Chemical Process Safety
Professor Shishir Sinha
Department of Chemical Engineering
Indian Institute of Technology Roorkee
Lecture 07
Toxicology
Elimination, Responses, Treatment

Welcome to this toxicological elimination module. In this particular module, we will study about the various elimination techniques in theoretical, that how once toxicant enters into the body system, then how we can eliminate it in a theoretical way, what are the various responses for those toxicants and where they may give their symptoms, where may they get deposited over the period of time and what are the prima facie or primary treatment to handle such type of scenario when anybody get exposed with the toxic substance.

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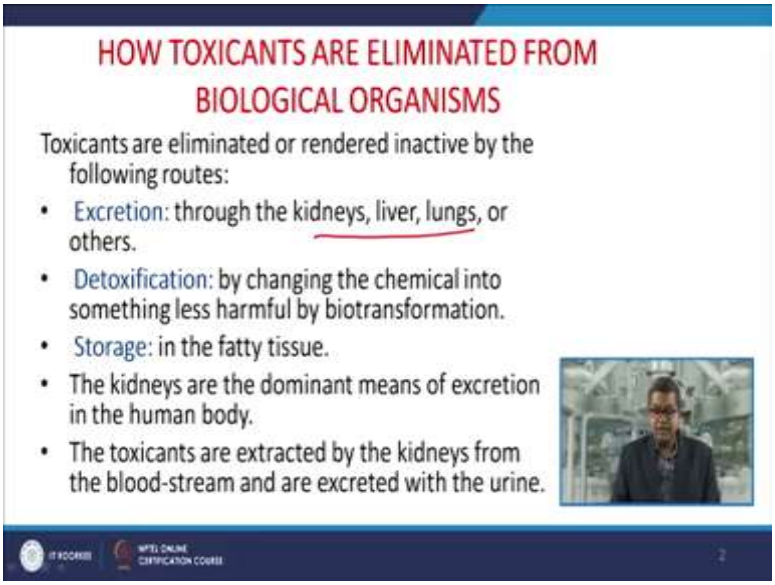

So, first thing is that if a toxic substance enters into the biological organism, then how we can eliminate it. So usually there are three basic ways through which they can be eliminated from biological system. One is the excretion through kidney, liver, lungs or other ways of means, this usually the first three things like kidney, liver and lungs it is being provided by the nature, so once you are exposed to that toxic environment or somehow by the inhalation or dermal absorption, you are encountered with this toxic substance then the kidney, liver and lungs they try to repel the effect of that particular toxicant into the body system.

Another route is the detoxification, by changing the chemical whatever chemical enter into the body system into something which is less harmful through the biotransformation.

Remember by actuation of your human body, by contamination your human body is tuned to repel the effect of that particular toxicant and in this particular process they release certain hormones, certain enzymes to detoxify that foreign chemicals.

The last option is the storage and usually the toxicant or toxic substance they may get deposited into the fatty tissues, either in the decomposed form or as such.

Now, among all available elimination tools, the kidneys are the dominant means of excretion in the human body and you may see that if anybody is having the kidney problem sometimes they may go to the dialysis, et cetera to remove the toxic substance from the body system or through the blood stream. The toxicants are extracted by the kidney from the blood stream and they are excreted with the urine.

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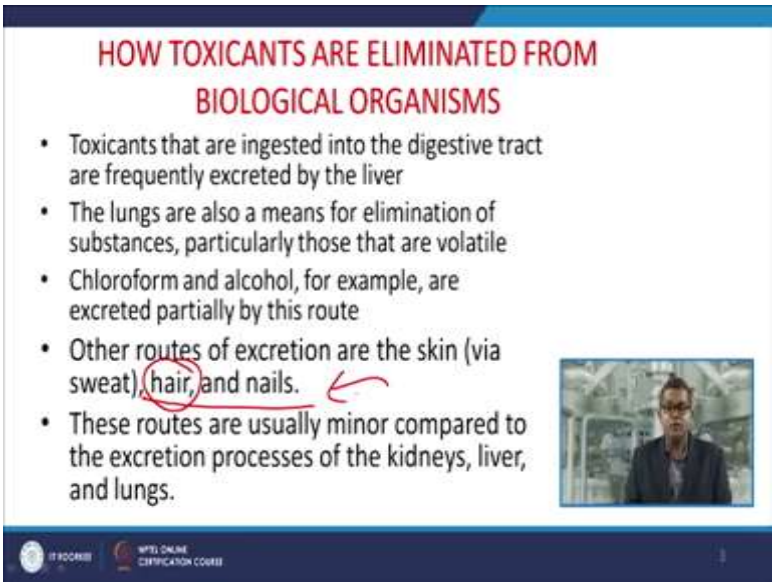

Now, toxicants that are ingested into the digestive tract are frequently excreted by the liver. So, once they become the part and parcel of blood stream, then with the help of liver then body system can detoxify, body system can remove their toxicant. Lungs are also means of elimination of substance particularly those which are volatile in nature.

Now, this is again the thing when you expose or you are working in a environment and sometimes toxic substance may get release, first thing is that when if you inhale or sometimes through the mouth if it goes into the body system, your lungs, et cetera that nature gave you another thing that you try to resist the things by sneezing, by coughing, et cetera.

So chloroform and alcohol for example they excreted partially by this route of lung. Other route of excretion are skin via sweating, hair, nails, et cetera. And sometimes you may experience that the color change in nail give a prominent information that something is going wrong within your body system, maybe the contamination of a toxic substance, maybe your body is not working properly.

So you need to identify those symptoms and there are so many evidences in the history like one of the most prominent story is that toxification of Napoleon Bonaparte. He was given a regulated quantity of arsenic and the first hand after his death his hairs was analysed by physician and they found that he was toxified by arsenic.

Now these routes are usually minor compared to the excretion processes of kidney, liver and lungs, but importance of these routes cannot be overlooked.

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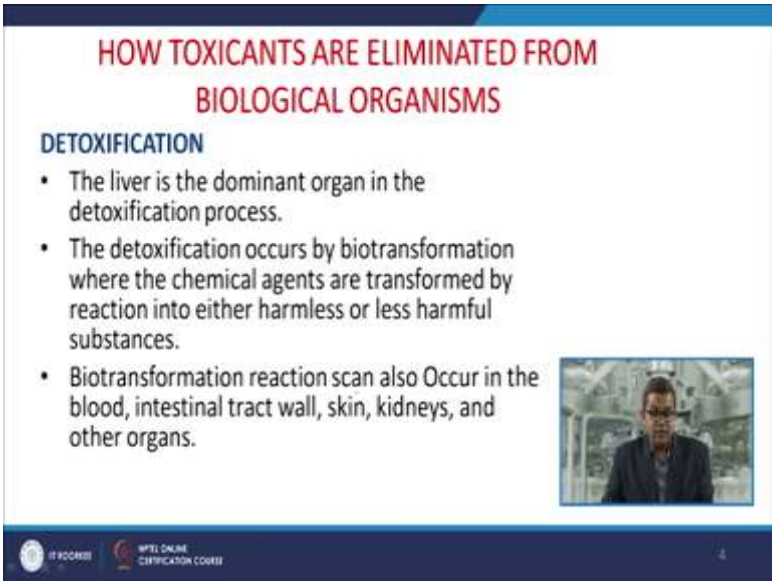

Now detoxification; liver is the dominant organ in the detoxification process. The detoxification usually occurs by the biotransformation where the chemical agents are transformed by reaction into either harmless or less harmful substances and biotransformation reaction can also occur in the blood, intestinal tract wall, skin, kidney and other organs.

Now remember, sometimes this biotransformation is useful to detoxify your body and sometimes it is highly undesirable. The reason is that whenever you come into the contact of any kind of toxic substance which after decomposition may produce a lesser harmful toxic substance and it may get deposited into the fatty tissues and the later part of your life it may create a problem. So be careful while adopting this detoxification route.

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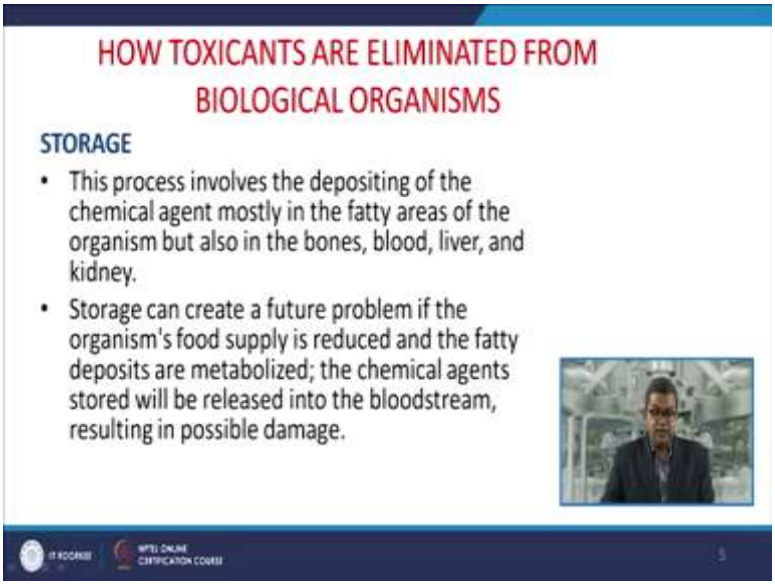

Now storage, this particular process involves the deposition of chemical agent mostly in the fatty areas of the organism, but also in the bones, liver, blood, kidney, et cetera. Now, when you are young then definitely you can overcome such type of scenario, but the later part of life when these chemicals or your body is not supported by the fatty tissue formation then definitely this may create a problem.

So that is why the storage can create a future problem, if organism food supplied is reduced and the fatty deposits are metabolized over the period of time. The chemical agents stored will be released into the blood stream and resulting the possible damage. So you may experience by seeing all parts of society that some people those who are working in the chemical factory the later part of their life they may encounter several other disease which are uncommon in nature.

So this type of thing is again creates a problem and sometimes that these decomposed product which are deposited into the fatty tissues may create a gene problem, mutagenic problem, et cetera. Now, once we study the different (())(8:13) responses of the toxicant to the biological system, we must see the thing into two aspects, those responses which are irreversible in nature or those responses which are reversible in nature. So sometimes these toxicants may create a genomic problem which are highly irreversible.

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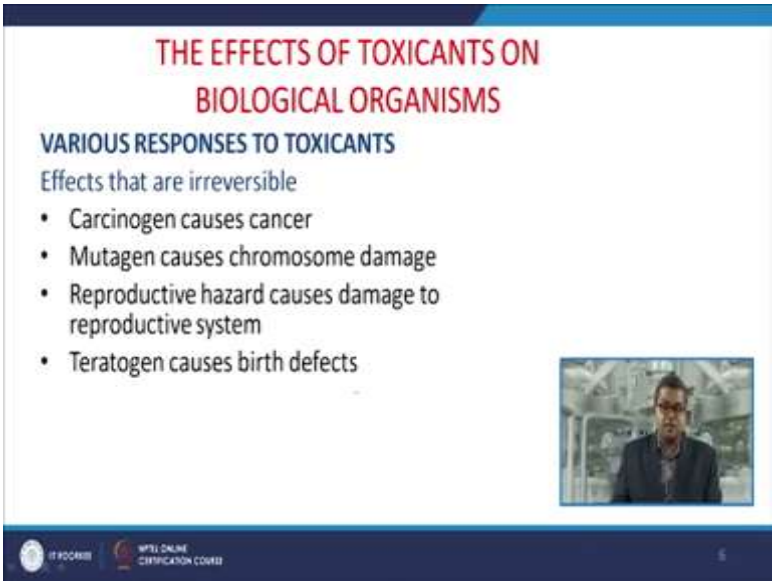

So we have enlisted different type of responses of the toxicant like Carcinogen they causes the cancer. Mutagens they causes the chromosome damage and sometimes like methyl isocyanate they created a problem still say after 30, 40 years still the people are suffering for those kind of ailments. Reproductive hazards cause damage to the reproductive system. The teratogen they cause the birth defect.

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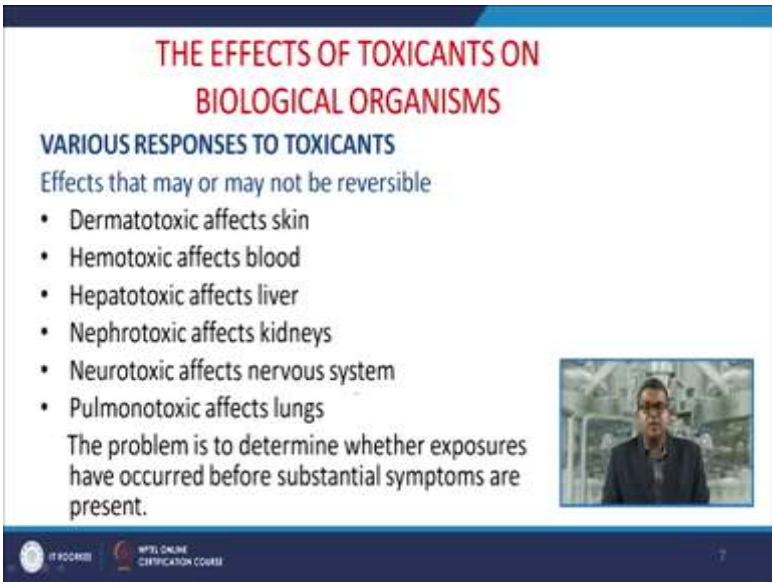

Now sometimes you may experience certain responses those who are reversible or may not reversible like dermatotoxic affects the skin, sometimes you may experience that your skin may get contaminated with the toxic substance maybe either in the vapour form or in the

liquid form and there are permanent damage to the skin or sometimes the skin is decolorized, et cetera.

Hemotoxic they usually affects the blood, hepatotoxic that affects the liver and sometimes there are certain deposition may take place into the liver and those effects are quite visible in the liver function. Nephrotoxic usually affects the kidney so the detoxification step is hampered. Neurotoxic affects the nervous system. Recall the world war when the Germans they use the nerve gas or mustard gas, they particularly affected the nervous system.

Pulmonotoxic affects lungs because it attributed to the dangers. The asbestos sheets or a lead particles, they may destroy the available surface area for oxygen and carbon dioxide exchange with the blood.

So the problem is to determine whether exposures have occurred before substantial symptoms are present, so you need to assist that particular problem before going ahead with the toxicological studies.

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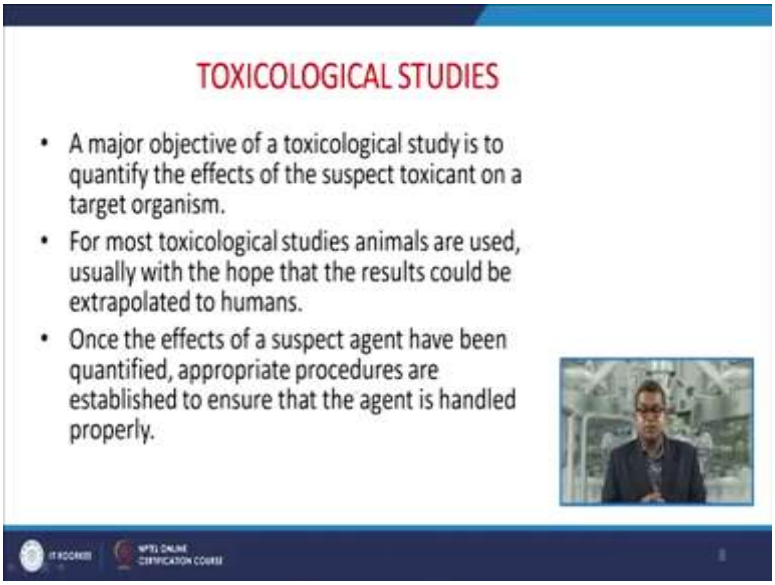

The major objective of toxicological study is to quantify the effects of suspect toxicants on the target organs. So, how we can identify those things, we will study. The most toxicological studies the animals are used, but within the regulations or regulatory body supervision, usually with the hope that you can extrapolate those result with the human being and sometimes it proves to be beneficial and sometimes it not!

So once the effects of suspect agent have been quantified, the appropriate procedures are established to ensure that agent is handled properly. And then you may go ahead that what are the symptoms, how you can detoxify it and how it can be stored and how your body system is being protected from the contamination.

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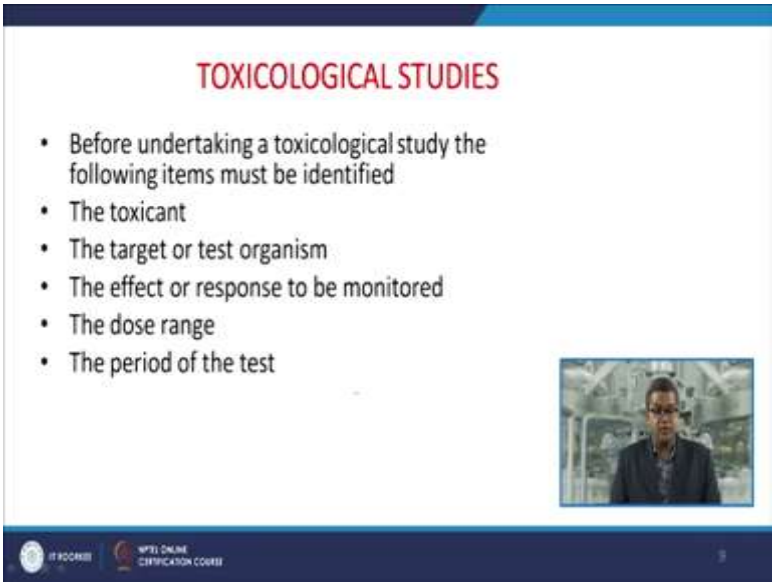

Now before we go ahead with the toxicological study because once you start your step, you must know that who is your enemy! So before you undertake any kind of toxicological study you must identify the following five factors. The toxicant, what is the toxicant? What its MSDS says Material Safety Data Sheet says? What are the different limits?

Then what is the target or test organ? Where it is going to affect first? Where it is going to deposited first? Which organ is responsible for the detoxification? So you must identify those target or test organs.

The effect or responses to be monitored. Now remember there are two type of responses, one is based on the primary symptoms. Suppose you are working in chlorine environment, so first symptom you may experience the dryness of the skin and irritation to your eyes. So this responses must be monitored and this is a clear cut indication that something is wrong within the system.

Then if it enters into the biological system, which system is going to be effected? And how it can be affected? Sometimes you may experience the stomach ache, sometimes you may experience some problem related to the kidney.

The fourth aspect is the dose range. See, it all depends on various factors including your age suppose if I am young or you are young then definitely you may require a certain higher quantity of those doses compared to their kid having a age of say 5 to 10 years or having the elder person who is having the age of 60 plus. What is my physique? What is my sex? So it all depends on the dose range, because dose range is a primarily factor through which you can monitor your responses. It is just like you take a 1 peg of wine, then definitely your dose, your responses would be different compared to if you take 3, 4 different peg of wines, then what is the period of test that is how much and what is the time duration of exposure?

Because ultimately by this way you can analyse that whether it is acute exposure, sub-acute exposure, chronic exposure or sub chronic exposure. So while taking any kind of toxicological studies you must remember 5 different points.

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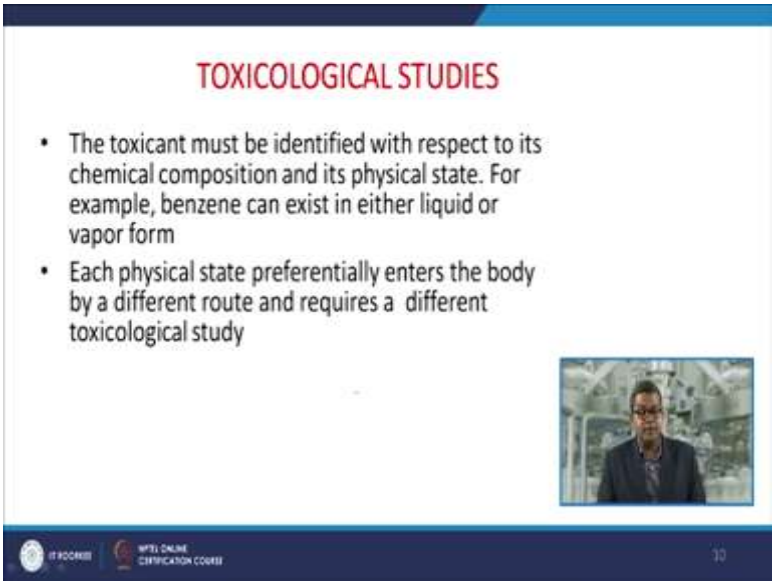
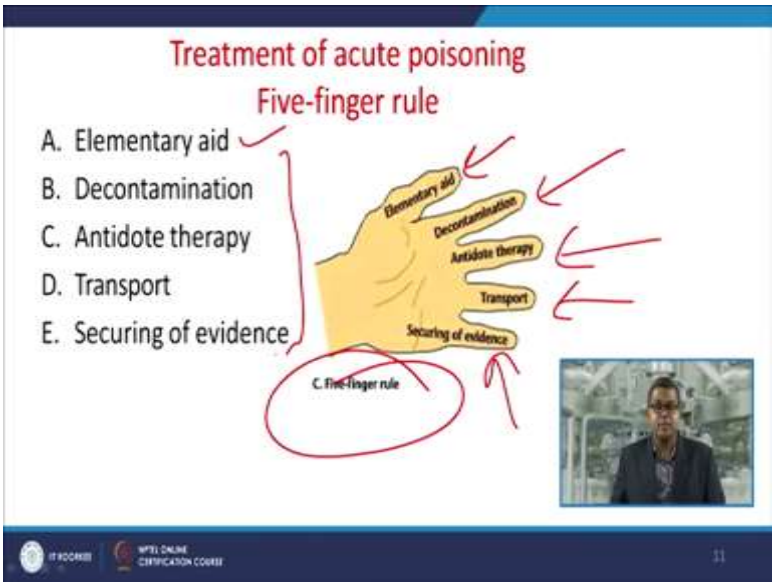


Now, toxicants must be identified with respect to the chemical composition, its physical sate. For example, benzene can exist in either liquid or vapour form. So the entry route will be different because if it is in the liquid form one may take the benzene through the injection route and if it is in a vapour form then he or she may take through the inhalation. So the entry route will be different, as well as the target organ would be different. And simultaneously the responses and other things would be different. So you must identity with respect to its chemical composition.

And each physical state preferentially enters the body by a different route, requires a different toxicological studies. So the whole line of action would be different if you are taking this thing into account. (Refer Slide Time: 15:38)



Now, while going for a treatment of any kind of toxic substance for acute poisoning, et cetera you must remember the five-finger rule. What is the elementary aid covered with this A, how we can decontaminate it, what is the antidote therapy, how the person or human being been transported to the safe place, and how we can secure the evidence? So this is the five-finger rule. Because each and every aspect is essential. I am going to discuss this particular thing in detail in the subsequent slides.

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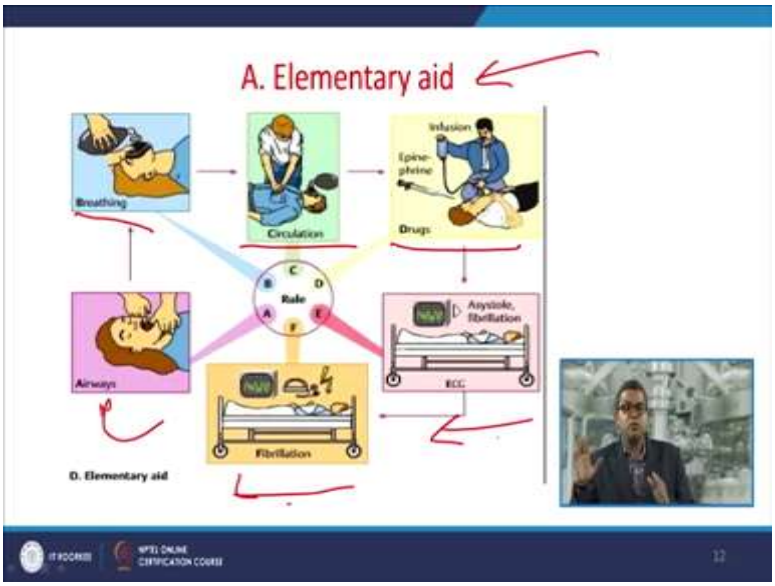

Now, first thing is that once anybody is contaminated with the toxicological toxic substance, then you must provide the elementary aid so that primarily you can decontaminate the things, you may start the detoxification process, this may be by the breathing, the circulation with the help of primary drug, you may go for hospital for the ECG, then fibrillation, then different type of airways.

So everybody, see this is the first thing because you are practically aware about the toxic substance. So you must adopt this type of elementary aid to elementarily detoxify the things.

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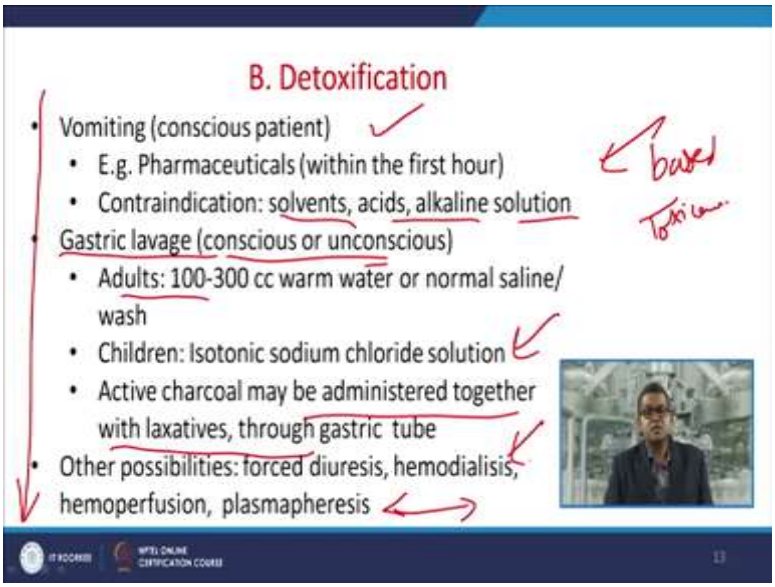

The second thing is that Detoxification. Now, these are the usual routes of detoxification. By vomiting may be with the help of pharmaceuticals within the first hour that may be with the help of stomach wash, et cetera may be with the help of solvents, acids, alkaline solution that is purely based on your toxicant. It may be the gastric, may be conscious or unconscious. Adult, it may require the 100 to 300 cc of warm water with the normal saline, stomach wash.

The children, isotonic sodium chloride solution, this is one of the most usual way. Sometimes active charcoal may be administered together with different laxatives, through gastric tube so that the other routes of detoxification or other routes of excretion may be active. The other possibilities like forced diuresis, hemodialisis, hemoperfusion, plasmapheresis these are the different other routes and remember all these things must be administered by trained person.

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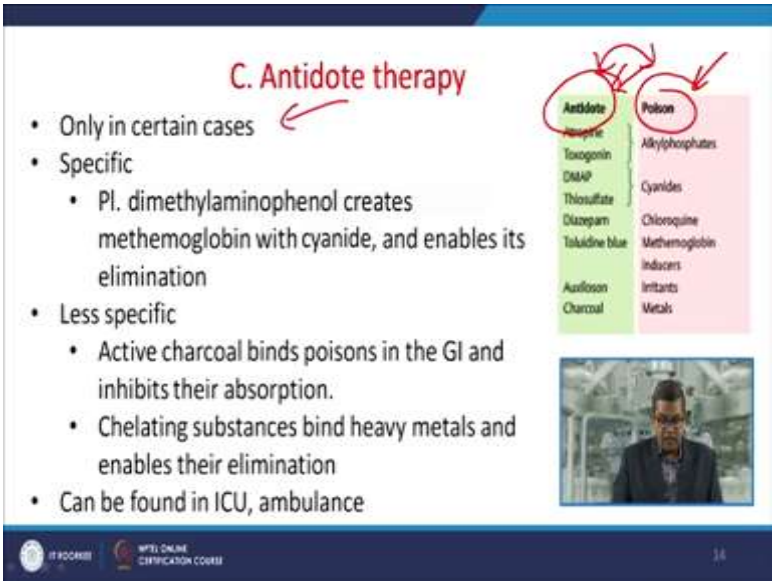

There are certain antidote therapy, these are applicable to various specific cases. Now these cases must be defined a priori. The reason is that for various kind of poisons there are antidotes, there are availability of antidotes, the only thing is that you must be well communicated. The problem in the Bhopal tragedy happened, the prima facie, the information supplied to that the civil authorities that it is a chlorine leak, but it was not, it was a methyl isocyanate leak, the primary treatment for chlorine leak is to take as much as water as you can, but it is the fatal for MIC because MIC is highly reactive to water and it creates the cyanide poisoning.

So you must aware that what is the remedy and it should be well communicated, so if you are working in a plant, all kind of information must be available ready hand and the same thing is applicable for antidote therapy because if there is anything poison, then the antidote must be well communicated. It must be less specific.

Active charcoal binds poison in the GI and inhibits their absorption, you must know all these things. Chelating substance bind heavy metals and enable their elimination. All these things can be found in ICU, ambulance. So the first hand thing is required in this case is that the knowledge of material safety datasheet. Once you know that how hazardous this particular chemical is then you can go ahead with this type of therapy.

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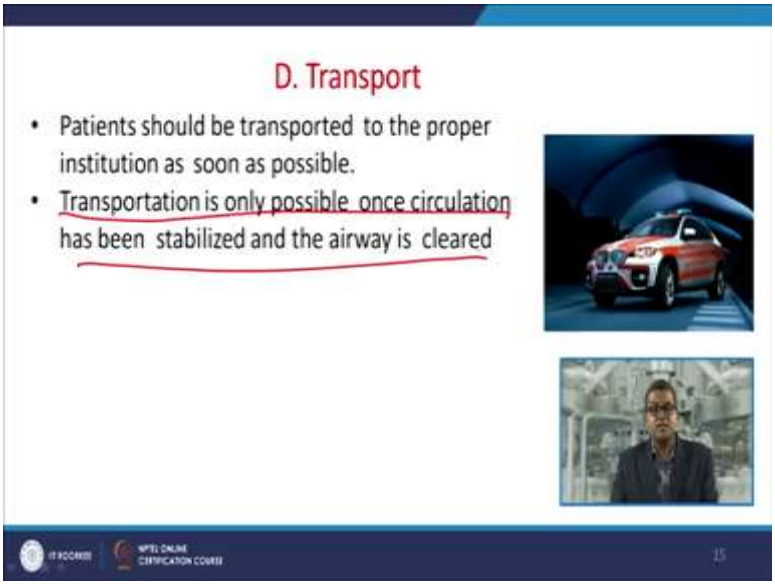

Now, once the things are not working like antidote therapy is not working, detoxification use of detoxification or primary treatment is not working, the patient or those person, those who are get contaminated with the toxic substance should be transported to the proper institutions or hospitals for a medical care as soon as possible. This transportation is only possible when circulation has been stabilized and airway is cleared. The reason is that in during the process you may be in a position to detoxify the things.

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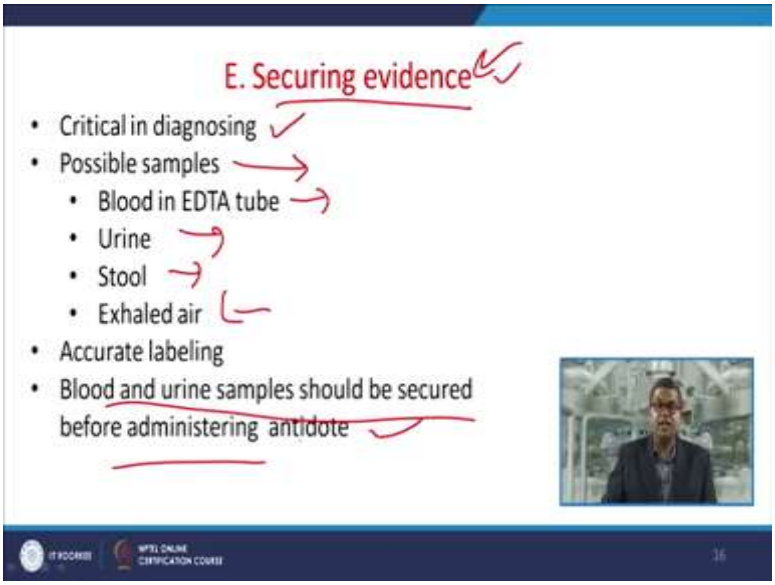

Now, remember securing the evidence is extremely important, the reason is that this not only provides the legal help, but also it gives a proper information that what is the chemical, how

it was released, how the person was exposed to that particular chemical, what are the different reasons? So once the things are stabilized, you must secure the evidence.

Again I am giving you one example of a Bhopal Gas Tragedy, that the first time when the MIC was released and people became fatal, fatal, fatal then the first autopsy which took place after a day or so, then they found out after the stomach that they found out there is a cyanide poisoning. Then they scrutinized the things that how this cyanide came into picture and then they found out that this is the Methyl-isocyanate, primarily they were treating for chlorine.

So securing and disgave the information that MIC was leaked and then reverse engineering gave a proper information. So securing evidence is extremely important. This is critical in diagnosis that what is the substances, what is the route of entry, what was the target organ? This can be carried out with the help of sampling, blood, urine, stool, air, et cetera and you must perform the accurate labeling from where the sample are collected, what is the age, what is the sex, how concentrated toxicant was?

Blood and urine samples should be secured before administering any antidote because sometimes because I told you in the previous modules that water may become the fatal, only thing is that the right dose differentiates between the poison and a remedy. So, suppose for chlorine water is the antidote, but for MIC it is not, so blood and urine sample should be secured, analysed before you administered any antidote.

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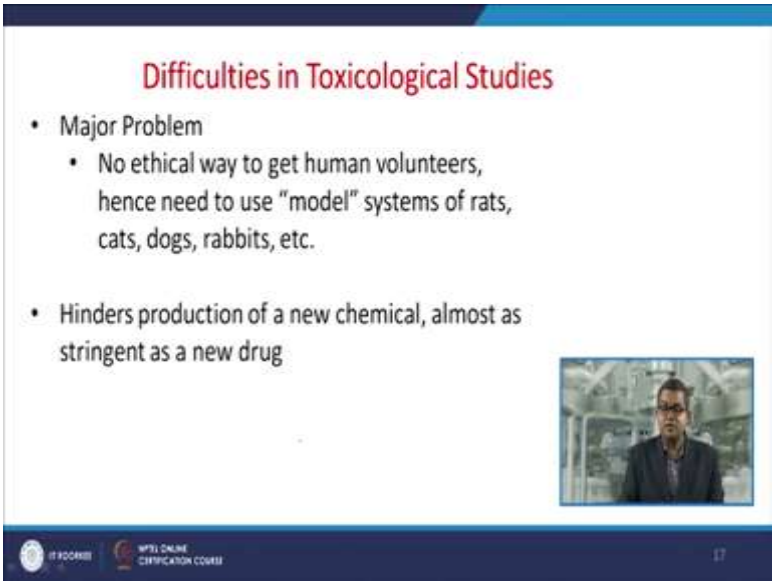

Now, there are various difficulties associated with the toxicological studies, the major problem is that there is no ethical way to get human volunteer, hence used to model system,

we are bound to have some certain model system like rates, cats, dogs, rabbits under the administrative control of certain ethical societies.

Now this hinders the production of new chemical, almost has stringent as a new drug because you are not getting the proper samplers. So in this particular chapter we have discussed the different type of excretion, remedial measures, et cetera. And in the subsequent studies, we will discuss that how we can go ahead with the various toxicological studies, what are the different parameters, those who administered the proper toxicological studies, how we can get, how we can create the dose versus response curve because these dose versus response curve was an integral part of the toxicological studies. So by this way thank you very much.