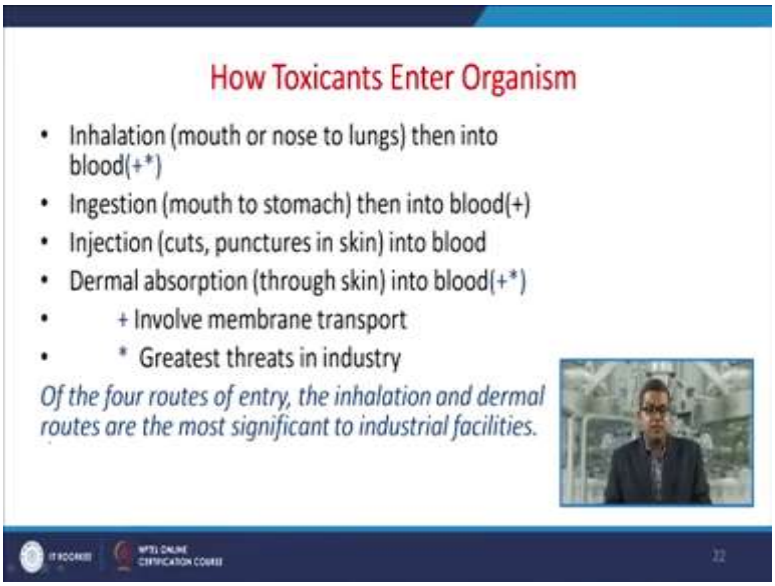

Now, first question arises that how toxicant can enter into biological system? First is inhalation through mouth, nose to lung and then into the blood stream. Ingestion via mouth to stomach, suppose by mistake you have taken the benzene, benzene is available in both liquid

and vapour phase. So by any chance you take the liquid benzene and you take through your mouth then it may become the part and parcel of your blood stream.

Injection with the help of some certain cuts, puncture in skin and sometimes people may deliberately inject certain poisonous substances into your body system and sometimes by mistake any poisonous system may enter through your medicine or any other injection route, so sometimes cuts and your blood vessels are exposed to the atmosphere and if you are working in a toxic vapour environment and those toxic vapour may get in contact with the blood stream so it may become the part and parcel of your body system.

Dermal absorption through skin into the blood, sometimes there are certain components because the dermal skin, skin plays a very vital role in absorption and because of their pores, because of the hair follicles, et cetera. So through dermal absorption into the blood stream they involve the membrane transport and this is the greatest threat to the industry. So out of four routes the inhalation and dermal absorption routes are the most significant to the industrial facilities because whenever you encounter to any kind of cuts, puncture in the skin definitely your first attention is towards to take the first-aid so your attempt is to minimize the exposure of those cuts to the atmosphere.

So dermal; because you skin sometimes your skin is exposed to the environment and inhalation because you cannot avoid this thing because you have to breathe. So that is why the out of four routes the inhalation and dermal routes are most significant route of the entry.

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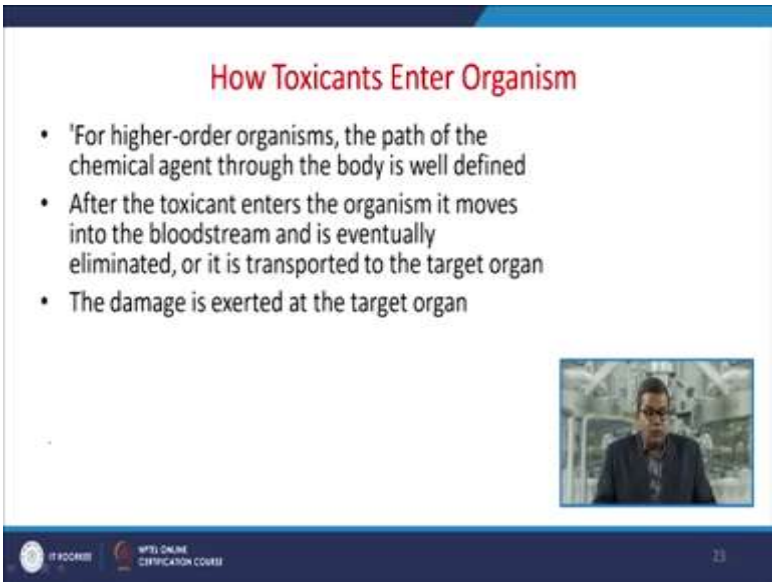

Now, for higher-order organism, the path of chemical agent through the body is well defined because either if you take through dermal absorption or you take the inhalation because it will go through upper respiratory tract then the lower respiratory tract and then it will become the lungs it will become the part and parcel of the lungs and in the lungs with the Bronchi and alveoli it may become the part and parcel of your blood stream and through blood circulation it can go upto anywhere.

So after the toxicant enter into the organism it moves into the blood stream and eventually eliminated or it is transported to the target organ. The beautiful thing given by the nature is that whenever your body is contaminated to any foreign body the foreign chemical then first of all body tries to retaliate all those things by the various symptoms, so you need to identify those symptoms first and simultaneously body reacts in an adverse manner to overcome the effect of those particular toxicant, so you must utilize that capability.

Now, if it is not then you have to take certain external things to overcome the effect of those toxicant. So the damage is exerted at the target organ if you fail any kind of or by any chance you are unable to remove all the toxic effect into the body system then the damage is exerted with the target organ.

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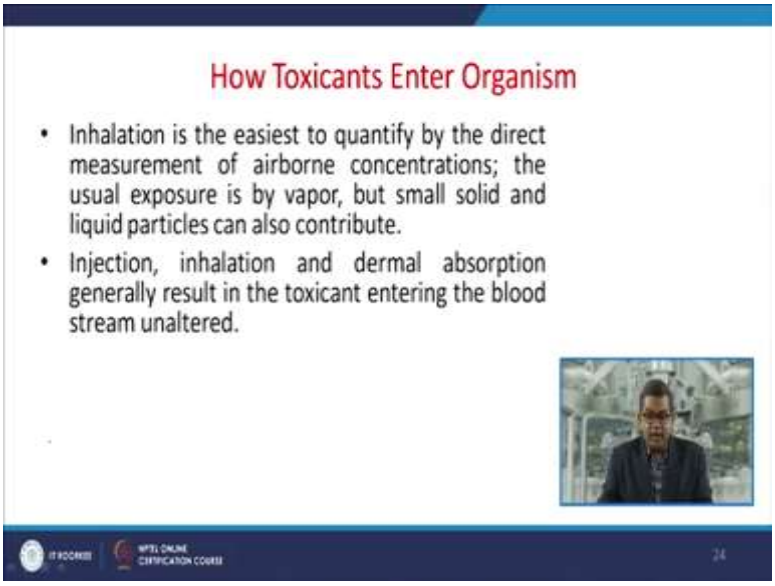

Inhalation is the easiest to quantify by the direct measurement of airborne concentration, the usual exposure is by vapor, but small solid and liquid particles can also contribute, sometimes missed, sometimes small solid particles they are supported by (())(21:00) et cetera they may

create a problem. Injection, inhalation and dermal absorption generally result in the toxicant entry into the blood stream they are usually unaltered.

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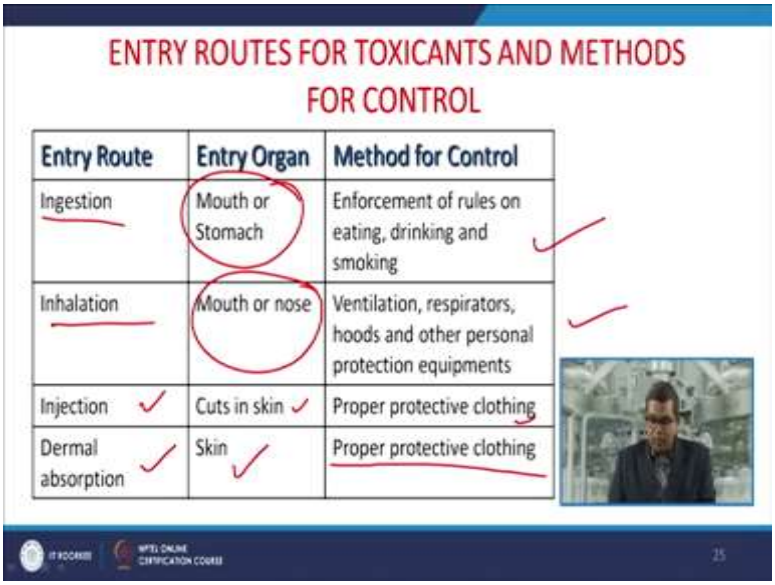

Now, in this particular table we can summarize that there are four different entry route, ingestion the entry organ is mouth or stomach you can control this entry by the enforcement of rules on eating, drinking and smoking. Inhalation that is again from the mouth or nose, you may adopt the method of control in terms of ventilation, respirator, hoods and other personal protection equipment so that the concentration of those toxicant may below the lower level.

Injection usually happens in the cuts in skin or through deliberation, you must have a proper protective clothing. Dermal absorption again it may happen or entry through the skin, you must have a proper protective clothing. So these four things are the rule of thumb and whenever you study the toxicological study you must know these four rule of thumb.

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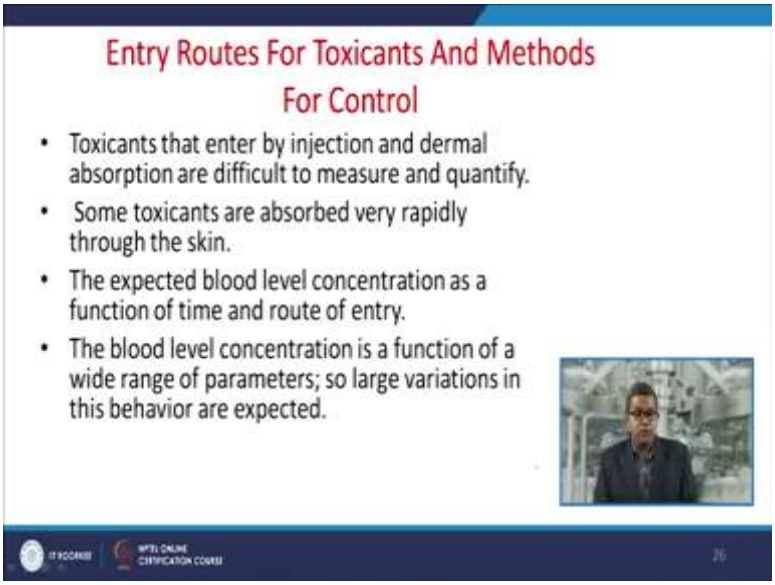

Now, entry routes for toxicant and method for control deals with the toxicant that enter by the injection and dermal absorption are different to measure and quantify. Some toxicants are absorbed very rapidly through skin based on their molecular structure, based on their concentration to the atmosphere. The expected blood level concentration as a function of time and route of entry the blood level concentration is a function of a wide range of parameter, so large variation in this behaviour are expected.

Again there are because there are n number of parameters those who govern this particular aspect. So as an engineer we must identify that what are those parameters and if you are unable to find out those all those parameters you must enlist four, five different major parameters.

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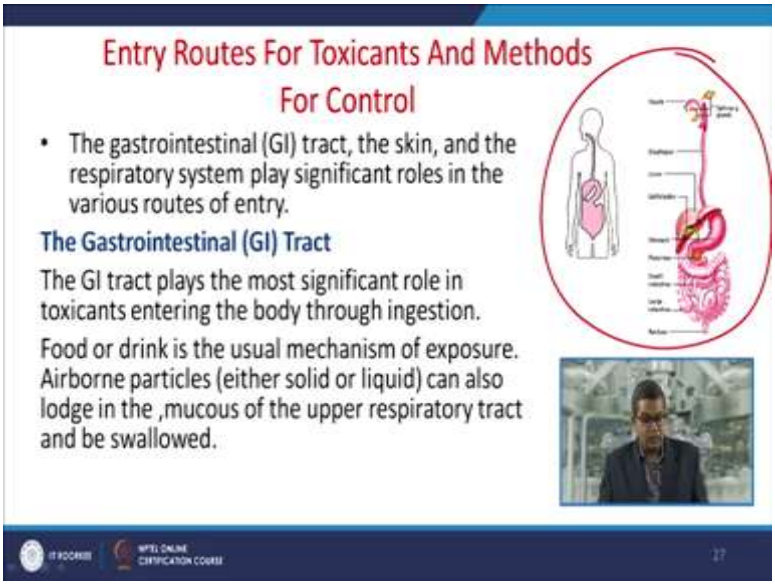

The first prominent route of toxicant entry into the biological system is gastrointestinal tract, the gastrointestinal tract apart from skin and other respiratory system plays a significant role in the various route of entry. The GI tract as depicted in this particular figure plays a most significant role in toxicant entry entering the body through ingestion. Food, drink is the usual mechanism of exposure. Airborne particles either solid or in a liquid form can also lodge into the mucous and the upper respiratory tract and be swallowed.

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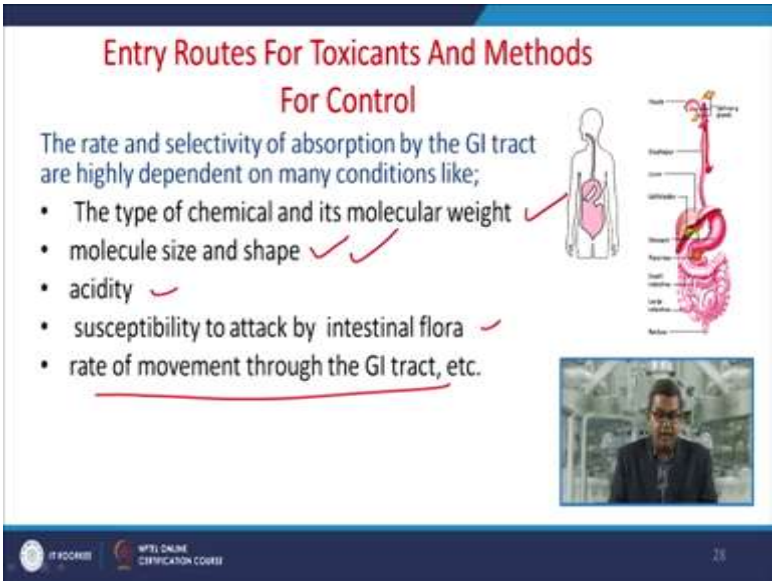

The rate and selectivity of absorption to the GI tract are highly dependent on many conditions that what kind of chemical and its molecular weight because the heavier the molecular weight the entry maybe a little bit different compared to the lighter molecular weight component, what is the molecular size and shape? Like benzene is having the cyclic molecule then it may

create other problems rather than the linear molecules, what is the acidity and basicity of the component? What are the chances to attack by the intestinal flora because I told you that your body system is designed in such a way that it retaliates to the foreign body and suppose you encounter with the toxic substance so initially your intestinal flora attack to that particular toxic substance.

The rate of movement of that particular component to the GI tract that is again based on this parameter and molecular size and shape.

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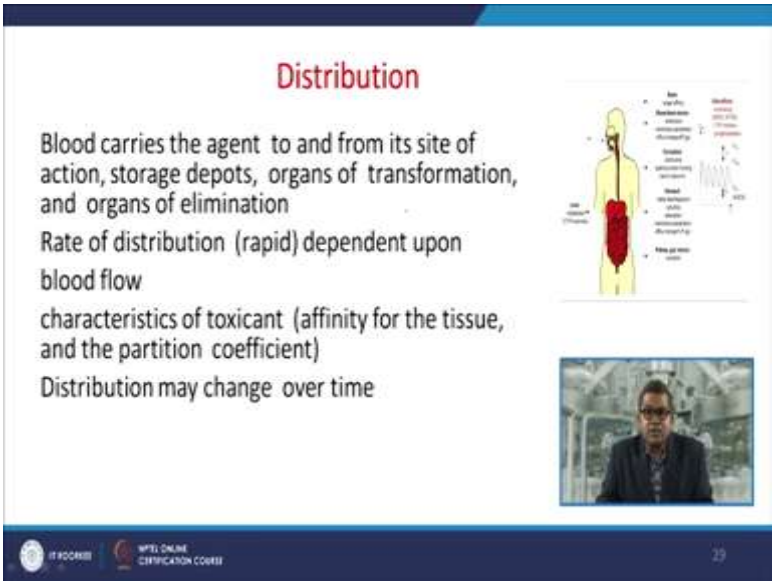

Now, next aspects when this toxic substance enters through your GI tract the next concept is how it distributed to your body system? So blood carries this is usually they are carried by the blood stream, so blood carries the agent to and from its site of action, storage depots storage depots sometimes the fatty tissues, bone marrows, et cetera organs of transformation and organs of elimination.

Now, rate of distribution depends upon the blood flow characteristics of toxicant affinity for the tissues and partition coefficients and distribution may change over the time. Again there are several factor govern this particular aspect that is what is the molecular size, molecular weight, age of the host, etc.

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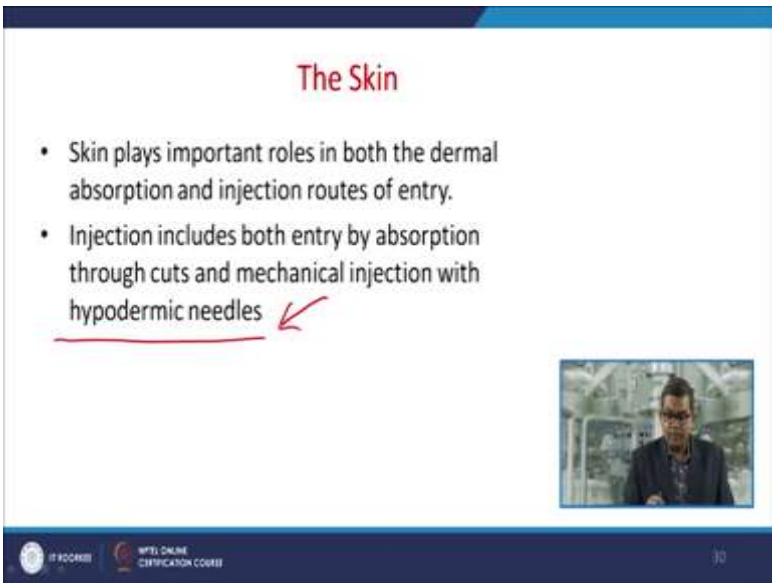

The next route of entry is your skin. Skin plays important role in both the dermal absorption and injection route of entry. Now injection includes both entry of absorption through cut and the mechanical injection with the hypodermic needles. So usually sometimes either in the medicinal way or sometimes deliberately this type of effect plays a vital role.

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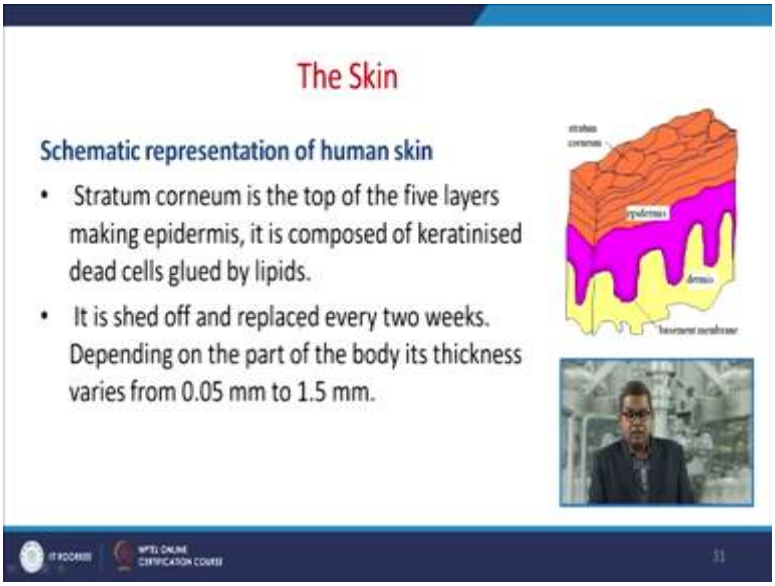

Now, this is the schematic representation of human skin. Now stratum corneum is at the top of the five layer making the epidermis usually composed of keratinised dead cells glued by the lipids. Now these are the keratinised cells glued by the lipids that lipids are fatty tissues. So whenever you are growing up or you are young those fatty tissues may get deposited over the period of time. And if after the aging these fatty tissues may get decomposed so it is quite evident that when you become older and older the wrinkles they form because of the decomposition of those fatty tissues.

So it is shed off and this stratum corneum it is shed off and replaced every two weeks, so depending on the part of the body its thickness varies from 0.05 mm to 1.5 mm, so most thickest part is your palm.

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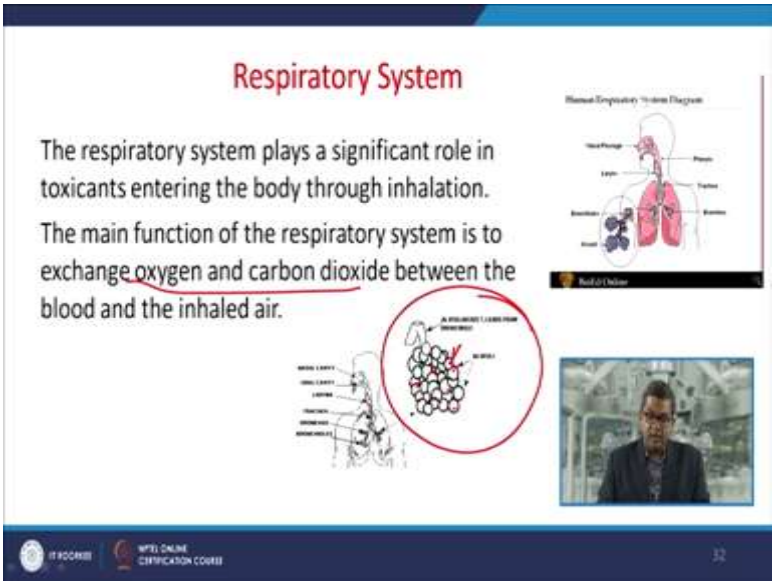

The respiratory system, the respiratory system plays a significant role in toxicant entry into the body through inhalation, you can avoid, you can cover up your all skin but you cannot avoid the inhalation because you cannot avoid breathing. The main function of respiratory system is to exchange oxygen and carbon dioxide between the blood and inhaled air. So these are the main sects or alveoli or bronchi through which the carbon dioxide and oxygen they are exchanged from the blood stream.

So by any means if they get blocked then the available surface area for this carbon dioxide and oxygen exchange is diminished and you may experience a breathing problem. And sometimes there are so many chemicals those who destroy the active sides available at this port and sometimes certain solid particles those who are having the low size or in the micron size they may get deposited in these (())(28:28) by blocking the active surface area.

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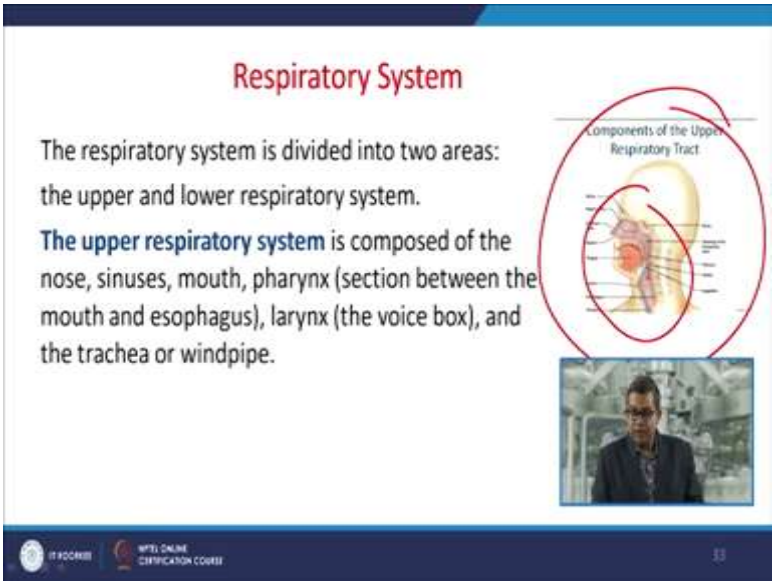

The respiratory system is divided into two areas, the upper and the lower respiratory system. The upper respiratory system is composed of nose, sinuses, mouth, pharynx, larynx that is the voice box and the trachea or windpipe. So you can see I do not know how much visible is this figure, but you can see all these things in this particular figure.

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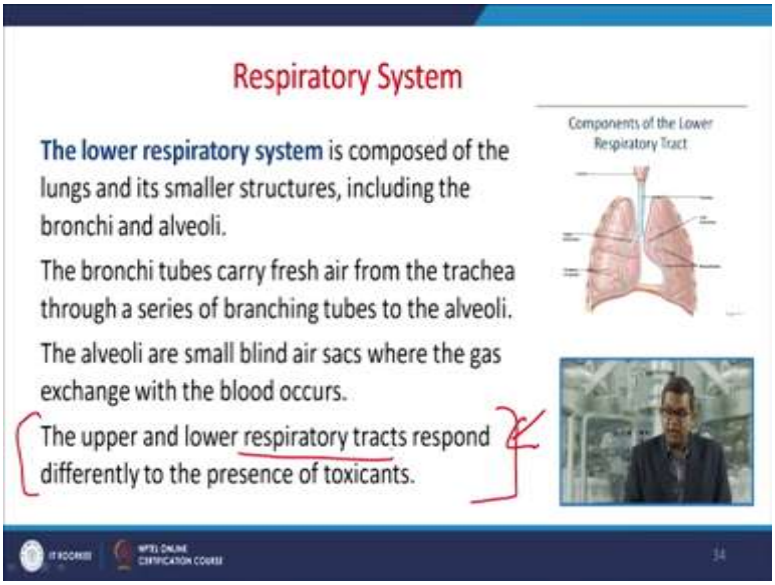
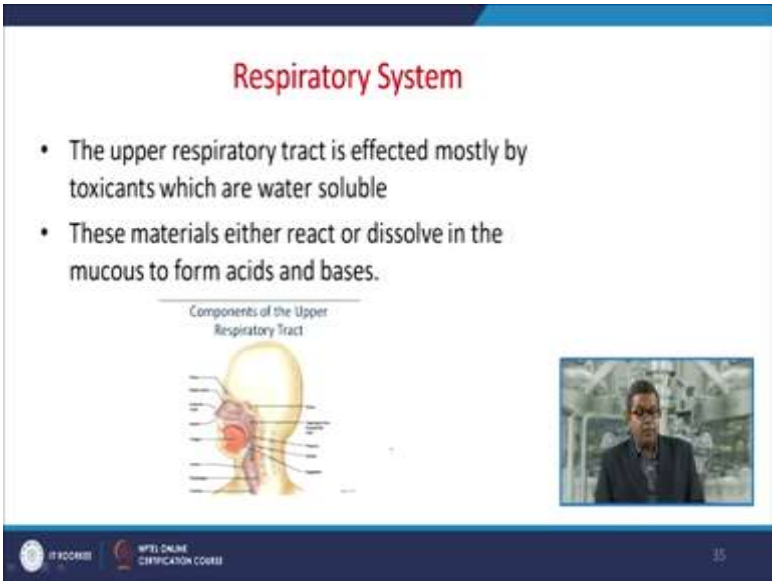


The lower respiratory system is composed of the lungs and the small structures like bronchi and alveoli which I showed in the previous figures. The bronchi tubes usually carry the fresh air from the trachea through a series of branching tubes to the alveoli. These alveoli are small blind air sacs where the gas exchange with the blood stream. The upper and lower respiratory tracts respond differently to the presence of toxicants. Now remember this is a key factor

when we are discussing because we cannot overlook the importance of inhalation so you must know that which chemical affects which respiratory tracts! (Refer Slide Time: 29:46)



The upper respiratory tract is effected mostly by the toxicants which are water soluble, remember your body is having sufficient quantity of water. These materials either react or dissolve in the mucous to form acid and bases.

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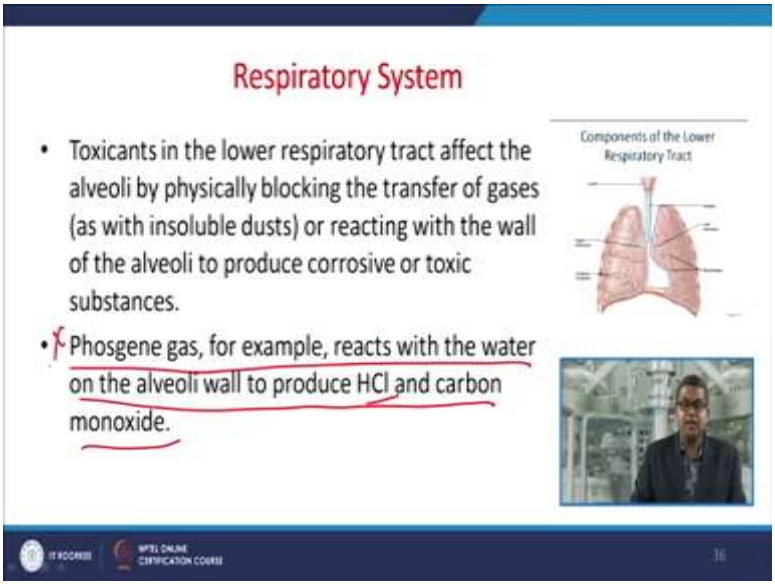

The toxicant in the lower respiratory tract affect the alveoli by physically blocking the transfer of gases as with the insoluble dust or reacting with the wall of the alveoli to produce the corrosive or toxic substances. Remember phosgene, for example they reacts with the water on the alveolis wall to produce HCL and carbon monoxide and both the things are dangerous.

Like suppose, in case if you are in presence of phosgene gas and by any means you inhale this phosgene gas, so it may react with the water present in your body system or in your lungs or in your lower respiratory tract to produce the HCL and carbon monoxide, carbon monoxide is very reactive to your blood stream and HCL is having the corrosive property. So it may destroy the inner wall of either alveoli or bronchi, so the blood vessel may get exposed, so they can be more reactive to a carbon monoxide.

And moreover, the available sites or the available surface area for oxygen carbon dioxide exchange diminishes, so be particular, so this is the effect of one of the effect of any toxic gas.

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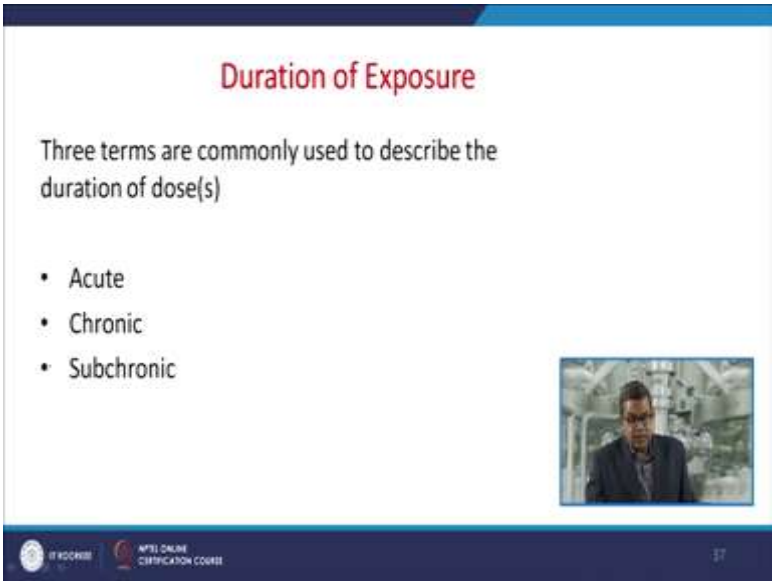

Now, as far as the toxic effects are concerned, it depends, another parameter is that duration of exposure, usually in engineering term we talk about three terms which are used to describe the duration of any dose or exposure Acute, Chronic, Subchronics. In the subsequent parts we will, we will study all these things under these three heads.

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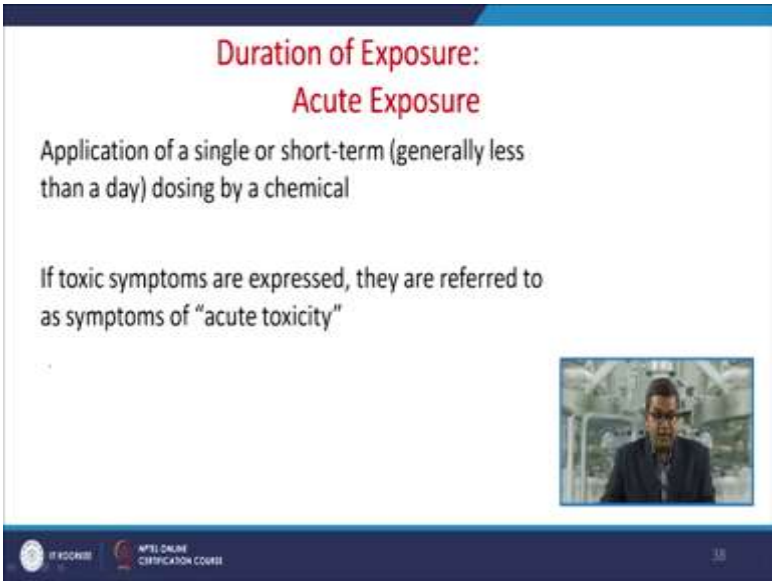

Now, Acute Exposure, application of a single or a short term generally less than a day dosing by a particular chemical or sometimes spontaneous exposure. Now, if toxic symptoms are expressed, they are referred as symptoms of “acute toxicity”.

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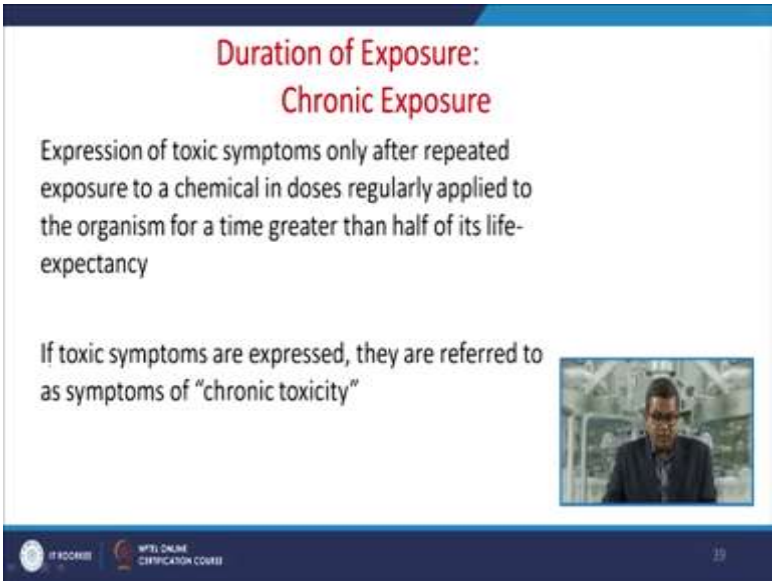

Now, Chronic Exposure, the expression of toxic symptoms only after repeated exposure to a chemical in doses regularly applied to the organ for a time greater than half of its life expectancy. So, sometimes if you are working in say ammonia environment, so gradually you may get exposed to those environment and sometimes because of our nature of body we may get acclimatized and we cannot experience the adverse effect of ammonia and sometimes our body is acclimatized to give the prima facie symptom like suppose first hand if you expose to the chlorine environment, you may experience the irritation, you may experience the skin dryness, et cetera.

But if you are continuously working in that particular environment, your body may get tuned in such an environment so you may not experience, only thing you experience is if there is any change in the chlorine concentration, then you may experience that something going wrong. So this may be a chance of a chronic exposure.

Now, if toxic symptoms are expressed, they are referred to as the symptoms of "chronic toxicity".

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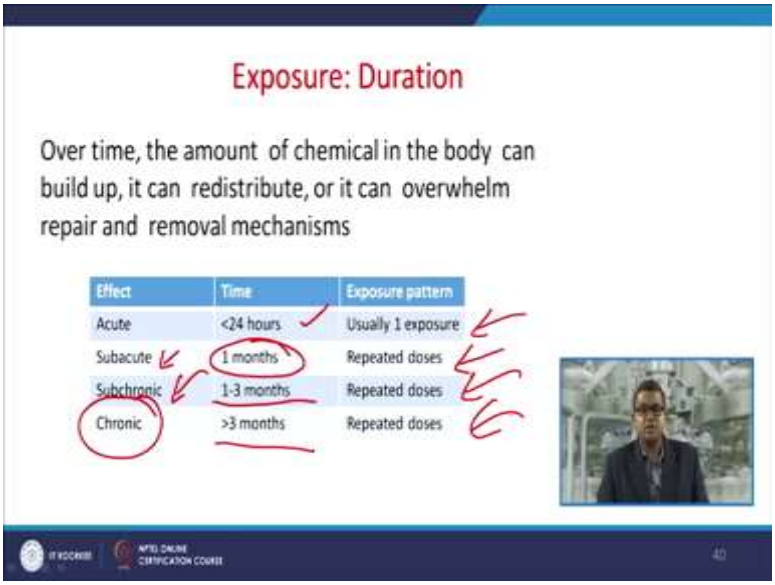

Now, usually in this particular table discuss that over time, the amount of chemical in the body can build up, it can redistribute, or it can overwhelm repair and removal mechanisms. Because based on the duration, they may become the part and parcel of your blood stream and they may get deposited in the various your body parts of your human body.

Now, there are 4, 5 different fore effects. Acute, usually the time domain is less than 24 hours and sometimes it is attributed to 1 exposure.

The Subacute, the new term usually the time of exposure is 1 month and sometimes you may get the repeated doses. Repeated doses; sometimes every dose is not having the same concentration, sometimes it is on the higher side, sometimes it is on the lower side.

Subchronic, usually 1 to 3 months, repeated doses.

And the chronic one, it is greater than 3 months. So, suppose you are working in an industry and the work place is and your small dose, small amount of toxic release it may club under the head of chronic and you may experience the repeated doses, maybe the stagnant doses, maybe the fluctuating doses, so this is the exposure pattern.

So in this particular module, we have discussed about the different aspects of toxicity, the different definitions of toxic substance, toxic, toxicity, toxin, etc. Then different routes of entry through which any toxicant can become the part and parcel of your body system and what are the different qualitative analysis through which we can analyse the exposure of toxic substance. Thank you.